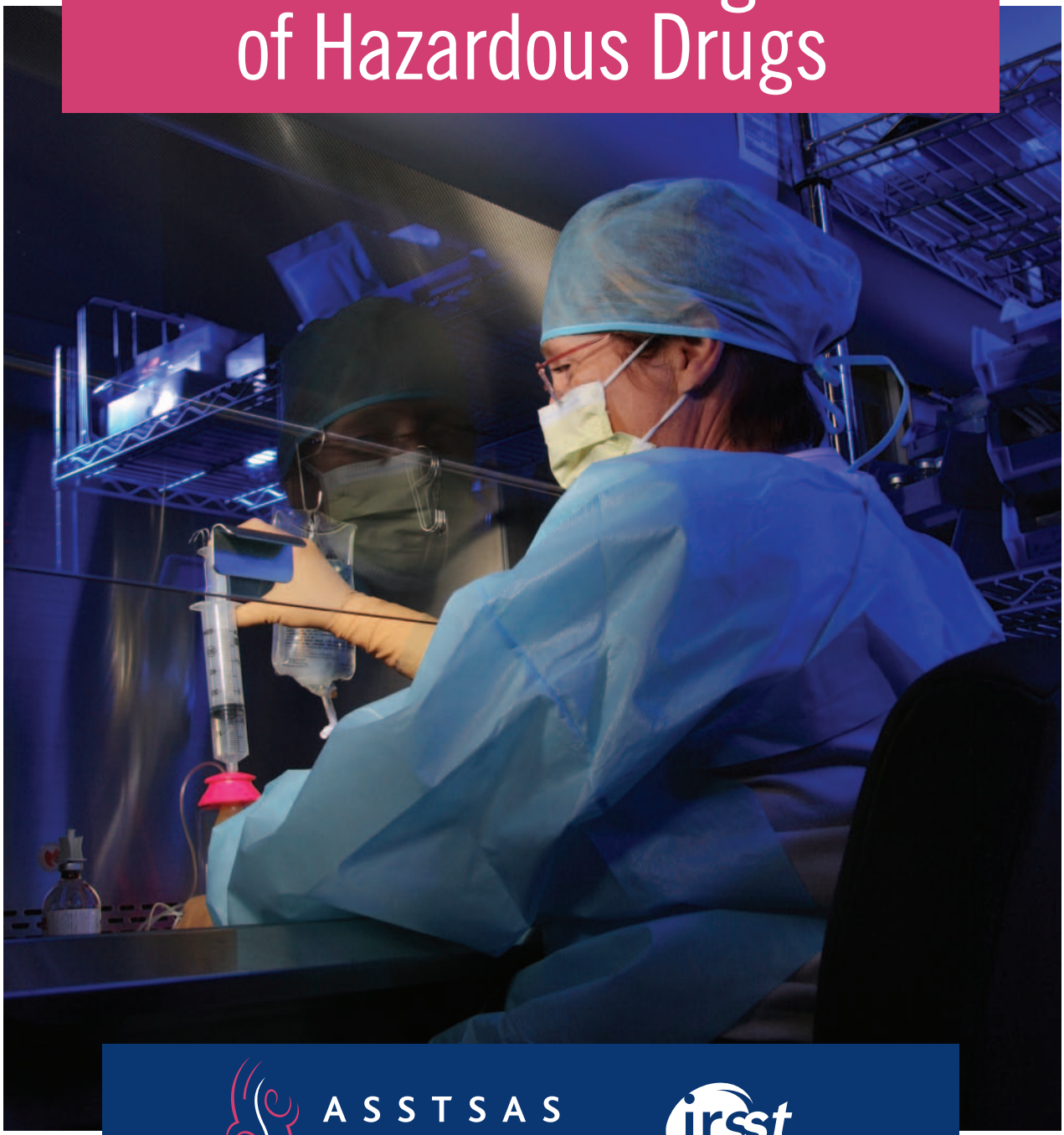
Prevention Guide

Safe Handling of Hazardous Drugs



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– optimize working conditions to improve the health and workplace quality of life of workers, while promoting productivity and taking into account the safety of the institutional clientele.

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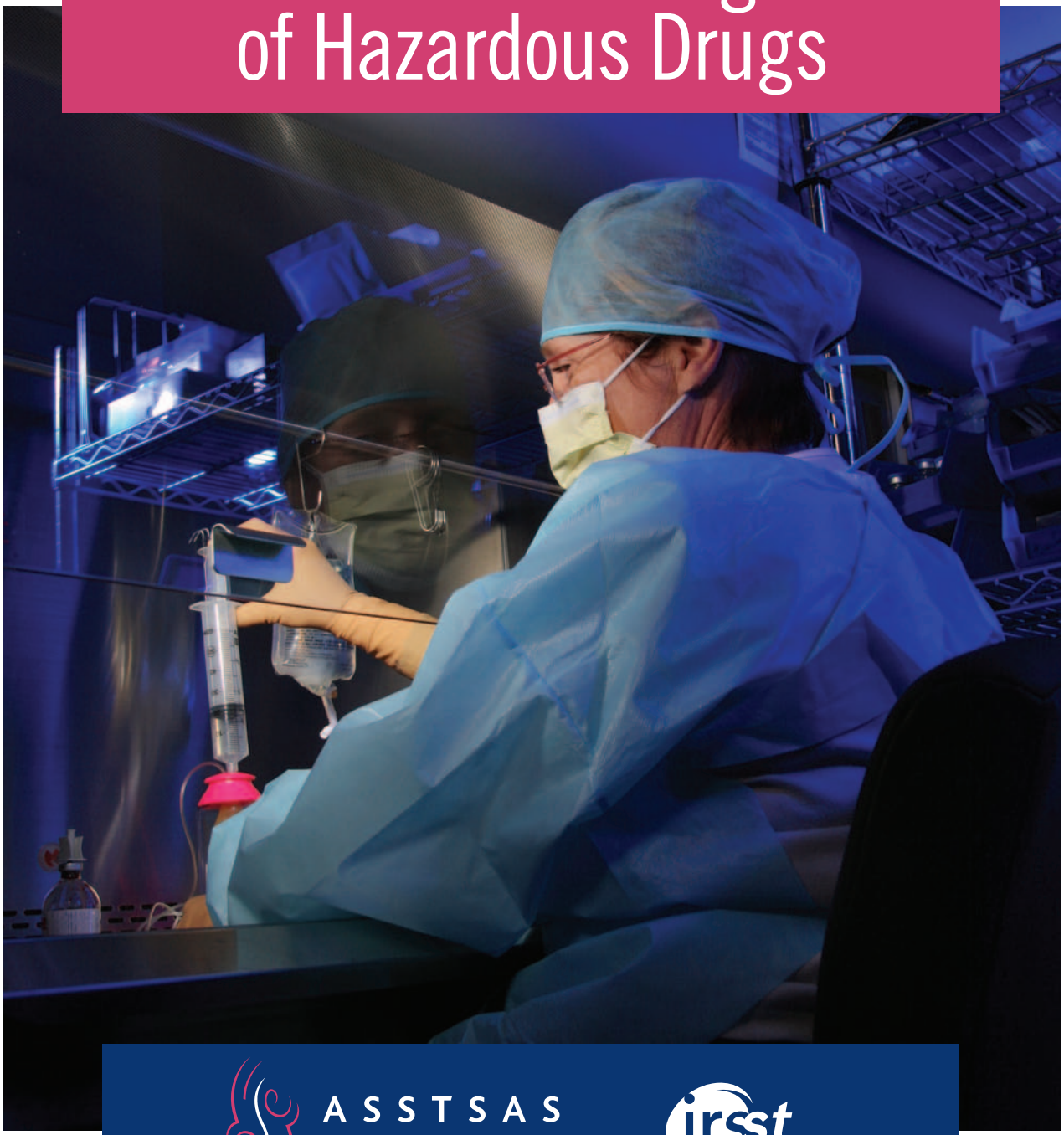

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Representatives from the following organizations and institutions have contributed to the preparation of this guide and have approved its contents.

Association des pharmaciens des établissements de santé du Québec	Centre hospitalier universitaire de Sherbrooke
Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales	Centre hospitalier universitaire Sainte-Justine
Association québécoise d'établissements de santé et de services sociaux	Centre universitaire de santé McGill
Association québécoise des assistant(e)s-techniques en pharmacie	Institut de recherche Robert-Sauvé en santé et en sécurité du travail
Association québécoise des infirmières en oncologie	Institut national de santé publique du Québec

This guide has been developed by the Working Committee on the Safe Handling of Hazardous Drugs established by the Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS).

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This document is available on ASSTSAS and IRSST web sites : **www.asstsas.qc.ca**
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ISBN: 978-2-89618-017-2

Code: 270-0508 (GP65A)

Symbols and Abbreviations

APES	Association des pharmaciens des établissements de santé du Québec [Association of Quebec Health Care Institution Pharmacists] *
AQATP	Association québécoise des assistant(e)s-techniques en pharmacie [Quebec Association of Pharmacy Technicians] *
AQESSS	Association québécoise d'établissements de santé et de services sociaux [Quebec Association of Health Care and Social Service Institutions] *
AQIO	Association québécoise des infirmières en oncologie [Quebec Association of Nurses in Oncology] *
ASHP	American Society of Health-System Pharmacists
ASSTSAS	Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales [Joint Sector-based Association for Health and Occupational Safety for the Social Sector] *
ASTM	American Society for Testing and Materials Standards
ATP	Assistants techniques en pharmacie (Pharmacy Technicians [PT])
CHQ	Corporation d'hébergement du Québec [Quebec Corporation Providing Technical Expertise and Financing to the Health and Social Service Sector] *
CSA	Canadian Standard Association (Association canadienne de normalisation [ACNOR])
CSHP	Canadian Society of Hospital Pharmacists
INSPQ	Institut national de santé publique du Québec [Quebec National Institute of Public Health] *
IRSST	Institut de recherche Robert-Sauvé en santé et en sécurité du travail [Robert Sauvé Occupational Health and Safety Research Institute] *
LSST	An Act respecting occupational health and safety (RSQ, c. S-2.1)
MSDS	Material Safety Data Sheet
MSSS	Ministère de la santé et des services sociaux [Department of Health and Social Services] *
NIOSH	National Institute for Occupational Safety and Health
NSF	National Sanitation Foundation
ONS	Oncology Nursing Society
OPQ	Ordre des pharmaciens du Québec [Quebec College of Pharmacists] *
OSHA	Occupational Safety and Health Administration
PPE	Personal Protective Equipment
RPA	Respiratory Protection Apparatus (Respirator)
RSST	Regulation respecting occupational health and safety (RRQ, S-2.1, r. 19.01)
USP	United States Pharmacopoeia

* Free translation/description

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PREAMBLE

In September 2004, the United States National Institute for Occupational Safety and Health (NIOSH) published an alert recommending more stringent preventive measures for the preparation and handling of hazardous drugs. This document quickly attracted attention in Quebec, where a number of institutions began questioning their preventive measures. The AQESSS Montreal Prevention Committee, as well as a number of institutions and organizations, have turned to the ASSTSAS for answers regarding medical and biological monitoring. In addition, some institutions whose pharmacy departments were being remodelled or were about to undergo remodelling wished to ensure the implementation of the proper measures, e.g. the type of pressure gradient required between the *clean room*, the antechamber and the general pharmacy.

In 1995, the ASSTSAS – whose mission is to promote occupational health and safety in health and social services institutions – had published a prevention guide in this regard, which it was planning to revise in 2005. Due to the issuing of the NIOSH recommendations, this revision was completed earlier.

Following a review of the reference material and extensive work in collaboration with a university hospital (CHUS) to assess the applicability of the NIOSH recommendations, the ASSTSAS felt it necessary to draw on the expertise and assistance of other stakeholders to produce a prevention guide which would reflect the diversity of the issues and points of view.

The Association thus formed a committee with mandate to produce a prevention guide for the safe handling of hazardous drugs in Quebec health care institutions.

This committee included professionals and stakeholders from the health care network with expertise and an interest in the hazardous drug issue. They have been introduced in a previous section. Some members were included in this committee in view of their expertise, while others were delegated by organizations with an interest in the issue (APES, AQATP, AQESSS, AQIO, CHQ, INSPQ, IRSST, MSSS). All of the members were asked to confer with their peers and collaborators in their respective environments.

This guide sets out the Committee's recommendations regarding how to safely handle hazardous drugs. It refers to practices which may present a risk of exposure to those working closely with or at a distance from these drugs.

The recommendations contained in this guide are in keeping with the general recommendations of the majority of recent guides published in North America, Europe and Australia. This guide does not claim to address every issue, as some require further research. If necessary, updates will be published to supplement or clarify information regarding some of these issues.

The measures proposed in this guide should be considered recommendations; they are not normative and are not mandatory. Each workplace is to implement them based on its individual circumstances.

While the guide is primarily intended for health care workers, some recommendations apply to users of the health care network and their families. These recommendations are intended to protect these individuals from direct contact with sources of contamination and to ensure harmonization between institutional and home care. Patients and families who are properly informed regarding hazardous practices will be able, in turn, to help protect workers.

1 INTRODUCTION

1.1 Guide Preparation

The Committee's recommendations are based on a number of research documents, guides and guidelines (see box below). The Committee has analyzed every recommendation in each of these documents to verify their applicability to the Quebec environment and to provide concrete information regarding their implementation.

Documents Upon Which the Recommendations of This Guide are Based	Code*
APES. Recueil d'informations pharmaceutiques en oncologie, October 2003.	APES
ASHP Guidelines on Handling Hazardous Drugs, June 2006.	ASHP
ASSTSAS. Médicaments dangereux et autres médicaments (Guide de prévention), 1995.	ASSTSAS
Buchanan & Schneider. Compounding Sterile Preparations, (ASHP), 2005.	CS
CSA. Handling of Waste Materials in Health Care Facilities and Veterinary Health Care Facilities, (Standard: CAN/CSA/Z317.10-01), approved in February 2003.	CSA
CSHP. Guidelines for the Handling and Disposal of Hazardous Pharmaceuticals, 1997.	CSHP
NIOSH Alert – Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health-Care Settings, September 2004.	NIOSH
ONS – Safe Handling of Hazardous Drugs, 2003.	ONS
OPQ. Norme 95.01: La préparation des produits stériles en pharmacie, 1995.	OPQ
OSHA Technical Manual: Controlling Occupational Exposure to Hazardous Drugs, (Section VI, Chapter 2), 1999.	OSHA
United States Pharmacopoeia - Chapter 797 ; - other chapters.	USP

* This code is used in the "Reference" Section below each guide recommendation.

Many questions go unanswered in the reference material. For example, can the same protective gown be worn after a break or a meal or should a new one be worn each time? Should one or two pairs of gloves be worn when administering drugs? What should be the pressure gradient between the *sterile* preparation room, the airlock and the rest of the pharmacy? What medical monitoring program should be recommended for the workers? None of this material offers satisfactory answers to all of these questions and the many others raised.

The Committee has attempted to answer them by reviewing the scientific literature. In the absence of scientific data, we asked for professional advice and used common sense. This enabled us to address a fair number of these questions. Further research will undoubtedly lead to a definitive answer to other questions. In the event of continuing uncertainty, we elected to base our recommendations on a few clearly-defined guidelines (See 1.2.2).

A "prepublication" version of the guide has been sent to a number of concerned individuals and organizations for their comments. The final guide takes these comments into consideration as much as possible.

1.1.1 Survey Regarding Practices in the Health Care Network

In addition to the review of reference material, the Committee used a questionnaire to determine the preventive measures being used in Quebec on March 31, 2006, in particular, compliance with the NIOSH recommendations. All of the Pharmacy Department Heads in institutions with more than 100 beds (at least 50 short-term care beds) received the questionnaire by email (61 questionnaires sent). The response rate was 87%. In 89% of cases, the questionnaire was completed in conjunction with the Nursing Department. Non-respondents received two email reminders and one telephone reminder. The results of the survey provide an overview of the current practices in the network.

The summary results of the survey are contained in Appendix 3; the detailed results were published in a trade journal (Pharmactuel, Vol. 40, No. 1, January-February 2007, pp. 37 – 42 www.pharmactuel.com). Another, Canada-wide, survey regarding the sterile preparation practices in the pharmacy (including the preparation of hazardous drugs) was conducted during the winter of 2006-2007. The Quebec results were published in a trade journal (Pharmactuel, Vol. 40, No. 4, August-September 2007), while the results for the rest of Canada were published in the Canadian Journal of Hospital Pharmacy (publication pending).

1.2 Terminology and Guiding Principles

1.2.1 Terminology

Hazardous Drugs – In this guide, the term "*hazardous drug*" is used to describe all of the drugs on the list included in the NIOSH recommendations. Theses drugs are deemed hazardous because, due to their effects, they pose a danger to workers. The NIOSH list will be used for the purposes of this guide.

Must, should, may –This document is only a guide; its recommendations have no legal or normative value. The measures proposed must be considered recommendations only. Most are described using the term "should".

When a recommendation is supported by a law, regulation or standard, the term "must" is used.

In addition, in some cases, the term "may" is used with respect to a measure which is "recommended", but whose implementation may vary according to local circumstances.

Glossary – A glossary defines the main terms found in this guide (Appendix 1). The words in *italics* refer to the glossary.

1.2.2 Guiding Principles

The Committee members have adopted guiding principles to direct the decision-making process when recommendations are based on incomplete knowledge or when a consensus was difficult to reach. These principles are based on the Cadre de référence en gestion des risques pour la santé dans le réseau québécois de la santé publique (Guidelines for Risk Management in the Quebec Public Health Network) developed by the Institut national de santé publique (National Public Health Institute) (INSPQ, 2003). The guiding principles underpin the Committee's orientation in its choice of recommendations. Four principles have been retained in the Committee's recommendations.

1.2.2.1 Priority: The Protection of Human Health

Health is seen from a global standpoint, encompassing the concepts of maintaining and improving public health and safety and disease prevention. Our first concern was for the protection of those working directly with hazardous drugs, as well as for the protection of the patients and their families. The guide thus places a high priority on the protection of human health. While aware that other concerns (for example, economic) may come into play, the role of the Committee is not to plead the case of other considerations. We have, however, taken these concerns into account as much as possible, without jeopardizing the protection of health.

1.2.2.2 Scientific Rigor

The recommendations must be based on the best evidence and knowledge available, must be supported by the scientific opinions of experts in all of the relevant disciplines and must be the result of a structured, systematic approach.

1.2.2.3 Prudent Practice

The principle of prudent practice has been applied, i.e., that preventive measures be taken when there is reasonable evidence to indicate that the situation may have significant harmful effects on health – even when the scientific evidence is not conclusive and there is continuing uncertainty.

For example, there are no known values regarding the limits of safe exposure to a hazardous drug. This uncertainty requires the application of the principle of prudent practice, i.e., the recommendation of preventive measures to minimize exposure to hazardous drugs to the greatest extent possible, in keeping with the provisions of occupational health and safety regulations regarding products suspected of being carcinogenic.

1.2.2.4 Management

The Committee focused on strengthening the ability of individuals and organizations to make informed decisions regarding the management of the risks related to hazardous drugs. This is the reason for this prevention guide, i.e., to provide stakeholders with all of the information required to exercise their judgment in an informed manner.

1.3 Guide Structure

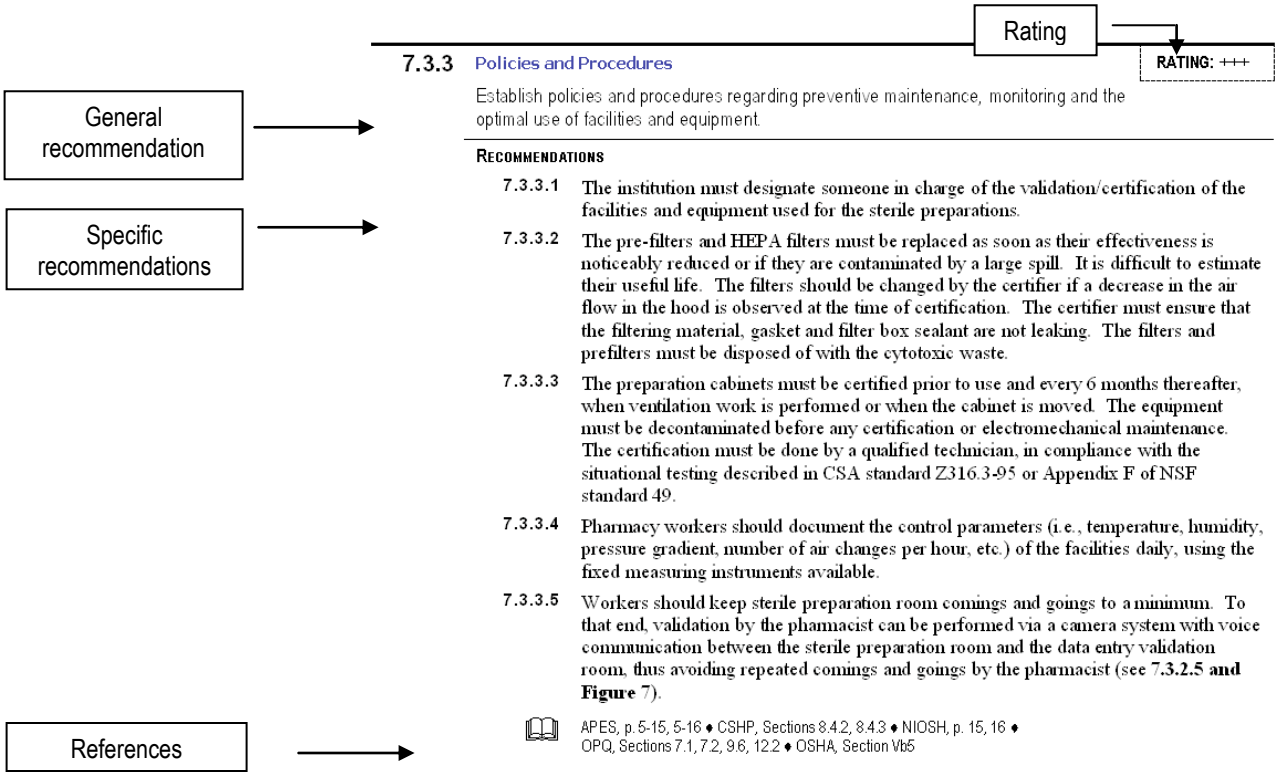
The first three chapters are an introduction, describing the risks related to hazardous drugs and establishing prevention objectives.

Chapter 4 describes the general preventive measures that apply to every step of the medication circuit in the institution.

The order of the other chapters is based on the medication circuit in the institution: receiving of the drugs and their transport to the pharmacy, unpacking and storage, preparation, administration, etc.

Each chapter is structured the same way:

- description of issues and risks related to the step concerned;
- identification of individuals at risk of exposure;
- preventive measures discussed and documented; these are presented in the following manner:



- Rating: the Committee assigned a confidence rating to each general recommendation, based on an evaluation scale regarding the level of scientific evidence supporting the recommendation. This scale has three levels:
  - +++ refers to strong evidence;
  - ++ refers to moderate evidence;
  - + refers to limited evidence and is the subject of discussion in the scientific literature;
  - in some cases, the rating applicable to the general recommendation does not apply to a specific recommendation; in this instance, the rating applicable to the specific recommendation appears in brackets following the recommendation.
- General recommendation: the title of the recommendation is in boldface and the wording is general in nature.

- Specific recommendations: each general recommendation is followed by one or more specific recommendations.
- References: this Section indicates whether the recommendation is also found in the guides of the organizations cited. The data are listed according to the page or Section of the guide (e.g. ASHP, page 1174; OSHA, Section Vc) where there is a similar recommendation. If a reference organization is not listed in this Section, that organization's guidelines do not include recommendations in that specific area.

Chapter 15 details the recommendations regarding medical and environmental monitoring.

Various items are described in a number of appendices: drug list, procedures, etc.

1.4 Additional Sources of Documentation

The work of the Committee resulted in the compilation of numerous documents related to the hazardous drug issue. The ASSTSAS Web site has a Section regarding hazardous drugs which includes the following tools and documents:

- questionnaire distributed to the institutions and link to the publication;
- summary of discussions with NIOSH;
- link with the CHQ documentation regarding facility standards;
- INSPQ offer of services regarding environmental monitoring;
- suggested bibliography;
- relevant hyperlinks (e.g. guidelines, guides, alerts proposed by various organizations, WHMIS, Material Safety Data Sheet (MSDS)).

This Section will be updated periodically.

1.5 Guide Updates

The store of knowledge regarding the risks related to hazardous drugs and how to prevent them is constantly growing and is continually being supplemented by new material.

Moreover, as previously stated, some of the issues dealt with in this guide are not as well-supported by scientific evidence as others. With time, we feel that new light will be shed on some of these areas. Both the ASSTSAS and the Working Committee members will continue to follow this matter closely, in order to keep the guide current.

We plan to publish updates as more knowledge becomes available. These will be posted on the hazardous drugs page of the ASSTSAS Web site.

2 RISKS RELATED TO THE USE OF HAZARDOUS DRUGS

2.1 Hazardous Drugs

2.1.1 Definition of a Drug

In Quebec, a drug is defined as any substance or mixture of substances that can be used:

- for the diagnosis, treatment, alleviation or prevention of an illness, disorder, abnormal physical or psychological condition, or their symptoms, in people or animals; or
- to restore, correct or modify the physiological functions of people or animals.

There are two widely-used international classifications of drugs. The World Health Organization suggests the use of the anatomical, therapeutic and chemical (ATC) classification, while the American Hospital Formulary Service (AHFS) has a similar classification system. The Régie de l'assurance-maladie du Québec (Quebec Health Insurance Board) uses the AHFS classification as the Quebec frame of reference. The list of *hazardous drugs* proposed by NIOSH (Appendix 2) also uses this classification.

This therapeutic classification groups the drugs according to their primary pharmacological effects (e.g., class 10:00 – *antineoplastic* agents, class 68:00 - hormones and substitutes, etc.).

For the purposes of this guide, *antineoplastic drug* includes such terms as anticancer drug and chemotherapy, as well as the drugs classified as such in the AHFS classification.

2.1.2 Definition of a Hazardous Drug

NIOSH considers a drug to be hazardous if studies involving humans or animals show that it has one or more of the following six characteristics.

Characteristics according to NIOSH	**Definitions**
Carcinogenic (GDT)*	Applies to any substance or agent capable of promoting or causing the development of a cancer or a lesion which could be the starting point of a cancer. Quasi-synonym: carcinogen, cancerogen The terms "carcinogenic" and "oncogenic" should not be confused. "Carcinogenic" is used to refer solely to malignant tumours, while "oncogenic" is used to refer to both benign and malignant tumours.
Teratogenic (GDT)*	Applies to substances capable of causing congenital malformations due to an action on the embryo.
Genotoxic (ASHP)	Applies to substances with the ability to damage the genetic material (DNA) and cause mutations.
Reproductive Toxicity (ASHP)	Applies to substances affecting fertility (e.g., miscarriages, late fetal death, infertility).
Organ Toxicity at Low Dose (ASHP)	Applies to substances with a toxic effect on an organ or on health at a low dose (e.g. liver damage, local necrosis of exposed tissue, etc.).
Similar Drugs (ASHP)	Applies to substances whose structure and toxicity are similar to those of a drug declared hazardous based on one of the above criteria.

* GDT: Grand dictionnaire terminologique (French/English terminology database)

NIOSH has compiled a list of hazardous drugs (Appendix 2) based on these criteria. On October 30, 2006, this list included 136 drugs, two-thirds of which are antineoplastic drugs used primarily for the treatment of cancer. Aside from the hazardous drugs used in oncology, the list includes hazardous drugs from the following therapeutic classes: some antibiotics and anti-infectives (08:12, 08:40), some antivirals (08:18), androgens (68:08), estrogens (68:16:04), gonadotropins (68:18), oxytocics (76:00), some vaccines (80:12), topical retinoids (84:36), immunosuppressive agents (92:00) and other unclassified agents (92:00).

This list is to be updated annually by NIOSH, which estimates that approximately 30 new hazardous products will be added each year. NIOSH (2007) thus carried out a consultation process, completed in September 2007, to update the list of hazardous drugs published in 2004. Two lists were involved in this process - a list of 62 new drugs marketed in the United States since the publication of the first NIOSH list and which met the above-mentioned hazardous drug criteria (e.g. amiodarone, valproic acid, pemetrexed, bevacizumab, pimecrolimus, ziprasidone, bosentan, bortezomib, sirolimus, etc.) and a second list of 85 drugs presumed to be safe (e.g. clozapine, hyaluronidase, darbepoetin alfa, infliximab, amifostine, ranibizumab, saquinavir, adalimumab, trastuzumab, efalizumab, etc.)[1].

These lists include, for each drug, an evaluation of the five hazardous drug criteria (see table above), including the teratogenicity rating assigned by the FDA when the drug was marketed. Unfortunately, the original list published in 2004 does not include a detailed table of this nature. This information is contained in the hazardous drug *Material Safety Data Sheet* [MSDS] available from the manufacturer.

At present, the regulatory system does not require drug manufacturers to distribute Material Safety Data Sheets, contrary to what is the case for the manufacturers of hazardous products governed by the *Hazardous Products Act.* The members of the Committee feel that detailed information regarding carcinogenicity, teratogenicity, genotoxicity and the general toxicity of drugs should be more accessible to Quebec health care professionals.

Until regulatory prescriptions allow the sharing of this information in Canada, the reader can refer to the list proposed by NIOSH and to various on-line sources which provide the detailed data sheets for a number of these hazardous drugs (see the ASSTSAS Web site at www.asstsas.qc.ca).

NIOSH considers that the precautions in its guide apply equally to every drug on its list. The Working Committee believes that these precautions apply unequivocally to all antineoplastic drugs, regardless of whether they are used in oncology or to treat other conditions (e.g. methotrexate for arthritis). However, some precautions could be adapted for other categories (e.g. hormones), based on the specific risks for each category. Unfortunately, the current documentation did not allow the Committee to prepare (as it would have liked) a list of precautions adapted on the basis of the toxicological characteristics of certain drug classes. Therefore, the recommendations in this guide are to be considered general recommendations. It is our hope that updates will allow the development of more targeted recommendations.

In a preliminary version of this guide (during the consultation process in 2006), the Committee proposed compiling an A list (hazardous drugs which are antineoplastic or with a high exposure risk) and a B list (other hazardous drugs with a lower exposure risk and a use outside oncology). However, upon reflection, the members agreed that it would be difficult to compile two lists, primarily because the information allowing assessment of the risk posed by each drug is difficult to collect and requires advanced expertise, as well as because the Committee was unable to establish objective scientific criteria allowing the drugs to be assigned to one list or the other.

[1] CDC – NIOSH – Process for updating the list of hazardous drugs for the NIOSH Alert on Hazardous drugs – NIOSH Docket #105 ; http://www.cdc.gov/niosh/review/public/105/default.html [Accessed on July 1, 2007].

On September 20, 2007, the ASHP responded to the consultation proposed by NIOSH to update its list, suggesting two levels of risk:

- low risk: drugs which pose a low risk for workers, particularly intact medications forms. Gloves would be required; however, masks and gowns would be optional. Once opened, crushed or broken, these drugs would require additional precautions;
- high risk: drugs which pose a high risk for workers, such as parenteral antineoplastic drugs and recognized or probable carcinogenic drugs, according to IARC (International Agency for Research on Cancer) and the NTP (National Toxicology Program). All of the NIOSH guide precautions would apply to these drugs.

In general, the ASHP supports the compilation of a list of hazardous drugs, particularly the antineoplastic drugs. However, it has suggested to NIOSH that it review its initial 2004 list with respect to certain drugs (Bacillus Calmette-Guerin, oxytocin, epinephrine and oral contraceptives). The ASHP feels that the inappropriate assignment of the "hazardous" label to certain drugs (i.e., if the evidence is insufficient to conclude that there is a genuine risk of occupational exposure) may have a major practical, professional and economic impact on the health care system. According to the appendix proposed by the ASHP, further discussion is required prior to assigning "hazardous" status to a number of drugs (e.g. risperidone, valproic acid, amiodarone, etc.).

The guide thus proposes general preventive measures for the hazardous drugs used outside oncology. Each health care institution must assess the risks in its facility and apply the appropriate protective and preventive measures.

2.1.3 Growing Use of Hazardous Drugs

The use of hazardous drugs (in particular, antineoplastic drugs used in oncology) is increasing for a number of reasons.

On the one hand, there has been an increase in the number of cancer cases, which account for almost 30% of deaths in Quebec annually (Boothroyd, 2004). The National Cancer Institute of Canada estimates the number of new cases of cancer in Quebec in 2006 at 38,300. According to the data from British Columbia, the number of individuals receiving chemotherapy increased by 43% from 1996-1997 to 2001-2002. There is every reason to believe that the situation is similar in Quebec (MSSS, 2003).

On the other, the hazardous drugs used are more potent and are more often used in combination and at higher doses. They are also used to treat conditions other than cancer. For example, the immunosuppressive properties of methotrexate also make it useful for treating arthritis and other conditions.

In hospitals, antineoplastic drugs are most often used in the pharmacy, oncology units, some outpatient clinics, the operating room and care units. In the United States, it is estimated that, during the course of their work, 5.5 million workers are exposed to hazardous drugs or their wastes.

Home use is also increasing. According to a survey conducted in the local community service centres (CLSC) in 1999-2001, 35.6 % had been involved in administering intravenous antineoplastic drugs in the homes of patients (Boothroyd, 2004). There is a trend toward performing certain treatments in the home if this can be done safely for the patient. In the United States, 90% of chemotherapy treatments are performed in the outpatient clinic or in the patient's home.

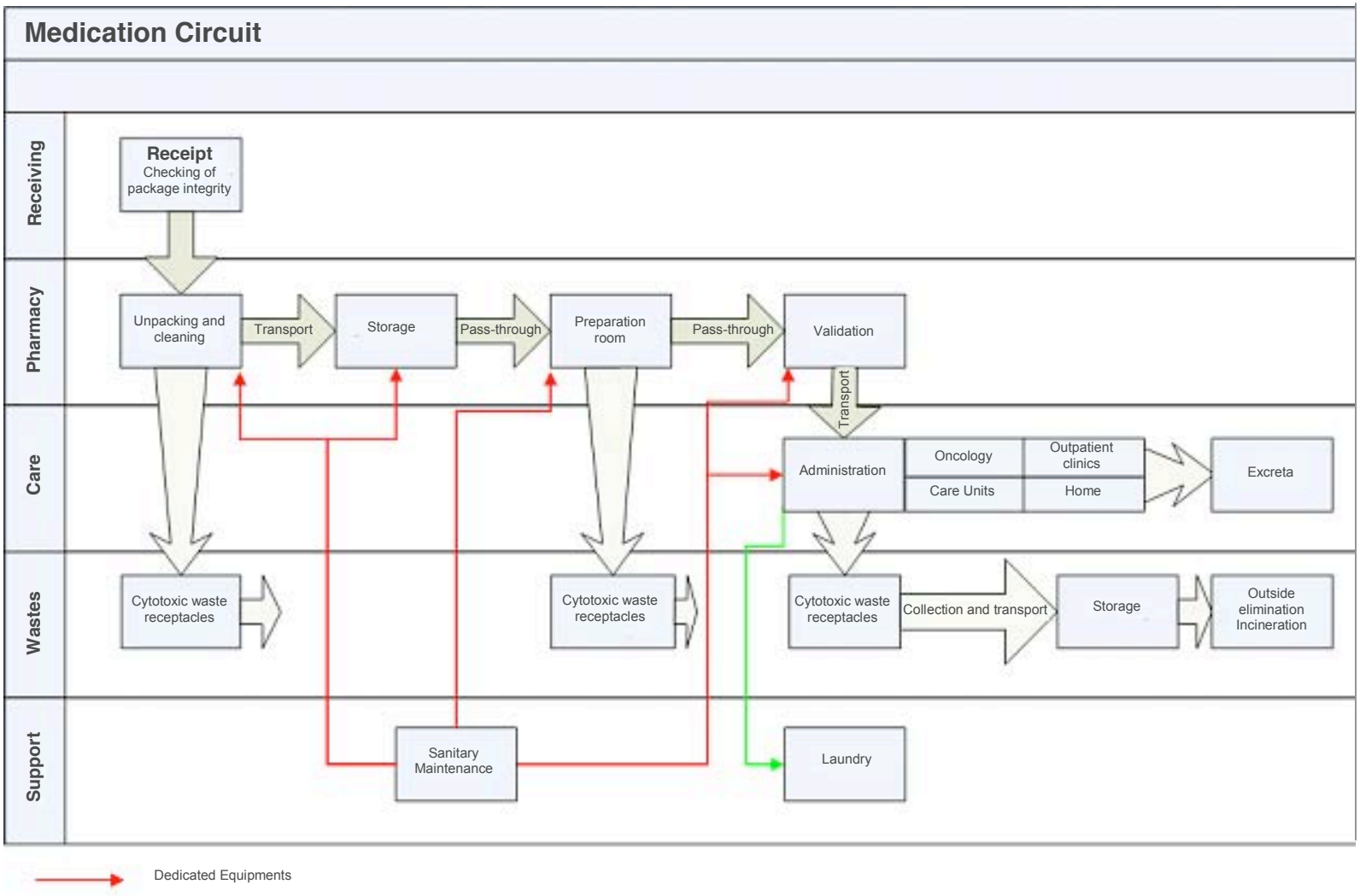
2.2 Exposure to Hazardous Drugs

2.2.1 Who is at risk for exposure to hazardous drugs?

Exposure is possible throughout the medication circuit in the hospital or at home. The medication circuit includes all of the steps through which the drug travels – from the receiving dock to the storage facility - as well as its preparation, administration, elimination in the excreta and in its wastes. In October 2005, the MSSS published a report regarding the computerized and robotic systems for drug distribution in Quebec health care institutions. This report proposed a 54-step medication circuit (MSSS 2005). When making its recommendations, our guide uses the main steps of the medication circuit. These are illustrated in Figure 1.

A number of individuals may be exposed throughout this circuit, i.e., the receiving and transport workers, pharmacists and pharmacy technicians, the physicians, nurses and inhalation therapists who administer the drugs, the nurses and patient service associates involved in patient care following the administration of hazardous drugs, the hygiene and sanitation workers, the waste management workers, the laundry workers, etc.

Figure 1. Medication Circuit



2.2.2 Hazardous Drug Entry Routes into the Body

Hazardous drugs may enter the body through skin absorption, ingestion, accidental injection (e.g. needlesticks) or inhalation.

Skin absorption is the main known penetration route and occurs through direct contact with contaminated surfaces or objects. For example, contact with the contaminated exteriors of drug vial is one source of contamination. Contaminated work surfaces, the excreta and bedding of patients treated with antineoplastic drugs, drug leaks, etc. are other sources of exposure. Most often, the contamination is spread by the hands; this is why the wearing of gloves and handwashing are such important preventive measures.

Ingestion can occur through eating contaminated food or by putting contaminated fingers or objects (in particular, pencils) in the mouth.

The significance of inhalation as an exposure route has not been clearly established. A number of studies report low levels of dust or particles in the air. However, these studies do not usually check for the presence of vapours, despite the fact that it has recently been determined that some drugs are volatile (Turci, 2003, Kiffmeyer, 2002, Opiolka, 2000, Connor, 2000). Contamination can occur through the inhalation of drug vapours.

In view of the fact that some hazardous drugs are capable of generating vapours, appropriate preventive measures must be taken (for example, a biological safety cabinet which does not recirculate the air in the room). The drug particles can turn into vapour in a few seconds or minutes, depending on the product. A study by Kiffmeyer (2002) demonstrated that the six drugs studied (carmustine, cisplatin, cyclophosphamide, etoposide, fluorouracil, fosfomycin) are capable of evaporating. Measurements of cyclophosphamide in gaseous form revealed the presence of the drug in 7 out of 20 samples.

However, as the drug monographs do not generally include data regarding the volatility of hazardous drugs, it is not possible to compile a list of these.

2.2.3 Potential Sources of Exposure

Exposure can occur at any step in the medication circuit, i.e., creation of aerosols during the preparation or administration of hazardous drugs, leaks or spills during transport or handling, contact with contaminated surfaces or objects, contact with wastes or excreta; etc.

Table 1 summarizes the target workers and primary potential sources of contamination at each step of the circuit. In addition to those individuals involved in the main steps of the medication circuit, we should not forget the biomedical engineering workers, who may have to become involved to maintain or repair the pumps and equipment used to administer the drugs. In view of the local variability of practices and potential sources of exposure, it is difficult to establish a single risk hierarchy based on potential sources of exposure.

While the majority of hazardous drugs are stored, prepared and administered in a limited number of locations (i.e., oncology pharmacy, care units, outpatient clinics, etc.), they can also be administered elsewhere in the institution (e.g. operating rooms). The guide does not suggest recommendations according to location type. It is up to the Occupational Health and Safety Program Manager to apply the general recommendations to specific situations (e.g. using an appropriate *transport container* between the pharmacy and the operating room, as well as making appropriate operating room waste receptacles available in the rooms where hazardous drugs are administered, etc.).

Table 1. Medication Circuit Steps, Exposed Workers and Main Sources of Exposure

Medication Circuit Steps	*Potentially Exposed Workers*	*Potential Sources of Exposure to Hazardous Drugs*
Receiving and Transport *(Chapter 5)*	Receiving or transport clerks (e.g. stock-keeper, storeroom clerk) Hygiene and sanitation workers Pharmacy Department workers (e.g. pharmacist, clerk, pharmacy technician)	Damaged or contaminated packages or *delivery containers* Breakage of a container due to a fall or other cause
Unpacking and Storage *(Chapter 6)*	Pharmacy Department workers (e.g. pharmacist, clerk, pharmacy technician) Hygiene and sanitation workers	Damaged or contaminated packages or delivery containers Contamination of outside surfaces of drug vials from the manufacturer
Drug Preparation *(Chapter 8)*	Pharmacy Department workers (e.g. pharmacist, clerk, pharmacy technician) Hygiene and sanitation workers Maintenance workers (e.g. biomedical engineering workers or preparation cabinet certifier)	The handling of hazardous drugs, particularly during their preparation (i.e., reconstitution, dilution, bagging or filling of syringes, etc.) may be a major source of work environment contamination, even in the general areas of the pharmacy. The lack or ineffectiveness of measures to contain these sources (e.g. air recirculation hood, diffusion of contaminants outside the *sterile* preparation room) may contribute to worker exposure. Direct contact with contaminated vials from the manufacturer. Direct contact with hazardous drugs during handling (e.g. when counting solid oral forms, contact when adding diluent, when agitating the drug container, when transferring the solution into another container, such as a syringe, bag or other administration device). Direct contact with the bins or trays used to transport hazardous drug preparations (e.g. syringes, bags containing hazardous drugs) during their packaging or transfer to the care units or outpatient clinics. Contact with contaminated equipment (e.g. the plunger of syringes containing drugs, the pumps during their maintenance or repair or the HEPA filters during their replacement). Exposure to hazardous drug particles or vapours in the immediate vicinity of the preparation cabinet due to leaks through the front opening. Such leaks may be caused by rapid arm movements or obstruction of the front filter grille of the cabinet.

Medication Circuit Steps	*Potentially Exposed Workers*	*Potential Sources of Exposure to Hazardous Drugs*
Transport and Storage Following Preparation *(Chapter 9)*	Pharmacy Department workers (e.g. pharmacist, clerk, pharmacy technician) Outpatient clinic and patient care unit workers (e.g. nurse, patient service associate) Transport workers (clerk, etc.)	Breakage of a drug container due to a fall or other cause (worker exposure and environmental contamination due to the spread of liquids, powders or aerosols or through the diffusion of vapours). Direct contact with a drug container (as the outside of the container may be contaminated).
Administration of Drugs *(Chapter 10)*	Care unit, outpatient clinic and home care workers, i.e., nurses, patient service associates, physicians, inhalation therapists Pharmacists Hygiene and sanitation workers Other patients and families of patients	Leaks or creation of aerosols when priming or removing air from tubing, if this is not done in the preparation cabinet; Leaks or creation of aerosols during the connecting and disconnecting of syringes and tubing from the injection ports; Contamination through contact with poorly-cleaned drug bags, tubing or syringes during the preparation step. The drug containers or drug preparation transport trays may also be contaminated; Inhalation of aerosols during aerosolized administration (ribavirin, pentamidine); Surface contamination (gloves, etc.) and inhalation of particles when handling or crushing pills; Contact contamination when applying creams or ointments; Accidents: needlesticks, breakage of drug containers, spills; Direct contact due to projections, splashing or vapour inhalation during special procedures such as *hyperthermic intraoperative intraperitoneal chemotherapy* (HIIC) (operating room or intensive care unit).
Patient Care *(Chapter 11)*	Care unit / outpatient clinic / home care workers (e.g. nurse, physician, inhalation therapist, patient service associate) Other patients, families of patients Hygiene and sanitation workers Biomedical engineering workers	The body fluids of patients who have received chemotherapy contain drug residues. Contact with patient excreta, bedpans, sheets or wash water may be a source of contamination.

Medication Circuit Steps	*Potentially Exposed Workers*	*Potential Sources of Exposure to Hazardous Drugs*
Management of Wastes, Accidental Exposure, Spills and Returns *(Chapter 12)*	Receiving or transport clerks (e.g. stock-keeper, storeroom clerk) Waste collection workers Pharmacy Department workers (e.g. pharmacist, clerk, pharmacy technician) Care unit / outpatient clinic / home care workers (e.g. nurses, physicians, inhalation therapists, patient service associates) Other patients, families of patients Hygiene and sanitation workers	The transfer of hazardous drugs and contaminated supplies to waste receptacles can cause exposure, as can the handling of these receptacles (e.g. when closing bags, during transport, etc.). While the waste receptacles are relatively leakproof, contaminated fluids may leak out if the receptacle tips over. If the waste receptacles are not closed, there is a risk of aerosol propagation or vapour diffusion. Spills constitute an exposure risk due to potential direct contact with hazardous drugs or their spread into the air as aerosols or vapours. This may occur at any step of the medication circuit.
Hygiene and Sanitation *(Chapter 13)*	Hygiene and sanitation workers	Inadequate cleaning increases the exposure of all staff working in areas where hazardous drugs are handled. Contact with contaminated surfaces (e.g. counters, furniture, etc.), wastes, excreta, soiled bedding, rags and mops used to clean contaminated areas (toilets or floors in the rooms of patients who have received hazardous drugs, preparation or administration areas, etc.). Ingestion via contaminated hands or by eating or drinking in these areas. *Cleaning* of hazardous drug spills or the stools, urine or vomitus of patients who have received hazardous drugs.
Laundry *(Chapter 14)*	Laundry workers	Possible contact with contaminated bedding in some laundries. Inhalation of particles on the sheets in some laundries.

2.3 Data Regarding Exposure and Its Effects

2.3.1 Contamination of the Work Environment

Many studies have confirmed the presence of contamination in areas where hazardous drugs are handled, including the pharmacy, oncology units and the rooms of patients who have received chemotherapy.

Since 1990, at least 14 studies have measured surface contamination by one or more drugs (those most often measured are cyclophosphamide, ifosfamide, fluorouracil, and methotrexate). All of the studies showed measurable amounts of drugs in the work environment.

A study conducted in 1999 (Connor, 1999) in six Canadian and American hospitals revealed the presence of contamination, by at least one of the three drugs measured, in 75% of pharmacies and 65% of drug administration areas. In the preparation areas, the contamination was often higher outside the hood than inside. The authors noted that the hood does not offer complete protection and that the preparation techniques are very important. The level of contamination was lower in the administration areas; the most contaminated areas were the floor around the patient's chair or bed, the arms of the patient's chair and the work table or counter.

The preparation and administration areas are not the only trouble spots. A study conducted in Holland in 2005 also showed contamination in the rooms of patients who had received chemotherapy (Fransman, 2005). For example, all of the urinals and bedpans, all of the cloths used to wash the patients and 60 to 82% of the cloths and mops used to clean the room were contaminated with hazardous drug residue. This contamination resulted, in turn, in contamination of gloves or hands and, occasionally, the forearms and foreheads of the nurses or cleaners. In a number of cases, the workers were not wearing gloves. Wearing gloves reduced hand contamination by 1.6 to 4 times, depending on the task concerned. Bussières *et al.* published a summary of the contamination data in an Institut national de santé publique du Québec newsletter (Bussières, 2006b).

In summary, contamination of the work environment has been well-documented by many authors. Assessments performed in a number of Quebec institutions as part of a pilot study carried out with the INSPQ indicates that a similar situation exists in Quebec.

2.3.2 Health Effects of Exposure

According to the Alert issued by NIOSH in 2004, "Working with or near hazardous drugs...may cause skin rashes, infertility, miscarriage, birth defects and possibly leukemia and other cancers".

Despite improvement in the safety of pharmacy department practices, recent studies have shown that the workers may still be exposed. During the past decade, a number of investigators have demonstrated that concentrations of various hazardous drugs could be found in the urine of those administering or preparing the drugs (Sessink 1992, Ensslin 1994, Nygren 1997, Turci 2003, Fransman 2006, NIOSH 2004, Bussières 2006). This finding is of even greater concern as these drugs can have toxic effects (as noted in the NIOSH document). The carcinogenic effect of some drugs in animals is recognized and research tends to demonstrate that these drugs may promote the development of new cancers in the individuals treated. Table 2 lists certain drugs known to be carcinogenic or probably carcinogenic in humans (Connor, 2006).

The consequences of occupational exposure are, however, difficult to document and the study results lack consistency because the facilities and work methods are constantly changing. *Genotoxic* effects have been demonstrated and adverse reproductive effects, such as fetal death, congenital malformations, infertility and an increased risk of leukemia, are a real concern (NIOSH 2004, Dranitsaris 2005, Fransman 2007, Bussières 2006).

The only statistically significant finding of a recent systematic review and meta-analysis of the health effects of hazardous drugs was an increased risk of spontaneous abortion in exposed workers (OR 1.46; CI 1.11 - 1.92 [see "Risk Measurement" box]) (Dranitsaris, 2005). While not statistically significant, the other effects are not ignored, in particular, an excess risk of congenital malformations (OR 1.64; CI 0.91 – 2.94) and stillbirth (OR 1.15; CI 0.75 – 1.82). Because of their number and size, however, these studies do not allow a significant degree of accuracy.

A more recent study performed in Holland reported a low, but significant, excess risk of prematurity (8%) and intrauterine growth retardation (11%) in nurses exposed to cyclophosphamide. The investigator also reported a low excess risk of leukemia – from 0.27 to 40 additional cases per million female workers exposed during their professional lives (Fransman, 2007).

Risk Measurement

OR: *odds ratio*

The odds ratio is a measure of association which provides a good estimate of the risk related to exposure. Thus, an OR of 1.45 basically means that there is an excess risk of 45% versus a group of non-exposed individuals.

CI: *confidence interval.*

A measure of association such as the odds ratio (OR) usually comes with a confidence interval at 95% (95% CI). This interval expresses the statistical precision around the measure of association. If the 95% CI does not contain the value 1, for example (1.10 – 1.95), it can be said that the result is statistically significant at the threshold of 5% ($p < 0.05$). More specifically, the interval (1.10 – 1.95) should include the true value 19 times out of 20 (the value of 5% has been adopted by the scientific community as the threshold for statistical significance). However, if the CI does contain the value 1, for example (0.9 – 1.2), the result is not statistically significant.

Table 2. Antineoplastic Drugs or Drug Combinations Known to Be Carcinogenic or Probably Carcinogenic in Humans and Available in Canada

Group 1 *Known To Be Carcinogenic in Humans**	*Group 2A* *Probably Carcinogenic in Humans**
Azathioprine	Carmustine
Chlorambucil	Lomustine (Ceenu)
Cyclophosphamide	Cisplatin
Busulfan	Doxorubicin HCl
Melphalan	Imatinib (Gleevec)
Tamoxifen	Etoposide
Thiotepa	Mechlorethamine HCl
Mustargen, vincristine and procarbazine	Procarbazine HCl
Combination of etoposide, cisplatin and bleomycin	Teniposide

* Classification established by the International Agency for Research on Cancer (IARC)

2.3.3 Worker Contamination

The risk for workers depends on the toxicity of the drugs to which they are exposed and their level of exposure to these drugs. Exposure depends on a number of factors:

- the work performed: preparation, administration, cleaning, etc.;
- its frequency and duration;
- the quantity of hazardous drugs handled;
- compliance with good work techniques: proper hoods, wearing of protective equipment, work techniques.

The skin is the known primary exposure route. Contamination of the hands and, less frequently, the forearms and forehead account for 87% of contaminated body areas (Fransman, 2004).

This exposure often results in whole body contamination, detectable through the presence of drugs in the urine. In 18 studies, 16 detected the presence of drugs in the urine, including 4 where the workers did not handle any drugs. These cases are thought to represent indirect contamination through contact with contaminated surfaces.

There is no safe exposure standard. In view of the seriousness of the potential effects, prudent practice requires that the exposure be reduced as much as technically possible. Turci *et al.* use the acronym ALARA, i.e., "as low as reasonably achievable" (Turci, 2006).

While an acceptable level has yet to be determined by occupational health and safety organizations, publications in this regard should be monitored by the scientific community. For example, in its August 15, 2006 update, the United States Pharmacopoeia mentions a maximum acceptable environmental contamination threshold of 1 ng/cm^2 for cyclophosphamide. This exposure value can be verified in Quebec workplaces using the environmental monitoring tests developed by the INSPQ at the request of the Working Committee (see Appendix 5). To help the institutions interpret their results, a summary of the contamination values from 34 studies was published in the INSPQ toxicology newsletter (Bussières *et al.*, 2006b)

The members of our Committee do not recommend measuring biological contamination levels in workers (other than for research purposes), as it is currently impossible to interpret the results (see Section 15).

2.3.4 The Importance of Prevention

All of these studies clearly demonstrate the need for the stringent application and intensification of preventive measures.

The risks for the worker can be substantially reduced if he works in a controlled environment, such as a vertical laminar flow hood, in a properly ventilated area, using the recommended protective equipment and safe work techniques.

For example, a recent study performed in Holland reported an 8- to 25-fold reduction in the level of glove contamination during work in the hood and a 25- to 6000-fold reduction in contamination in the hood from 1993-1999 to 2005. (Fransman, 2005). This improvement can be attributed to concentrating drug preparation in the pharmacy, heightened worker awareness and a tightening of the preventive measures.

The same attention must be paid to every step of the medication circuit. The study also reported contamination in workers providing care to patients who had received antineoplastic drugs. Here, as the risk is not perceived to be as high, the preventive measures were not always as stringent.

Training also plays an important role in reducing contamination. Favier (2002) demonstrated a 3.2-fold reduction in the frequency of hand contamination and a 7-fold reduction in the amount of drug found on the hands. Prior to the training, 100% of gloves and 70% of hands were contaminated, despite the use of standard means of protection. Following training regarding proper handling procedures, 45% of gloves and 20% of hands were contaminated.

There are *closed-circuit systems* for preparation and administration which have proven effective in significantly reducing the level of contamination in both the workers and the work environment. The PhaSeal® system has been

studied and recognized to be effective (Wick, 2003; Spivey, 2003; Connor, 2002; Harrison, 2006; Au, 2006). Other systems are also available (e.g. Tevadaptor®). The cost-effectiveness ratio of closed-circuit systems or those limiting the risks of contamination (particularly in the context of Quebec health care) has not yet been determined. We are encouraging evaluative research to determine the role of this type of technology in Quebec practice.

In a pilot study performed in 2007 with the INSPQ Toxicology Laboratory and CHU Sainte-Justine, environmental contamination levels below 1 ng/cm^2 of cyclophosphamide, ifosfamide and methotrexate were measured in most of the 75 samples taken from 5 sites outside the cabinet in a non-optimal environment without closed-circuit preparation equipment. Following the relocation of this satellite pharmacy, in June 2007, to an environment in keeping with the guidelines set out in this guide, without a closed-circuit system, new measurements confirmed the lack of environmental contamination in an equivalent number of samples. It is thus possible to significantly reduce environmental contamination through training and the use of various preventive measures (data on file, not yet published).

How can the effectiveness of existing preventive measures be ensured? Regular environmental monitoring appears to be the best way to validate the preventive measures implemented. It should be stressed that there are currently no standards regarding drug contamination of the environment, nor any safe level of worker exposure. Stringent, regular monitoring of the work environment will at least allow the detection of any change in exposure levels and determination of the cause, in order to make the necessary corrections. The analyses proposed by the INSPQ Toxicology Laboratory will be useful in assessing the contamination by three products (see Appendix 5 and Chapter 15).

3 PREVENTION OBJECTIVES AND ACTION PLAN

Any prevention process must have an objective. The Committee is proposing one general objective and two specific objectives.

3.1 General Objective

To reduce health care worker exposure to the lowest level possible, while preserving the integrity of the drug and the health of the patients and their families.

3.2 Specific Objectives

- To reduce the environmental contamination level as much as technically possible.
- To eliminate the biological contamination of workers.

The ultimate objective is to ensure that workers are not contaminated. Absorption of hazardous drugs exposes workers to the risks related to hazardous drugs. Unlike the patient, the worker derives no benefit from such exposure. Achieving these objectives requires the implementation of the general and specific recommendations contained in this guide.

3.2.1 Action Plan

This guide proposes an extensive review of the professional practices related to the health and safety of workers who may be exposed to hazardous drugs. It is directed, in particular, toward the Occupational Health and Safety Managers in each institution, the Heads of the Pharmacy Departments, the Directors of Nursing, and the union representatives of the workers concerned. The Committee members are proposing that those institutions wishing to review their practices adopt a structured approach, i.e.:

- that the institution create a Hazardous Drug Committee and designate its members (Section 4.1.2 of the guide suggests a list of the individuals who should, ideally, be part of the Committee);
- that all members of the Hazardous Drug Committee in each institution read this guide carefully;
- that the Hazardous Drug Committee assess the risks in its facility.

First, the potentially exposed individuals and their numbers, the products used and the frequency of their use must be identified. Although not mandatory in hospitals, the work station record prescribed by the Occupational Health and Safety Act (Section 52) may be used for this purpose.

Second, the Committee should also assess the compliance of the practices, equipment and facilities, based on the recommendations in this guide. The grid shown on the ASSTSAS Web site may facilitate this assessment.

Finally, the level of environmental contamination of the work areas likely to be contaminated (pharmacy, oncology clinic, rooms of patients who have received chemotherapy, etc.) must be checked. *[To this end, see Chapter 15 and Appendix 5 for information regarding the tests offered by the INSPQ]*. This overall assessment of the situation may help determine intervention priorities (among other things).

- This risk assessment will enable the Hazardous Drug Committee of each institution to determine the corrective measures to be implemented in the form of an action plan with an institution-specific timeline. The actions can be prioritized according to several criteria, i.e.:
    - the respective level of contamination in the pharmacy, administration areas (e.g. oncology clinics) and care areas (e.g. the rooms of patients receiving chemotherapy), as well as in all other areas assessed; in general, according to the data in the scientific literature, the pharmacy is more contaminated than the administration and care areas. However, depending on the facilities, equipment and practices, this situation may vary from one institution to another. In addition, the environmental assessment will allow the targeting of risk situations and possible solutions in a given area. For example, substantial contamination of drug transport bins may mean that the drug bags were poorly-cleaned when they left the preparation cabinet. Based on this observation, it is possible to improve the drug bag *cleaning* practices and introduce a periodic bin cleaning program.

- the effectiveness of the measure. The better an action can eliminate contamination at the source, the more effective it is. For example, washing the drug vials received from distributors will allow the removal of a source of contamination at the beginning of the preparation circuit.
- the feasibility and costs. When reading this guide, you will note that some measures are easy to implement and require practice modifications with no financial impact on the institution (e.g. separating the hazardous drugs from the other drugs in storage); other measures require a practice change with an acceptable financial impact (e.g. double gloving, purchase of appropriate cases for the transport of hazardous drugs, certification of work methods); finally, other measures have a substantial financial impact (e.g. retrofitting of the *sterile* preparation room in the pharmacy). It is thus reasonable to immediately implement the measures which can be put into practice quickly, with a view to implementing the more difficult measures over a longer period of time.

For information purposes, Table 3 illustrates the "traditional" classification of preventive measures.

Due to the current situation regarding preventive measures (as revealed by the results of the survey conducted in Quebec in the spring of 2006) (Appendix 3), we feel that this guide will lead to a revamping of work methods in health care institutions.

Each institution must prioritize its own actions. As seen above, the sources of exposure can vary from one institution to the next. The action plan must thus take into account the situation in each institution, including its level of contamination (which it will periodically be asked to document through the surface contamination analyses offered by the Institut national de santé publique (INSPQ) Toxicology Laboratory). In any case, the principle of prudent practice should be applied to every step of the medication circuit. In short, this guide cannot set a single timeline for the province of Quebec as a whole, due to the variability of the situation in each institution.

Table 3. Classification of Preventive Methods

Preventive Methods	*Examples*
Engineering controls Layout of the premises and use of equipment to reduce the risk Collective protection	Hood or isolator Ventilation Closed-circuit preparation or administration system Needleless systems
Work practices	Preparation techniques in the hood Drug administration techniques Techniques for removing the PPE Cleaning of the premises (to avoid spreading the contamination) Collection of *cytotoxic waste* Spill recovery
Organization	Hazardous drug inventory, data sheets (with update) and identification with labels Training for positions at risk of exposure and assessment of techniques Environmental monitoring Procedure in the event of spills Post-accidental exposure follow-up procedure Damaged goods return procedure Respiratory Protection Program Management of cytotoxic waste Etc.
Personal protective equipment (PPE) Personal protection, dependent on the level of compliance with the recommendations	Gloves Gowns Face protection *Respirator (RPA)*

4 GENERAL PREVENTIVE MEASURES

This guide makes general and specific recommendations regarding preventive measures. This Section describes the general preventive measures that apply to every step of the medication circuit.

4.1 Preventive Measures

4.1.1 Hazardous Drug Preventive Management Program and Manager

RATING: +++

Designate a manager for the Risk Prevention Management Program related to the use of hazardous drugs in the institution.

RECOMMENDATIONS

4.1.1.1 The Occupational Health and Safety Program Manager, working closely with those concerned, should coordinate the implementation of the Risk Prevention Management Program related to the use of hazardous drugs, in addition to chairing the institution's Hazardous Drug Committee.

4.1.1.2 The Head of the Pharmacy Department or the designated pharmacist must assume the responsibilities described in the Ordre des pharmaciens du Québec standard in effect.

APES, p. 5-3 ♦ ASHP, p. 1175 ♦ CSHP, Section 3.1 ♦ OPQ, Sections 4.1, 4.2

4.1.2 Hazardous Drug Committee

RATING: +++

Establish a Hazardous Drug Committee.

RECOMMENDATIONS

4.1.2.1 This committee should include, at the very least, one representative from each of the following departments and services: occupational health and safety, pharmacy, nursing, hematology-oncology (physician), inhalation therapy, hygiene and sanitation, technical service, risk management.

4.1.2.2 This committee should be mandated by the hospital administration to ensure the implementation and follow-up of the Risk Prevention Management Program related to the use of hazardous drugs.

4.1.2.3 This committee should meet at least twice a year to discuss the hazardous drug situation.

ASHP, p. 1175 ♦ CSHP, Section 4.1.2 ♦ OPQ, Section 3.1.2

4.1.3 Hazardous Drug Preventive Management Program

RATING: +++

Establish a Hazardous Drug Preventive Management Program.

RECOMMENDATIONS

4.1.3.1 The Hazardous Drug Preventive Management Program should include, at the very least, the following:

- an annual self-assessment of compliance with the recommendations of this guide, taking into account the steps of the medication circuit (see the assessment grid on the ASSTSAS Web site);
- an environmental monitoring program, as well as an environmental measures record;
- policies and procedures allowing the implementation of the recommendations of each section of this guide, according to the local assessment of the risk;
- an annual update of the policies and procedures;
- a training program, with an accompanying assessment;
- a hygiene and sanitation program;
- a monitoring and preventive maintenance program regarding the infrastructures (e.g. sterile preparation room) and equipment (e.g. hoods);
- proper, approved sets of *personal protective equipment*, as well as a respiratory protection program;
- an updated list of hazardous drugs. Any drug being used for the first time (e.g. investigational drug) is to be evaluated to determine whether it should be considered a *hazardous drug*, using the six criteria defining a drug as hazardous (see Section 2.1.2);
- the list of hazardous drugs should be readily accessible to the workers exposed at every step of the medication circuit;
- identification of the hazardous drugs in the management information systems, using a special code to generate a hazardous drug list. This list should specify both the trade name and the generic name, as well as the AHFS class;

  In the reference material, the *MSDS* is the tool generally recognized as being the most comprehensive regarding the following: risk identification, first aid, measures regarding fire, measures in the event of a spill, handling and storage, exposure prevention and personal protection, physical, chemical and toxicological properties, environmental information, waste management, transportation, etc. Under the Food and Drugs Act, the manufacturer is not obligated to provide a material safety data sheet for a hazardous drug, contrary to what is the case for the hazardous goods regulated by the Hazardous Products Act. We encourage the Pharmacy Departments to keep a list of hyperlinks to access the MSDSs for hazardous drugs.
- a communication plan, including quick, easy access to the hazardous drug list, technical data sheets and policies and procedures;
- an annual report regarding the situation.

4.1.3.2 The workers and families of patients should not eat, drink, chew gum, apply makeup or store food in the areas where hazardous drugs are stored or handled.

APES, p. 5-5 ♦ ASHP, p. 1175, 1182 ♦ CSHP, Sections 4.1, 4.2, 8.1, 8.2.3, 8.9.5 ♦ NIOSH, p. 10, 11 ♦ ONS, p. 43 ♦ OPQ, Sections 3, 4.3, 4.4.1, 9.2.2, 12.5, 14 ♦ OSHA, Section Va, Vb1, Vc6, VIIc

4.1.4 Continuing Education and Orientation Program

RATING: +++

Establish a Hazardous Drug Continuing Education and Orientation Program for All Exposed Workers

RECOMMENDATIONS

4.1.4.1 The Occupational Health and Safety Program Manager should designate an individual in each sector concerned to be responsible for continuing education and orientation regarding hazardous drugs; the learning objectives should be mutually agreed upon.

4.1.4.2 The hazardous drugs must be transported, prepared, reconstituted, administered and disposed of by properly-trained workers. Individuals in contact with excreta from patients who have received hazardous drugs or with objects soiled by such excreta must also receive proper training.

4.1.4.3 The Continuing Education and Orientation Program should, at the very least, include the following:

- definition of the health risks of hazardous drugs;
- identification and detection of these risks;
- use of personal protective equipment, including the proper *respirators*;
- emergency plan in the event of a spill or accidental exposure; a spill can occur at any step of the medication circuit.

4.1.4.4 The Continuing Education and Orientation Program should include the elements specific to each sector concerned and should be updated annually, if necessary.

4.1.4.5 The Training Program should include an assessment tool for each sector:

- an annual assessment of the quality of *sterile* handling in preparation cabinets;
- an annual assessment of the quality of handling in drug administration;
- an annual assessment of the quality of handling with respect to patient care;
- an annual assessment of the quality of handling with respect to hygiene and sanitation and *cytotoxic waste* management.

The use of fluorescein solutions is one tool for validating the quality of handling with respect to preparation and administration. Used with UV light, they help detect droplets or leaks during handling (Favier, 2003; Spivey, 2003; Favier, 2002; Harrison, 1996). The institutions can prepare fluorescein solutions using the above-mentioned references or purchase the ready-to-use kits available from certain suppliers.

4.1.4.6 The Program can include a mechanism for documenting worker participation in the training and assessment of the quality of handling activities.

4.1.4.7 The Program should include an annual spill simulation exercise. (See Appendix 4 for the spill procedure.)

APES, p. 5-5 ♦ ASHP, p. 1182 ♦ CSHP, Sections 4.2, 8.2.1, 8.2.2, 8.9.5 ♦ NIOSH, p. 11, 12, 16, 18 ♦ ONS, p. 43, 44 ♦ OPQ, Sections 4.3, 12.3 ♦ OSHA, Section VIII.

4.1.5 Identification and Safety

RATING: +++

Ensure safe storage and transfer of hazardous drugs at every step of the medication circuit.

RECOMMENDATIONS

4.1.5.1 Access to the Pharmacy Department must be restricted, at all times, to pharmacy workers.

4.1.5.2 Access to floor reserves and areas on care units where hazardous drugs are kept should be limited to the caregiving staff.

4.1.5.3 *Antineoplastic drugs* and their waste must be properly identified with the symbol described in CSA standard Z317.10, i.e., the symbol capital "C" and, under it, the words "CYTOTOXIC – CYTOTOXIQUE" in capital letters (Figure 2). Both the words and the symbol must appear on a dark grey rectangle. This logo is used for the antineoplastic hazardous drugs listed in Appendix 2 of this guide.

FIGURE 2
"Cytotoxic" Hazard Symbol

4.1.5.4 Other hazardous drugs (which are not antineoplastic agents) should bear a warning or a "CAUTION" label. There is currently no recognized symbol for identifying other hazardous drugs which are not antineoplastic agents (and therefore, *cytotoxic*). Committees in both the United States and Canada are working on such a symbol. In Canada, the Globally Harmonized System (GHS), which will eventually replace the WHMIS, should cover hazardous drugs and establish symbols based on the effects of products. It will not be in use, however, until 2008-2010. While the term "Caution" is general and does not refer solely to the recommendations in this guide, the Committee members have decided not to create another identification symbol while awaiting a decision from regulatory authorities. (++)

APES, p. 5-37 ♦ ASHP, p. 1175-76 ♦ CS. p. 65 ♦ CSA, Z317.10-01, Section 9.1.2 ♦ CSHP, Section 4.3 ♦ NIOSH, p. 12 ♦ ONS, p. 23 ♦ OPQ, Section 4.5 ♦ OSHA, Section Vc6

4.1.6 Integrity of Hazardous Drugs

RATING: +++

Check the integrity of hazardous drug containers.

RECOMMENDATIONS

4.1.6.1 Workers should check the integrity of hazardous drug containers throughout the medication circuit; in the event of a broken or damaged container, see Chapter 12.

ASHP, p. 1175 ♦ OPQ, Section 6.2.2

4.1.7 Protective Equipment

RATING: +++

Wear proper protective equipment for the handling of hazardous drugs and cytotoxic waste.

RECOMMENDATIONS

4.1.7.1 The proper protective equipment for the task (as described in Table 4) must be worn throughout the medication circuit. Under Article 51 of the LSST, it is the employer's responsibility to provide the necessary personal protective equipment.

4.1.7.2 Workers must wash their hands with soap and water before and after wearing protective equipment. An alcohol-based product may also be used before putting on gloves, to eliminate bacterial contamination. As these products do not eliminate chemical contamination, they must not be used after removing gloves.

4.1.7.3 Workers must visually inspect the protective equipment (gloves, gowns, respirators, etc.) before putting it on, to ensure that it is not defective.

4.1.7.4 The protective equipment must be put on and taken off according to a sequence that avoids chemical contamination of the worker or microbial contamination of the products. As they may be contaminated, the outside of the gloves or gown must not be touched with bare hands. Table 5 and Figure 6 *Procedure for Removing Gloves* describe the sequence to be followed to avoid self-contamination.

4.1.7.5 The protective equipment must be disposed of in a cytotoxic waste receptacle.

4.1.7.6 Workers must not wear the protective equipment outside the designated areas (e.g. sterile preparation room, airlock, treatment room).

4.1.7.7 **Gloves**

The gloves used to handle hazardous drugs must be powder-free, made of latex, nitrile, polyurethane or neoprene and comply with ASTM standard D-6978-05 (standard for chemotherapy gloves). Due to the allergenic properties of latex, other materials are often used. Vinyl gloves are not recommended, as they are more permeable to hazardous drugs. Gloves may be sterile or non-sterile. Workers should change gloves (single or double gloves) every 30 minutes or less (in the event of contamination, spillage, breakage, end of the procedure or technique or contact with another patient). All gloves have some degree of permeability to hazardous drugs. This permeability increases over time - 30 minutes is an average time that ensures protection.

4.1.7.8 Gown

a) The gowns used when handling hazardous drugs should be disposable, made of lint-free, low-permeability fabric, have long sleeves with adjustable cuffs and do up in the back. Polypropylene gowns coated with polyethylene or vinyl are recommended. Workers should change gowns halfway through their shift or every 3.5 hours or in the event of contamination, spillage, breakage, end of the procedure or technique. The supplier must be able to certify that the gown protects against hazardous drugs.

b) Most organizations recommend that a gown never be reused and that it be disposed of following use. This is the ideal scenario. If, however, for practical, economic or environmental considerations, it is decided to reuse a gown, it should be hung up outside traffic areas, folded in such a way that the potentially contaminated portion is to the inside. Alternatively, the outside can be turned toward the wall, provided that the wall is washed regularly. The maximum use time in all instances is that mentioned in paragraph 4.1.7.8a . (+)

c) When taking it off and putting it on, care must be taken not to touch the outside of the gown.

4.1.7.9 Cap

Workers must wear a disposable cap, when required, in accordance with the rules to prevent microbial contamination. The cap is to be changed halfway through each shift or after a total of 3.5 hours or in the event of contamination.

4.1.7.10 Face Protection

Face protection must be worn whenever there is a risk of splashing (e.g. during certain drug administration procedures). The use of a full face shield is preferable to safety goggles because it protects the entire face.

- Face shield: disposable face protection is available, e.g. a fluid-resistant, surgical-type mask, to which a plexiglass shield covering the eyes and forehead is attached (Figure 3). Its use eliminates the *cleaning* operation, which represents an additional contamination risk. There are also disposable full-face shields. Single-use equipment should not be cleaned.
  If a non-disposable, rigid plastic face shield is used, it must be cleaned with detergent and water following use, making sure that gloves and a protective gown are worn.

FIGURE 3
Disposable, fluid-resistant mask with attached shield

Note: These types of surgical masks must only be used to protect the skin from splashing. They must not be used for respiratory protection. Moreover, they have not been tested for resistance to penetration by hazardous drugs.

- Protective eyewear: if protective eyewear is used (less desirable solution), goggles (Category 2B) are the most suitable type. As they are not disposable, maintenance requirements must be considered. Disposable eye shields may be used; the plastic lens is discarded without being cleaned, while the frame is kept (and must, therefore, be

cleaned) (Figure 4). For further information, see *CSA standard Z94.3.1-02: Protective Eyewear: A User's Guide*. As the shield only protects the eyes, a fluid-resistant surgical mask should also be worn.

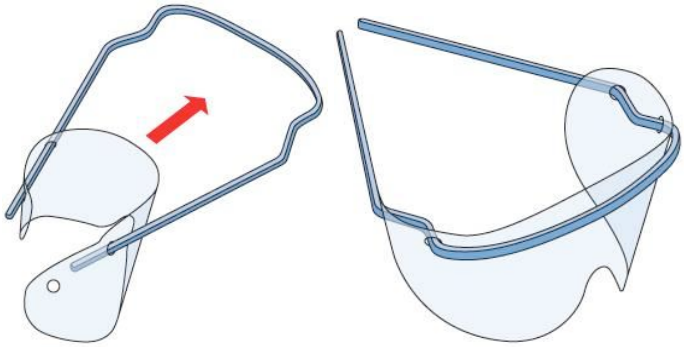


FIGURE 4
Disposable eye shield: the frame is reusable and must be cleaned. The lens is discarded without cleaning.

- Removing the protection: the face shield or protective eyewear must be removed by touching only the components that go around the head or ears; avoid touching the surface or sides of the shield or eyewear, as they may be contaminated.

4.1.7.11 Respiratory Protection Apparatus (RPA)

When required, a respiratory protection apparatus (respirator) must be used. The type of respirator depends on what is known regarding the risks and nature of the contaminant. In the case of hazardous drugs, there is no acceptable exposure value, the dose-effect relationship is not known and, in some circumstances, there is reason to be concerned about the vapours that may be generated by these drugs. We have therefore followed the principle of prudent practice in formulating our recommendations, i.e., it is better to err on the side of caution (while remaining realistic) when implementing the various recommendations.

- For the majority of tasks involving the handling of hazardous drugs, dust protection would be sufficient (full or half NIOSH-approved N-95 or N-100 filtering respirator/mask). In the presence of vapours, a respirator with chemical cartridges for organic vapours, combined with a dust filter, may be necessary (Figure 5). In the specific event of a spill, it may be appropriate (depending on the extent of the spill) to use a motorized or self-contained respirator.

FIGURE 5
Respirator with chemical cartridges and dust filter

- The choice of respirator must be made as part of the institution's Respiratory Protection Program, which should include a risk analysis, as well as the choice of respirators and the related training. A fit test is required to determine the appropriate size and model of the respirator. Thereafter, a seal-check test must be performed before each use. The Regulation regarding Occupational Health and Safety specifies that the Respiratory Protection Program must be established in accordance with CSA standard Z94.4-93 (Sect. 45) and describes the conditions of use (Sect. 46).

For additional information regarding respirators, see the *Guide pratique de protection*

respiratoire, 2e édition, (Practical Respiratory Protection Guide, 2nd edition), *IRSST, 2003*. [Available on line, in French only, at: http//www.irsst.qc.ca/fr/_publicationirsst_862.html]

4.1.7.12 Surgical Mask

Surgical masks do not provide respiratory protection against hazardous drugs. They may be used in the event of a respiratory tract infection to limit the risk of microbial contamination of the product (respiratory etiquette).

4.1.7.13 Shoe Covers

Disposable shoe covers must be worn when required. Shoe covers should be changed halfway through each shift or after a total of 3.5 hours or in the event of contamination, spillage or breakage. Aseptic practices include the wearing of shoe covers. In addition, in some cases where the floor may be contaminated (for example, in front of the hood in the sterile preparation room or in the event of a spill), the shoe covers prevent contamination of the shoes and, therefore, spreading of the contamination.

APES, p. 5-6, 5-7 ♦ ASHP, p. 1178-80 ♦ CSA, Z94.4-83 ♦ CSHP, Sections 8.2.4, 8.3 ♦ LSST, Art.. 49 and 51 ♦ NIOSH, p. 12, 13, 14, 17 ♦ ONS, p. 17-19 ♦ OPQ, Sections 8, 9.2.2 ♦ OSHA, Section Vb6

Table 4. Personal Protective Equipment Recommended According to Medication Circuit Tasks

Medication Circuit Steps	Gloves	Gown	RPA*	Face Protection	Cap***	Shoe Covers
Unpacking and cleaning	✓ (2 pairs)	✓	✓**			
Storage	✓ (1 pair)	✓				
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, vesical, intraperitoneal, *intrathecal*, liquid oral) or *extravasation*	✓ (1 pair)	✓		✓ (if risk of splashing)		
Solid oral administration (tablets)	✓ (1 pair)					
Topical administration (creams, ointments)	✓ (2 pairs)	✓		✓ (if risk of splashing)		
Aerosolized administration (ribavirin, pentamidine)	✓ (1 pair)	✓	✓	✓ (if risk of splashing)		
Patient care	✓ (1 pair)	✓		✓ (if risk of splashing)		
Handling of contaminated bedding on the wards	✓ (1 pair)	✓				
Waste management (collection and transport)	✓ (1 pair)	✓				
Spill or damaged or broken container	✓ (2 pairs)	✓	✓	✓		✓ (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)	✓				

* RPA = respiratory protection apparatus ** Not required if the unpacking area has an air exhaust mechanism (see 6.3.2). *** The wearing of a cap is related to sterile practices.

Table 5. Sequence of Operations for Putting on and Removing Personal Protective Equipment*

Putting On Equipment		Removing Equipment	
Preparation in the Pharmacy (2 pairs of gloves)			
In the airlock (clean area **)	1. Wash your hands 2. Shoe covers and cap: place the feet, one after the other, in the dirty area	In the sterile preparation room	1. Outer pair of gloves
In the airlock (dirty area)	3. Apply an alcohol-based gel to your hands 4. Inner pair of gloves (under the cuff of the gown) 5. Gown 6. Outer pair of gloves, over the cuff of the gown (this pair of gloves may also be put on in the sterile preparation room).	In the airlock (dirty area*)	2. Cap and gown*** 3. Inner pair of gloves 4. Shoe covers: remove by placing the feet, one after the other, in the clean area (avoid contact with the outer side)
		In the airlock (clean area*)	5. Wash your hands (clean area)
Administration of Drugs / Patient Care			
If wearing one pair of gloves	1. Wash your hands 2. Gown 3. Pair of gloves (over the cuff of the gown) 4. Face protection, if required	If wearing one pair of gloves	1. Pair of gloves 2. Gown 3. Face protection, if worn 4. Wash your hands
If wearing two pairs of gloves	1. Wash your hands 2. Pair of inner gloves (under the cuff of the gown) 3. Gown 4. Pair of outer gloves (over the cuff of the gown) 5. Face protection, if required	If wearing two pairs of gloves	1. Outer pair of gloves 2. Gown** 3. Inner pair of gloves 4. Face protection, if worn 5. Wash your hands

* Suggested procedure. It can be done another way if the sink is located midway between the clean and dirty areas.

** Clean area: should be free of chemical contamination (entry side area of the airlock). It contains the sink. Dirty area: may be chemically contaminated (sterile preparation room side). See 7.3.2.4

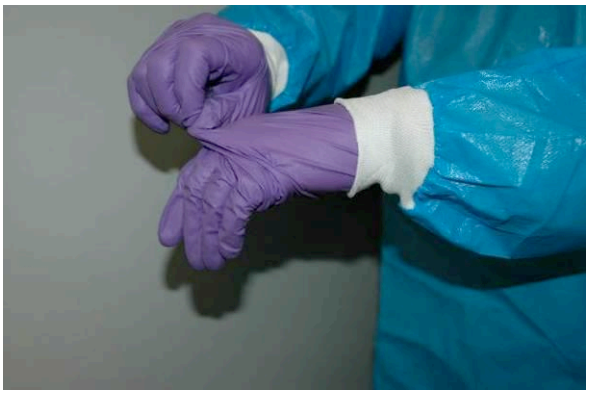
*** Special case: if the gown is kept on, but the gloves must be changed, it is recommended that the procedure shown in Figure 6 be followed.

1) To remove the outer pair of gloves (over the cuff of the gown).

Grasp the outer glove on hand 1 with hand 2 and pull off, touching only the outside of the glove, in order to avoid contaminating the inner pair.

Pull off outer glove 2 with hand 1, touching only the inside of the glove.

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



Pull on the gloves to free them from the cuffs of the gown. Touch only the outside of the gloves.

With gloved hand 1, remove the glove on hand 2, by grasping it on the outside.

With bare hand 2, insert the fingers under the cuff of the remaining glove and remove it.

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

5 RECEIVING AND TRANSPORT

5.1 Issues and Risks

Drugs from suppliers usually arrive at the institution's receiving dock. Depending on the institution, the unpacking and storage are done either upon receipt or in the pharmacy. In the first instance, the workers are not trained to handle hazardous drugs. It is thus preferable for these procedures to be performed in the pharmacy itself. In some institutions, delivery is made directly to the pharmacy.

5.1.1 Risks

Damaged parcels or containers represent a significant exposure risk. Liquid leaks can contaminate surfaces, while powders or aerosols can contaminate the air.

A container broken in a fall or in some other way may expose the workers present and contaminate the environment via the spread of liquids, powders or aerosols or through the diffusion of vapours.

Manufacturers and suppliers do not guarantee that the containers are free of contamination. The containers must thus be considered contaminated, unless effective packaging and segregation techniques have been used.

5.2 Exposed Workers

Receiving or transport clerks (e.g. stock-keeper, storeroom clerk)

Hygiene and Sanitation Department workers

Pharmacy Department workers (e.g. pharmacist, clerk, pharmacy technician)

5.3 Preventive Measures

5.3.1 Selection of Drugs

RATING: +++

Select hazardous drugs such that the risks are limited.

RECOMMENDATIONS

5.3.1.1 Institutions should ensure that purchases take into account the recommendations regarding hazardous drugs. If the purchases are made through group purchasing agreements, the Heads of the Pharmacy Departments involved should see to compliance with this recommendation.

5.3.1.2 Whenever possible, choose hazardous drugs whose distribution form limits exposure risks and facilitates preparation and administration. For example, if the choice is between an already diluted product and a powder which requires reconstitution, preference should be given to the product already in solution.

CSA, Z317.10-01, Section 4.1

5.3.2 Delivery Containers

RATING: ++

Ensure that the *hazardous drug delivery containers* from manufacturers and distributors are properly identified.

RECOMMENDATIONS

5.3.2.1 The Drug Purchasing Managers should ensure that:

- the manufacturers and distributors package hazardous drugs separately from other drugs. This recommendation is generally applied in Canada by the distributors of the *antineoplastic* drugs used in oncology. Until regulatory consensus has been reached in Canada regarding the necessary precautions for other hazardous drugs, we feel it is not very realistic to require distributors to provide separate packaging and labeling for other drugs not used in oncology.
- the manufacturers and distributors package antineoplastic drugs in a plastic bag placed inside a properly sealed cardboard box marked with the symbol C (cytotoxic). If this cardboard box is placed in a rigid delivery container, the container must also be marked with the symbol C (cytotoxic). The delivery container may contain other, non-hazardous drugs.
- the distributor cleans the delivery containers regularly.

For the sake of efficiency, these measures may be carried out at a regional or provincial level.

ASHP, p. 1175 ♦ NIOSH, p. 12

5.3.3 Handling Hazardous Drug Delivery Containers

RATING: +++

Ensure that hazardous drug delivery containers are unpacked in the Pharmacy Department.

RECOMMENDATIONS

5.3.3.1 The receiving dock workers should check the integrity of the delivery containers upon receipt; in the event of breakage or a damaged parcel likely to cause a spill, apply the Spill Protocol (Appendix 4).

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

5.3.3.3 The receiving dock or storeroom workers should not open the delivery containers. Only the Pharmacy Department workers are authorized to proceed with the unpacking and subsequent steps.

5.3.3.4 The delivery containers should be handled with care to avoid breakage of the hazardous drug containers and should not be left unattended in a corridor.

APES, p. 5-35 ♦ ASHP, p. 1175 ♦ OPQ, Section 6.2

5.3.4 Spill Kit

RATING: +++

Ensure the availability of a spill kit for the management of spills.

RECOMMENDATIONS

5.3.4.1 Damaged containers should be handled like spills. To limit exposure, a damaged container should never be returned to the manufacturer or distributor. The manufacturer or distributor must, however, be advised in writing and the event should be documented (e.g. supporting material, photos). See Section 12 regarding spills. (++)

5.3.4.2 A spill kit must be available in areas where hazardous drugs are received.

ASHP, p. 1175-76, 1183 ♦ CSHP, Section 8.15.3 ♦ NIOSH, p. 11, 12, 18 ♦ ONS, p. 31-32 ♦ OSHA, Sections Vc5, Vc6

6 UNPACKING AND STORAGE

6.1 Issues and Risks

Unpacking drugs can present an exposure risk if one or more containers inside the package are broken.

The scientific literature has shown that the outside of a number of drug vials coming directly from the manufacturer or distributor can be contaminated by detectable concentrations of *antineoplastic drugs*. In some cases, the vial packing cartons are also contaminated. Thus, even when there is no breakage during shipping, the handling of vials and bottles of hazardous drugs can be a source of exposure. Even if there is only a small amount on each vial, repeated exposure can be significant. Some authors have hypothesized that such contamination may partially explain the presence of antineoplastic drugs in the urine of workers (Favier, 2003).

In a collaborative pilot study conducted by the ASSTSAS, INSPQ and URPP (Unité de recherche en pratique pharmaceutique – CHU Sainte-Justine), the level of surface contamination was assessed on 40 vials of cyclophosphamide from two Canadian manufacturers. The results indicated the presence of contamination, but less than that reported in a number of other studies carried out in Europe and the United States. Several factors may contribute to the surface contamination of *hazardous drug* vials, including the methods of production, packaging and labeling, the storage and distribution processes, the occurrence of incidents (e.g. breakage during transport) and the use of protective film. The low number of vials and drugs assessed does not permit generalization of the conclusions of this study.

Cleaning the vials helps reduce contamination at the beginning of the medication circuit. However, the scientific literature does not specify which agent should be used to clean them. Pharmaceutical companies often use water to clean the vials. With the assistance of the INSPQ, the Committee compared the effectiveness of three cleaning methods, i.e., water alone, detergent and water, and premoistened towelettes (such as Wet-Ones). The use of a detergent and water solution or premoistened towelettes proved effective in removing 100% of the contamination. Water alone (0.5 mL) was not effective in every case. The tests were performed with cyclophosphamide.

These methods were not checked regarding drugs which are not soluble in water. To our knowledge, there is no synthesis tool allowing the quick determination of hazardous drug solubility for *decontamination* purposes. This is why gloves are always recommended when handing hazardous drug containers.

Breakage of a drug container falling off a counter or shelf may expose the workers present and contaminate the environment via the spread of liquids, powders or aerosols or through the diffusion of vapours.

6.2 Exposed Workers

- Pharmacy Department workers (e.g. pharmacist, clerk, pharmacy technician)
- Hygiene and Sanitation Department workers

6.3 Preventive Measures

6.3.1 Unpacking and Cleaning Area

RATING: ++

Set up a suitable unpacking and cleaning area limiting exposure risks for the handler.

RECOMMENDATIONS

NOTE: The pressure gradient values, air exchange values and other technical parameters, as well as the quality of the materials, will be specified in a document prepared by the *CHQ*. The general principles are outlined here.

6.3.1.1 The unpacking area should be a separate area, preferably a separate room.

6.3.1.2 The ventilation in the unpacking area should prevent the spread of contamination to adjacent rooms.

6.3.1.3 Local air exhaust should be provided in the unpacking and cleaning area (for example, a work table with an air exhaust grille on the wall).

6.3.1.4 To allow the safe handling of heavy *delivery containers*, the unpacking table should not have guards.

6.3.1.5 A sink should be installed in or near the unpacking area to allow the cleaning of drug containers.

6.3.1.6 There should be a receptacle for *cytotoxic waste* in the unpacking area, for the disposal of hazardous drug packaging and contaminated packing cartons.

ASHP, p. 6, 7 ♦ NIOSH, p. 12

6.3.2 Protective Equipment

RATING: ++

Wear proper protective equipment.

RECOMMENDATIONS

6.3.2.1 Exposed workers must wear a protective gown and two (2) pairs of gloves (see 4.1.7.7) when unpacking and cleaning hazardous drugs, from the opening of the delivery containers to the placing of the drugs in their storage space. If there is a risk of splashing, face protection must be worn (see 4.1.7.10).

Storage workers may wear a protective gown and one pair of gloves when handling hazardous drug containers.

6.3.2.2 The wearing of a *respirator* is not required for opening and unpacking drug parcels and containers if the unpacking area has a local air exhaust system. If it does not, workers should wear a *respirator* against dust (NIOSH-approved Class N-95 or N-100 full-face or half-face mask (see 4.1.7.11)).

ASHP, p. 1175, 1178, 1188 ♦ LSST, Art. 49 and 51 ♦ NIOSH, p. 12

6.3.3 Unpacking and Cleaning Procedure

RATING: ++

Establish an unpacking and cleaning procedure.

RECOMMENDATIONS

6.3.3.1 Workers assigned to unpacking should check the integrity of the delivery containers and their contents at the time of unpacking. In the event of breakage or leaking, they should treat the damaged contents as a spill (see 12.3.4.8).

6.3.3.2 Workers assigned to unpacking should cover the work table with a disposable, plastic-backed, absorbent pad on which to place the containers. This pad will also absorb any contamination.

6.3.3.3 The hazardous drug containers should be cleaned at the time of unpacking, before being placed in storage. To do so, the hazardous drugs must be removed from their individual packaging:

- if the drug is light-sensitive, provide a storage system limiting exposure to light.
- note that drugs removed from their packaging often cannot be returned to the manufacturer.
- do not remove the plastic film covering certain vials; this film is added by the manufacturer at the end of the production line, in order to limit contamination of the outside of the vials by hazardous drugs.

If containers are not cleaned at the time of unpacking, they should be stored separately from those which have been cleaned. Uncleaned containers should be cleaned before entering the preparation circuit.

6.3.3.4 All hazardous drug containers should be cleaned to reduce external contamination from the distributor or manufacturer. There is no ideal universal solvent. However, tests performed by the INSPQ at the Committee's request have confirmed that the use of a disposable cloth and a household detergent and water solution was effective in removing contamination on the outside of the vials. The use of premoistened towelettes (e.g. Wet-Ones) was also shown to be effective. (Note: The tests were done with cyclophosphamide. The cloth or towelette used was discarded after cleaning four vials.)

However, this procedure must not increase the risk of incidents/accidents due to damage to the hazardous drug label. The wearing of protective gloves is the first step to be taken prior to the *decontamination* of drugs. (+)

6.3.3.5 Plastic bins and safe carts (i.e., which limit the risk of falls/breakage) should be used for transporting hazardous drugs.

ASHP, p. 1175, 1183 ♦ NIOSH, p. 12 ♦ OPQ, Section 6.2.3

6.3.4 Waste

RATING: ++

Dispose of the delivery and hazardous drug containers in a safe manner.

RECOMMENDATIONS

6.3.4.1 Individual packaging for antineoplastic type hazardous drugs must be discarded with the cytotoxic waste.

6.3.4.2 Delivery container packaging which was not in direct contact with the vials (i.e., the carton, bubble wrap, filling, foam) may be discarded with the regular waste if they were not soiled (e.g. leakage, breakage of vials in the delivery container). These materials must not be used for other purposes.

6.3.5 Storage Area

RATING: +++

Establish a suitable storage area limiting the exposure risks for the handler.

RECOMMENDATIONS

NOTE The pressure gradient values, air exchange values and other technical parameters, as well as the quality of the materials, will be specified in a document prepared by the *CHQ*. The general principles are outlined here.

6.3.5.1 The storage area should be separate from the unpacking area, but may be adjacent to the data entry area. If it is in the same room as the data entry area or another area in which people work, ventilated cabinets must be used for storage.

6.3.5.2 The ventilation of the storage area should prevent the spread of contamination to the adjacent rooms.

6.3.5.3 The storage counters and shelves should have guards, to prevent the drug containers from falling and breaking. The containers may also be placed in bins to ensure better stability.

6.3.5.4 Hazardous drugs should be stored separately from other drugs (e.g. dedicated refrigerators and freezers or use of separate shelves). In addition, the storage spaces for antineoplastic drugs must be clearly identified with the "Cytotoxic" hazard symbol, while the storage spaces for the other drugs on the NIOSH list must be identified with a "Caution" label.

6.3.5.5 Bins and *storage containers* of the proper size must be used to avoid overflow or accidental breakage.

APES, p. 5-36 ♦ ASHP, p. 1175 ♦ CS, p. 66 ♦ NIOSH, p. 12 ♦ OPQ, Sections 6.1, 6.2 ♦ OSHA, Section Vc6

6.3.6 Spill Kit

RATING: ++

Ensure the availability of a kit to manage spills.

RECOMMENDATIONS

6.3.6.1 A spill kit must be available to manage spills in the oncology pharmacy. (See Appendix 4 for kit contents.)

6.3.6.2 Damaged containers should be treated like spills (see Section 12).

ASHP, p. 1175-76, 1183 ♦ CSHP, Section 8.15.3 ♦ NIOSH, p. 11, 12, 18 ♦ ONS, p. 31-32 ♦ OSHA, Section Vc6

7 PLANNING THE ONCOLOGY PHARMACY

7.1 Issues and Risks

Hazardous drug preparation presents a twofold challenge, i.e., limiting microbial contamination (to protect the patient) and limiting environmental contamination by hazardous drugs (to avoid worker exposure). This challenge is even greater when planning the *sterile* preparation room, particularly with respect to the direction of the pressure gradients, which protect both the product and the worker.

In 1995, the *Ordre des pharmaciens du Québec* published a standard (95.01) regarding the sterile preparation of drugs in the pharmacy. One of the recommendations was the presence of an *ISO 7* or *ISO 8* room for drug preparation, including a proper anteroom. This Quebec standard is very similar to the guidelines of the Canadian Society of Hospital Pharmacists. In 2004, the United States Pharmacopoeia published a standard concerning sterile preparations in the pharmacy (USP 797), specifying the procedures regarding the planning of facilities. In a summer of 2006 prepublication version of the update of this standard, USP added a section regarding the physical layout of pharmacies where hazardous drugs are prepared, which states that the sterile (ISO 7) preparation room should be under negative pressure. It also discusses the values with respect to gradient pressure and air exchange per hour, as well as other physical considerations.

In view of the growing body of knowledge and the still recent publication of the NIOSH recommendations, discussions are taking place throughout North America with respect to the definitive characteristics of the layout of the hazardous drug sterile preparation room and anteroom.

The Committee invited representatives from the *Corporation d'hébergement du Québec* (CHQ) to join us in our work. The CHQ has agreed to develop a set of standards for the planning of oncology pharmacies and preparation rooms following the publication of this guide. These standards will be posted on the CHQ site. Notwithstanding this future posting, our guide proposes general recommendations regarding the planning process. In view of the expertise of the CHQ and the standards related to the physical and mechanical aspects of the building, we will leave it up to them to specify the design parameters regarding (among other things) pressure gradient values, air exchange values and other technical parameters, as well as regarding the quality of materials.

The handling of hazardous drugs, particularly during preparation (i.e., reconstitution, dilution, bagging or syringe filling, etc.) can be a major source of workplace contamination. Failure to take measures to contain these sources (e.g. air recirculation hood) or their ineffectiveness (e.g. diffusion of contaminants outside the sterile preparation room) may contribute to worker exposure (pharmacy and housekeeping workers).

Some drugs release particles small enough to pass through the pores of HEPA filters; some are able to evaporate (e.g. cyclophosphamide, fluorouracil, etoposide, carmustine, cisplatin) (Turci, 2003, Kiffmeyer, 2002, Opiolka, 2000). Thus, *biological safety cabinets* which exhaust emissions to the outdoors (preventing their release into the room or building) are required.

7.2 Exposed Workers

- Pharmacy Department workers (e.g. pharmacist, clerk, pharmacy technician)
- Hygiene and Sanitation Department workers (e.g. oncology pharmacy cleaner)

7.3 Preventive Measures

7.3.1 Identification

RATING: +++

Clearly identify the entrances to the Pharmacy Department.

RECOMMENDATIONS

7.3.1.1 The oncology pharmacy premises (i.e., access door) must be identified with the "Cytotoxic" hazard symbol.

ASHP, p. 1175-76 ♦ OSHA, Section Vb1

7.3.2 Planning the Oncology Pharmacy

RATING: +++

Plan the oncology pharmacy for the preparation of hazardous drugs in accordance with the following recommendations.

RECOMMENDATIONS

NOTE The design parameters, such as the pressure gradient values, air exchange values and other technical parameters, as well as the quality of the materials, will be specified in a document prepared by the CHQ. The general principles are outlined here.

7.3.2.1 The oncology pharmacy should include a sterile preparation room and an ISO 7 airlock or an airlock in compliance with the recommendations of the *Ordre des pharmaciens du Québec*.
The pharmacy should also include an unpacking room/area (see 6.3.1), a storage room/area (see 6.3.5), a data entry room/area and a patient counselling room (see Figures 9 and 10).

7.3.2.2 There should be pressure gradients between the sterile preparation room, the airlock and the other rooms in the pharmacy, in order to avoid spreading contaminants from the sterile preparation area to the adjacent areas and bringing microbial and particulate contamination into the sterile preparation area. The pressure values are defined in the CHQ planning standard. With respect to the general principles, the most important variable for the efficacy of a sterile preparation room is whether it is airtight (to maintain the pressure gradients).

- The unpacking and storage areas should normally be under a slightly negative pressure; however, the airtightness of these areas cannot be ensured, contrary to what is required in the sterile preparation room and airlock.
- The sterile preparation room should be under negative pressure and the airlock under positive pressure.
- All of the air in the sterile preparation room, airlock and unpacking and storage areas should be exhausted to the outside of the building through a *HEPA filter*.
- The air in the pharmacy offices may be recirculated; however, as a precaution, this air should be recirculated to the pharmacy only.
- There should be monitoring and alarm systems with respect to the parameters of the ventilation and safety cabinets (monitoring of pressures, heat and humidity, etc.).

7.3.2.3 Workers must enter the sterile preparation room through the airlock. The drugs and preparation materials enter and leave the sterile preparation room through one or two pass-throughs, depending on the volume of activity. The use of two pass-throughs allows one to be used for the entry of materials and the other for their exit (in order to avoid cross-contamination).

7.3.2.4 Airlock

- A mechanism should prevent the opening of both doors of the airlock at the same time.
- The airlock should contain storage space (open shelves) for protective clothing (gowns, gloves, shoe covers, caps, masks), a small scrub sink with foot controls and soap and paper towel dispensers or an automatic hand dryer, an eye wash fountain, a chair (ideally, bolted to the wall to facilitate floor cleaning), a waste receptacle for the paper hand towels and another, for the disposable PPE, marked "*Cytotoxic waste*" + the letter "C"; some hooks for the gowns.
- The airlock should be divided into two separate areas, identified by a line on the floor or another form of demarcation:
    - a "chemically clean" area (airlock entry side), which should be free of chemical contamination. This area contains the sink and is where the workers put on the PPE.
    - a "chemically dirty" area (sterile preparation room side), where the PPE is removed.

7.3.2.5 Sterile Preparation Room

- The furniture in the sterile preparation room should be kept to a bare minimum, i.e., *sterile preparation cabinets*, space for a cart or a mobile work surface, *cytotoxic waste* receptacle.
- Inside the sterile preparation room, the preparation cabinets should be positioned to minimize the areas of turbulence, away from doors, drafts (i.e., heating and air conditioning) and high traffic areas. Figure 11 shows the proper distances when positioning preparation cabinets. The sterile preparation room should have a minimum surface area of $7m^2$ per preparation cabinet or comply with the CHQ set of standards.
- There should be a visual link (window) between the sterile preparation room and the pharmacy, in order to view the work in progress. A visual and voice communication system can also be provided to allow the pharmacist to validate the work without having to go in and out of the preparation room. This link can be established using a camera and an intercom (Figure 7). (++)

FIGURE 7
Camera system allowing remote validation by the pharmacist

- The layout should allow and facilitate the unimpeded cleaning of all surfaces (walls, floors, ceilings, doors, diffusers, windows). For example, rounding of the joints where walls, ceilings and floors meet, finishes resistant to *cleaning* products and alcohol, welded seam, no-wax vinyl flooring extending up the walls, elimination of all horizontal surfaces other than countertops.

7.3.2.6 **Pass-throughs**

The pass-throughs allow the transfer of drugs and equipment between the storage area, the data entry/validation area and the sterile preparation room (Figure 8).

- The compartment is large enough to accommodate the bins used to transfer the drugs and equipment.
- Both doors are glazed, close hermetically and cannot be opened at the same time.

FIGURE 8
Pass-through

7.3.2.7 Access to the sterile preparation room and the airlock should be strictly limited to trained, authorized workers. The equipment carts should go through a cleaning procedure before being allowed into the sterile preparation room. No carts should be removed from the sterile preparation room unless they are *decontaminated*. The carts should be cleaned periodically.

7.3.2.8 The layout should restrict worker traffic and reduce the possibility of workers crossing paths while working. Limit worker traffic, particularly near unpacking and storage areas (to avoid accidental breakage) and near preparation cabinets (to avoid interfering with their proper operation).

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

APES, p. 5-13 ♦ ASHP, p. 1176, 1181 ♦ CSHP, Sections 8.3.3, 8.4, 8.4.4 ♦ NIOSH, p. 12, 15 ♦ OPQ, Sections 7.1, 7.2 ♦ RSST, Art. 75-76

7.3.3 Policies and Procedures

RATING: +++

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

RECOMMENDATIONS

7.3.3.1 The institution must designate someone in charge of the validation/certification of the facilities and equipment used for the sterile preparations.

7.3.3.2 The pre-filters and HEPA filters must be replaced as soon as their effectiveness is noticeably reduced or if they are contaminated by a large spill. It is difficult to estimate their useful life. The filters should be changed by the certifier if a decrease in the air flow in the hood is observed at the time of certification. The certifier must ensure that the filtering material, gasket and filter box sealant are not leaking. The filters and prefilters must be disposed of with the cytotoxic waste.

7.3.3.3 The preparation cabinets must be certified prior to use and every 6 months thereafter, when ventilation work is performed or when the cabinet is moved. The equipment must be decontaminated before any certification or electromechanical maintenance.
The certification must be done by a qualified technician, in compliance with the field testing described in CSA standard Z316.3-95 or Appendix F of NSF standard 49.

7.3.3.4 Pharmacy workers should document the control parameters (i.e., temperature, humidity, pressure gradient, number of air changes per hour, etc.) of the facilities daily, using the fixed measuring instruments available.

7.3.3.5 Workers should keep sterile preparation room comings and goings to a minimum. To that end, validation by the pharmacist can be performed via a camera system with voice communication between the sterile preparation room and the data entry/validation room, thus avoiding repeated comings and goings by the pharmacist (see 7.3.2.5 and Figure 7).

APES, p. 5-15, 5-16 ♦ CSHP, Sections 8.4.2, 8.4.3 ♦ NIOSH, p. 15, 16 ♦ OPQ, Sections 7.1, 7.2, 9.6, 12.2 ♦ OSHA, Section Vb5

7.3.4 Sterile Preparation Cabinets

RATING: +++

Use sterile preparation cabinets consistent with the level of worker protection, as well as with the level of risk related to the nature and use of sterile preparations of hazardous drugs *(see **Table 6** for descriptions of the various types of cabinets)*.

RECOMMENDATIONS

7.3.4.1 Class II type B2 biological safety cabinets with protective glass (also called vertical laminar flow hoods) should be used. Class II B1 cabinets can be used in institutions where hazardous drugs are rarely prepared or as a back-up preparation cabinet. The B1 cabinets exhaust all of the air to the outdoors if the work is performed at the back of the cabinet, near the rear grille. However, this practice may be contraindicated from an ergonomic standpoint. Class III cabinets are now becoming available; these closed cabinets may limit (at least, theoretically) outside contamination of the sterile preparation room related to handling. Further investigation regarding the efficacy and ergonomics of these cabinets should be carried out before a general recommendation is made in this regard.

7.3.4.2 Generally speaking, *closed-circuit preparation systems* (PhaSeal®, Tevadaptor®) are not a substitute for Class II B2 or B1 preparation cabinets.

7.3.4.3 The biological safety cabinets should remain in operation 24 hours a day, 7 days a week, as recommended by the manufacturers. To conserve energy, the glass panel can

be lowered completely when the cabinets are not in use. To shut down the cabinets outside working hours to conserve energy, use a timer to make sure they are restarted 30 minutes before resuming work and stopped 30 minutes after finishing work; the ventilation in the sterile preparation room should always be adjusted accordingly. Clean the cabinet (i.e., floor, side walls, including the glass wall) after completing and before resuming work.

In the event of a stoppage (e.g. breakdown), *decontaminate* the cabinet and allow it to operate for at least 30 minutes before resuming preparation work.

7.3.4.4 A Class II A2 cabinet may be used in the sterile preparation room for non-hazardous drugs intended for oncology patients.

7.3.4.5 The cabinets may be positioned side by side, with a space of at least 0.3 metres between them (see Figure 11). Rolling carts may be used next to a cabinet to support the preparation activities. Smoke pattern tests may be performed at the time of certification to confirm that the layout does not interfere with the laminar flow inside the cabinet.

APES, p. 5-13, 5-17 ♦ ASHP, p. 1176-77, 1188 ♦ CSHP, Section 8.4 ♦ NIOSH, p. 13-16 ♦ ONS, p. 15 ♦ OPQ, Sections 7.1.9, 7.2 ♦ OSHA, Section Vb3 ♦ USP 797 ♦ proposed revision*

7.3.5 Non-sterile Preparation Cabinets

RATING: ++

Use non-sterile preparation cabinets consistent with the level of worker protection and the use of non-sterile preparations of hazardous drugs.

RECOMMENDATIONS

7.3.5.1 Class I biological safety cabinets exhausted to the outdoors may be used; when available, Class II B2 or B1 cabinets may also be used.

7.3.5.2 At the very least, a work area dedicated to the handling of non-sterile preparations of hazardous drugs should be used.

ASHP, p. 1176 ♦ CSHP, Section 8.7 ♦ NIOSH, p. 15

* http://www.usp.org/USPNF/pf/generalChapter797.html [Accessed on October 10, 2007]

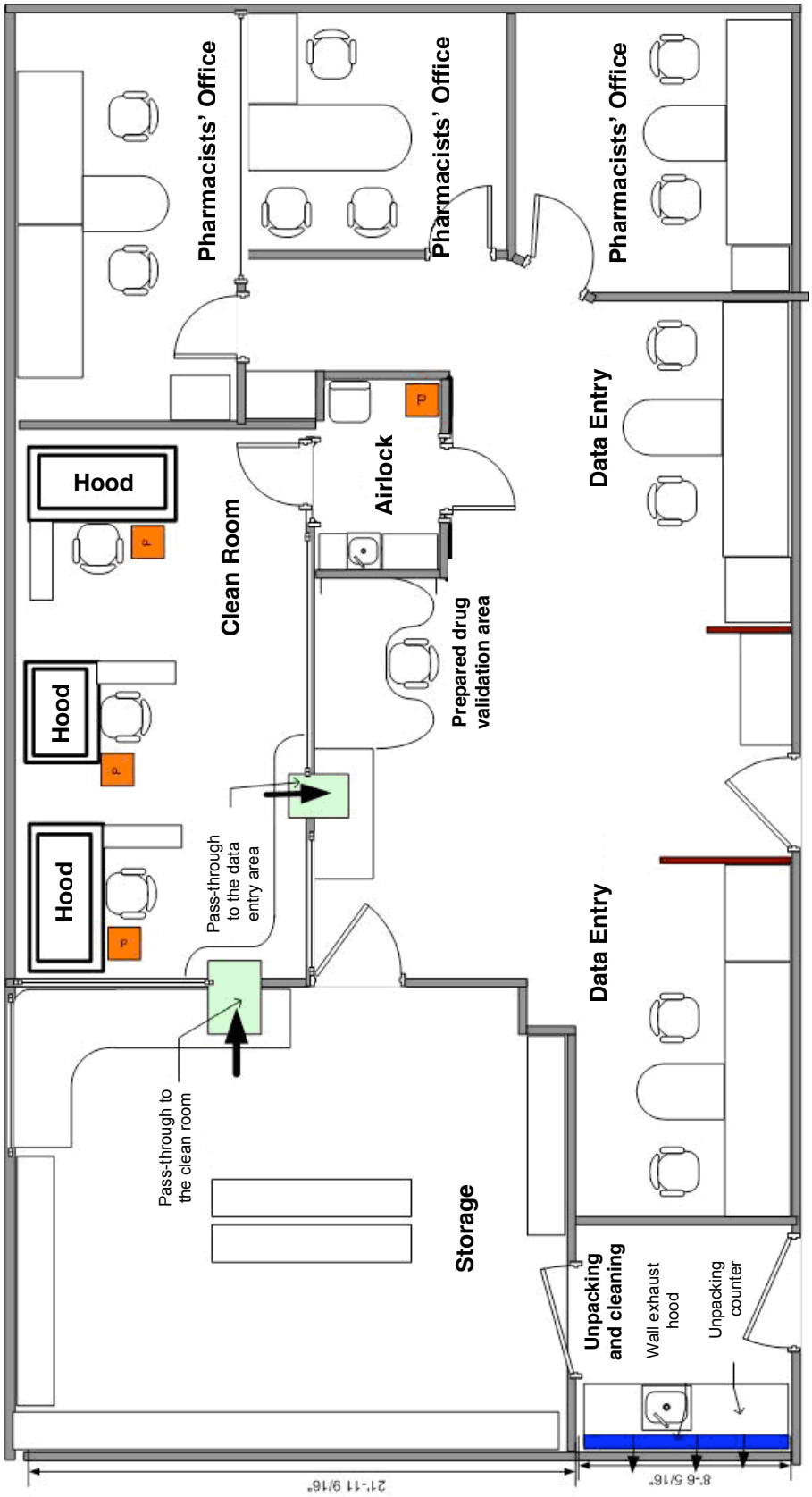


FIGURE 9
Sample layout of an oncology pharmacy with a high preparation volume

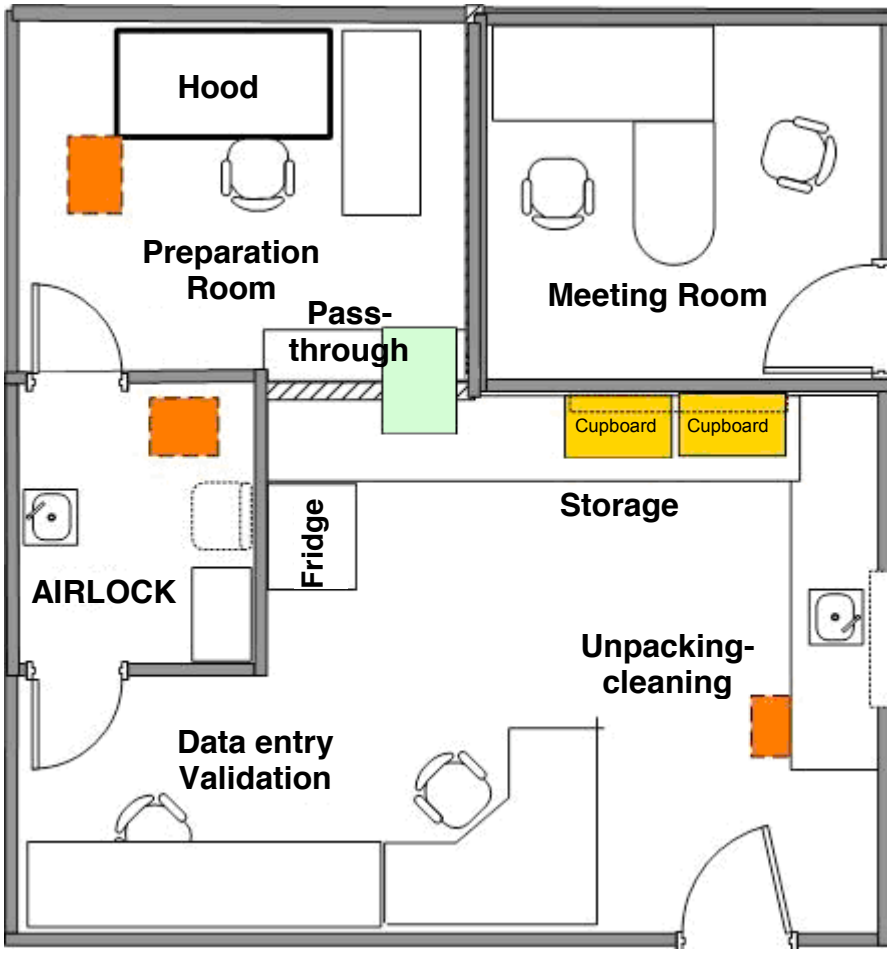


FIGURE 10
Sample layout of a small oncology pharmacy

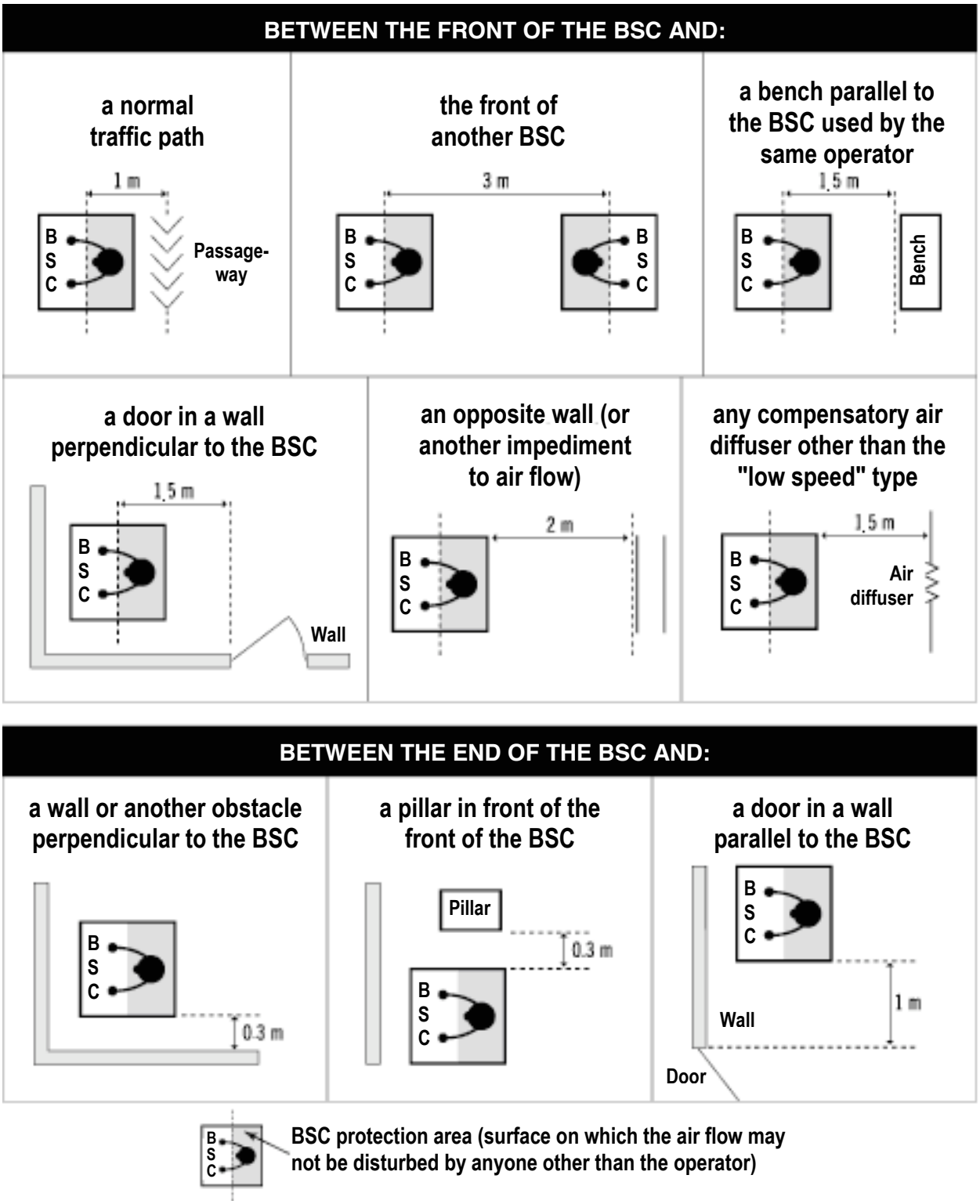


FIGURE 11
Minimum distances recommended for the positioning of biological safety cabinets
(Source: INRS, 2003)

Table 6. Features of the Various Types of Biological Safety Cabinets*

Classes and Types	Front Air Speed	Protection			Air Flow	Comments
		Workers	Product	Environ.		
Class I	75 ft/min** (0.4 m/s)	Yes***	No	Yes	The air is aspirated into the cabinet through the front opening and exhausted to the outdoors or into the room through a HEPA filter.	Usable for volatile or non-volatile toxic products (for volatile products, exhaust to the outdoors required)
Class II		Yes***	Yes	Yes	Front opening with descending air curtain that protects the product and inflow of air that protects the worker. Exhaust through a HEPA filter protects the environment.	
• A1	75 ft/min				70% air recirculated in the cabinet; 30% recirculated in the room or to the outdoors via a "thimble" connection. Ducts and plenums maintained under positive pressure.	Formerly, Type A. Not suitable for volatile toxic products.
• A2	100 ft/min (0.5 m/s)				70% air recirculated in the cabinet; 30% exhausted through a HEPA filter, either in the room or to the outdoors via a thimble connection. Ducts and plenums maintained under negative pressure.	Formerly, Type B3. Suitable for very small amounts of volatile toxic products, if exhausted to the outdoors.
• B1	100 ft/min (0.5 m/s)				30% air recirculated in the cabinet and 70% exhausted to the outdoors; hard-ducted through a HEPA filter. Ducts and plenums maintained under negative pressure.	Suitable for small amounts of volatile toxic products. May be used in institutions where preparations are infrequent.
• B2	100 ft/min (0.5 m/s)				100% of the air exhausted to the outdoors; hard-ducted through a HEPA filter. Ducts and plenums maintained under negative pressure.	Suitable for volatile toxic products. Recommended for hazardous drugs.
Class III		Yes	Yes	Yes	Cabinets totally enclosed and gas-tight. The work is performed through gloves attached to the cabinet panel. The air enters and exits through HEPA filters. Passage of equipment in and out through airlocks. Maintained under negative pressure.	Suitable for volatile toxic products. May be used for hazardous drugs.

* Table compiled using data from a number of sources, including the ASHRAE Handbook, ASHP, CDC, Health Canada, NIOSH.

** ft/min = feet per minute ; m/s = metres per second

*** Use of a cabinet does not prevent contamination of gloves and gowns due to improper handling techniques (leaks, splashes, etc.).

8 DRUG PREPARATION

8.1 Issues and Risks

The handling of *hazardous drugs*, particularly during preparation (i.e., reconstitution, dilution, bagging or syringe filling, etc.), can be a major source of workplace contamination. Failure to take measures to contain these sources or their ineffectiveness (e.g. air recirculation hood, diffusion of contaminants outside the sterile preparation room) may contribute to worker exposure.

The first source of contamination may be direct contact with contaminated vials from the supplier.

The second source of contamination may be direct contact with the *hazardous drug* during handling (e.g. counting out solid oral forms, contact when diluting the drug, shaking the container or transferring the solution to another container, such as a syringe, bag or other administration device). Hazardous drug tablets and capsules may be covered with a fine dust, which can be inhaled, absorbed through the skin or ingested or which can cause surface contamination. Liquid preparations can generate aerosols or be spilled. Finally, the crushing of solid oral forms can generate dust particles, which can be inhaled or which can contaminate the environment.

The third source of contamination may be direct contact with the bins or trays used to transport hazardous drug preparations (e.g. syringes, bags containing hazardous drugs) during their packaging or transport to the care units or outpatient clinics.

The fourth source may be contact with contaminated equipment (e.g. the plungers of drug-filled syringes) [Favier, 2005], the pumps (during their cleaning or repair) or the HEPA (filters during their replacement).

The fifth source may be exposure to hazardous drug particles or gases in the immediate vicinity of the preparation cabinet, due to leaks through the front opening (Kiffmeyer, 2002). Rapid arm movements or obstruction of the front grille of the cabinet may cause such exposure.

The recent guides published by NIOSH and ASHP recommend using *closed-circuit systems* for preparation (as well as for administration). The PhaSeal® system has been studied and found to be effective (Wick, 2003; Spivey, 2003; Connor, 2002; Harrison, 2006, Au, 2006). Other systems are also available (e.g.. Tevadaptor®). A recent study appears to indicate that only the PhaSeal® system is capable of containing vapours (Au, 2006). Figure 12 illustrates the PhaSeal® system.

While the use of closed-circuit systems has been shown to reduce contamination during preparation and administration, it does not entirely eliminate the risk of contamination, due to the limitations of this type of system and because other sources may be contributing to the contamination (vials whose exterior is contaminated, products which cannot be prepared using these systems, etc.).

The primary obstacle to the use of these systems is their high, recurring cost. Their cost-effectiveness ratio is not yet known, particularly in the context of care in Quebec. We are encouraging evaluative research to determine the role of this technology in Quebec practice. It should be stressed that, even if closed-circuit systems are used, the preparations should be compounded in *biological safety cabinets*.

The product never comes into contact with the air: a gas-tight membrane inflates or deflates depending on the pressure in the vial.

The system also allows closed-circuit administration, due to its gas-tight membranes.

FIGURE 12
PhaSeal® closed-circuit system

8.2 Exposed Workers

- Pharmacy Department workers (e.g. pharmacist, clerk, pharmacy technician)
- Hygiene and Sanitation Department workers
- Maintenance workers (e.g. biomedical engineering workers or preparation cabinet certifier)

8.3 Preventive Measures

8.3.1 Personal Protective Equipment

RATING: +++

Wear proper protective equipment.

RECOMMENDATIONS

8.3.1.1 Workers (pharmacists or pharmacy technicians) must wear a cap, shoe covers, a protective gown and two (2) pairs of gloves (see 4.1.7.7) to make *sterile* preparations of hazardous drugs in preparation cabinets. A surgical mask may be used by workers with a respiratory tract infection to reduce the risk of microbial contamination or if this is the practice in the institution.

8.3.1.2 Upon completion of sterile manipulations, the outer pair of gloves must be removed inside the preparation cabinet. Only the inner pair of gloves, next to the skin, must be worn for the labeling, bagging and transfer from the *sterile preparation cabinet*.

8.3.1.3 Outside the sterile preparation room, workers must wear 1 pair of gloves (see 4.1.7.7) if they come into contact with hazardous drug containers (e.g. workers removing syringes from their plastic bag for an additional verification, additional labeling). However, gloves are not required to handle the plastic bag.

APES, p. 5-6, 5-7 ♦ ASHP, p. 1178-1180, 1188 ♦ CSHP, Sections 8.2.4, 8.3.2 ♦ NIOSH, p. 12, 13 ♦ OPQ, Section 8

8.3.2 Organization of the Work

RATING: +++

Organize the work to limit microbial and environmental contamination.

RECOMMENDATIONS

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

8.3.2.2 Workers must proceed in a way that does not adversely affect the cabinet's effectiveness in protecting against hazardous drug exposure:

- never permanently obstruct the air return grilles (e.g. by covering them with material), to avoid disturbing the protective curtain of air;
- follow the manufacturer's instructions regarding the minimum work distances inside the cabinet; if there are no instructions from the manufacturer, work on a surface more than 10 cm away from the front and rear grilles and 15 cm from the side walls of the preparation cabinet;
- lower the protective window according to the manufacturer's recommendations. To protect the face and eyes of the worker, the bottom of the window should not be any higher than the worker's shoulders. The usual height of the opening is 20 cm.

8.3.2.3 Workers should proceed in a way that minimizes the risks of contamination:

- group the material required for a batch or preparation, to avoid having to frequently enter and leave the preparation cabinet (as arm movements, particularly lateral movements, break the protective curtain of air);
- limit the quantity of supplies and hazardous drugs in the cabinet, to avoid adversely affecting the laminar flow and to facilitate regular cleaning of the work surface;

- avoid sudden movements of the arms or hands in the front access area; slide the hands perpendicular to the front panel to enter and leave the cabinet. The cabinet air flow should be allowed to stabilize before resuming work;
- place the sterile products in the centre and the non-sterile products (e.g. waste receptacle) along the sides of the cabinet.

APES, p. 5-7, 5-8 ♦ ASHP, p. 1180-1181, 1188 ♦ CS, 72 ♦ CSHP, Section 8.6.2 ♦ ONS, pages 19, 21 ♦ OPQ, Sections 9, 9.1, 9.4 ♦ OSHA, Section Vc

8.3.3 Removal of Packaging

RATING: ++

Remove the packaging, when applicable, and clean all of the drug containers before taking them into the preparation cabinet.

RECOMMENDATIONS

8.3.3.1 If the vials were not *cleaned* at the time of unpacking (see 6.3.3), this should be done now, to remove any potential chemical contamination due to drug residues. The packaging should be removed and the hazardous drugs placed on a tray. The vials may be cleaned with a disposable cloth and a solution of detergent and water, from top to bottom. Premoistened towelettes (e.g. Wet-Ones) may also be used.

8.3.3.2 For sterility, the vials should be disinfected with ethyl alcohol or isopropyl alcohol 70% before being taken into the preparation cabinet. To do so, pour alcohol on a piece of sterile gauze using a wash bottle and wipe the containers, from top to bottom. The hazardous drug containers may also be sprinkled with alcohol using a wash bottle and then wiped with a pad or a piece of sterile gauze, from top to bottom. The first method is preferable, however, as it may help prevent projection of any drugs which may be on the containers. (+)

8.3.3.3 Supplies (e.g. syringes, solutions, sterile gauze, etc.) should be unpacked above the grille or in the first 10 cm of the hood. Unpack the critical parts of the material (e.g. needles, syringe tips, syringes without protective tips, sterile gauze) in the sterile area. If the supplies are unpacked before transfer into the preparation cabinet (e.g. infusion systems, solutions, etc.), disinfect them with alcohol (see 8.3.3.2).

ASHP, p. 1183, 1188 ♦ OPQ, Sections 9.4.2, 9.4.3

8.3.4 Handling Techniques

RATING: +++

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

RECOMMENDATIONS

8.3.4.1 Workers who prepare hazardous drugs should use dilution and sampling techniques that minimize exposure risks and pressure differences:

- unless using a closed-circuit system, a transfer device with a 0.22 micron hydrophobic filter should be used at all times; one device should be used for each drug container;
- a closed-circuit system (e.g. PhaSeal®, Tevadaptor®) may be used. While the scientific literature has demonstrated the effectiveness of this equipment in reducing contamination versus other preparation techniques, the cost-effectiveness ratio is still poorly-understood. We suggest their use in the following instances at the very least:
  - major, documented environmental contamination problem, despite compliance with the recommendations of this guide;

- ❖ inadequate infrastructure and upgrading not possible;
- ❖ very low preparation volume and lack of standard infrastructure;
- ❖ note that the use of a closed-circuit system must not allow preparations to be compounded outside a biological safety cabinet.

- ➢ the chimney technique using a needle and 0.22 micron hydrophobic filter may be used; the use of an ordinary needle or filtering needle is not recommended;
- ➢ the negative-pressure technique should no longer be used.

8.3.4.2 Workers should use administration containers that minimize exposure risks and pressure differences:

- ➢ use syringes and other devices with Luer-Lock fittings and proper connectors;
- ➢ do not fill syringes more than ¾ full, with the exception of vesical syringes for BCG with a closed-circuit system;
- ➢ avoid overfilling infusion bags by adding too much solution (i.e., a maximum acceptable volume can be established locally, in order to facilitate safe administration by the caregiving staff); when transferring to an infusion bag, be careful not to perforate the side of the injection port or the side of the bag;
- ➢ do not attach a needle to the syringes prior to transport to the drug administration site; instead, use standard Luer-Lock plugs on the syringes;
- ➢ use appropriate red seals on the bags containing hazardous drug additives, to avoid other additions/handling and exposure risks;
- ➢ correct the amount withdrawn prior to removing the needle from the vial;
- ➢ as much as possible, avoid using glass containers during preparation and administration, to reduce the risk of breakage;
- ➢ lightly tap the ampoules and vials to bring down the liquid or powder from the cap or neck; wrap the neck of the disinfected ampoule with sterile gauze before opening it; slowly pour the diluent into the ampoule or vial, down the side, and shake gently;
- ➢ upon completing a manipulation, do not put the protective tip back on the needle; dispose of the needle immediately.

8.3.4.3 Workers should perform certain preparation steps in the cabinet, to limit any additional handling of hazardous drugs by other health professionals:

- ➢ prime and remove the air from the tubing in a biological safety cabinet in the pharmacy before adding the hazardous drug to the infusion solution; otherwise, this may be performed at the patient's bedside;
- ➢ prepare hazardous drugs for inhalation (e.g. pentamidine, ribarivin) in a biological safety cabinet. The pharmacy should prepare the drugs in the administration device to avoid having to handle them during administration.

8.3.4.4 The Head of the Pharmacy Department must periodically check that the workers are trained in the preparation techniques; the implementation of a microbiological validation protocol is recommended to monitor microbial contamination.

APES, p. 5-8, 5-9 ♦ ASHP, p. 1178, 1180-82, 1188 ♦ CSHP, Sections 8.6.3, 8.6.4, 8.9.3 ♦ LSST, Art. 51
NIOSH, p. 12-14 + Alert p. 2 ♦ OPQ, Sections 9.4, 12.3 ♦ OSHA, Section Vc

8.3.5 Labeling

RATING: ++

Properly label the hazardous drugs such that microbial and environmental contamination is avoided.

RECOMMENDATIONS

8.3.5.1 Hazardous drug labels must inform those using these preparations of the nature of the drugs and the precautions to be taken. At the very least, the label must display the "Cytotoxic" hazard symbol or the word "Cytotoxic" (see 4.1.5.3) (*antineoplastic* drugs)

or "Caution" (other hazardous drugs). In the case of antineoplastic drugs, the irritant and *vesicant* potential must also be indicated. Moreover, the hazardous drug containers (e.g. syringes, bags) must display a standard additional label (i.e., cytotoxic or caution label).

8.3.5.2 While it is preferable to label the bag containing the medication following the preparation and cleaning of the container in the preparation cabinet, this practice has the potential for error in institutions with high volumes. Some authors prefer affixing the labels prior to preparation to avoid container/content errors, provided that the labels used allow cleaning of the container once the preparation is complete.

ASHP, p. 1175, 1181 ♦ LSST, Art. 51 ♦ OPQ, Section 11

8.3.6 Cleaning, Labeling and Final Packaging

RATING: ++

Clean the containers of the hazardous drugs to be administered.

RECOMMENDATIONS

8.3.6.1 The pharmaceutical assistant should clean the outside surface of the hazardous drug containers (e.g. syringes, infusion bags, tubing) in the preparation cabinet:

- remove the outer pair of gloves used during the cleaning procedure in the preparation cabinet, using a technique which avoids contaminating the freshly cleaned area (see the technique suggested in Figures 13 and 14);
- wipe the containers with a gauze pad soaked in sterile water or a detergent/water mixture (see 6.3.3.4). (+)

8.3.6.2 The labeling of hazardous drugs following sterile manipulations should be done outside the hood, wearing only the inner pair of gloves:

- place each hazardous drug container (e.g. syringe, bag), as well as the administration supplies (e.g. tubing), in a clear, leakproof, plastic bag (e.g. Ziploc® type) to facilitate identification by the nurse without having to remove the container from the bag. Photosensitive drugs should be double-bagged (one transparent bag and one opaque bag); the use of a single transparent bag may be acceptable if the transport containers are opaque and the drug is administered quickly;
- place the plastic bags containing the hazardous drugs on a work tray for transfer out of the sterile preparation room through the pass-through. The transport containers must not be taken into the sterile preparation room as they are used in the care units and outpatient clinics. A work tray can be used to organize the work flow inside the pharmacy (e.g. from the storage area to the sterile preparation room, from the preparation room to the data entry room, etc.);
- following final verification in the data entry room, the plastic bags containing the hazardous drugs should be placed in a rigid *transport container* (ideally opaque), properly identified with the "Cytotoxic" hazard symbol or the word "Caution", as applicable.

ASHP, p. 1179-80, 1188 ♦ CSHP, Sections 8.6.4.7, 8.9 ♦ NIOSH, p. 13 ♦ OPQ, Section 6.3.1 ♦ OSHA, Section Vc1f

8.3.7 Waste

RATING: ++

Choose a proper size and type of waste receptacle.

RECOMMENDATIONS

8.3.7.1 The waste from hazardous drugs (antineoplastic agents and other hazardous drugs) generated in the preparation cabinet must be disposed of in the waste receptacle placed inside the cabinet. This receptacle must be identified with the "Cytotoxic" hazard

symbol. Needles must be disposed of without being recapped. Avoid throwing drug containers to avoid splashing. The waste receptacle should be closed and sealed; it should be cleaned before removal from the preparation cabinet. For practical purposes, a single type of waste receptacle should be used in the cabinet for all hazardous drugs prepared in the oncology pharmacy. If a waste receptacle identified with the "Cytotoxic" hazard symbol is not used for the other hazardous drugs prepared outside the oncology pharmacy, the receptacle used should, at the very least, be marked "Pharmaceutical Waste – Incineration".

8.3.7.2 Hazardous drug waste generated outside the preparation cabinet must be disposed of in the *cytotoxic waste* receptacle placed outside the cabinet, in the preparation room. Avoid using the hands to compact waste in the receptacle.

APES, p. 5-8 ♦ ASHP, p. 1181 ♦ CSHP, Section 5.2 ♦ OPQ, Section 7.3.4

8.3.8 Cleaning of Biological Safety Cabinets and Other Equipment

RATING: ++

Introduce policies and procedures regarding the cleaning of the inside of the preparation cabinets.

RECOMMENDATIONS

8.3.8.1 Workers cleaning the inside of biological safety cabinets must wear a cap, shoe covers, a protective gown, two (2) pairs of gloves (see 4.1.7.7), a *respirator* and appropriate face protection (see. 4.1.7.10). (+++)

Due to the possible presence of vapours generated by the drugs inside the hood, a RPA should be used to protect the worker from dust and organic vapours (mask or half-mask with chemical cartridges or a canister to absorb organic vapours and dust) (see 4.1.7.11). (+)

8.3.8.2 The inside of the cabinet (i.e., floor, side walls, including the glass wall) should be cleaned daily, at the beginning and end of each shift. This cleaning should be performed by trained workers from the Pharmacy Department. The cabinet should be washed with a solution of detergent and water and subsequently rinsed with water (to reduce contamination from hazardous drugs). The *decontamination* should be followed by a *disinfection*, using the products and procedures recommended by the institution's Infection Control Department, in order to limit microbial contamination.
In addition to this daily cleaning, the work surface should be cleaned on a regular basis (i.e., every 60 minutes) or in the event of contamination or a spill.

8.3.8.3 Full weekly cleaning with detergent and water should be performed (including cleaning of the plenum under the work surface), followed by rinsing (see 8.3.8.2). The cleaning may be followed by decontamination with a solution of sodium hypochlorite 2.4% with a contact time of at least 10 minutes, after ensuring that, according to the cabinet manufacturer, it may be used on the type of surface concerned, as well. This procedure can also be used in the event of significant residual contamination. Rinsing should be performed following the cleaning.

Note. The scientific literature does not yet specify which type of cleaning and decontamination agent should be used (see Section 13.1).

8.3.8.4 The equipment (e.g. filling pumps, carts) used in the cabinet should be cleaned weekly.

APES, p. 5-14 ♦ ASHP, p. 1183, 1188-89 ♦ CSHP, Sections 8.4.1.3., 8.4.1.5 ♦ NIOSH, p. 16-17 ♦ ONS, p. 23 ♦ OPQ, Section 7.3 ♦ OSHA, Section Vb4

8.3.9 Preparing Non-sterile Hazardous Drugs

RATING: +++

Ensure optimal protection when preparing non-sterile oral hazardous drugs.

RECOMMENDATIONS

8.3.9.1 Exposed workers must wear a protective gown and one (1) pair of gloves (see 4.1.7.7) for the non-sterile preparation of drugs (e.g. counting drugs). They should wear two (2) pairs of gloves for topical or liquid preparations. The wearing of face protection is recommended if there is a risk of splashing (see 4.1.7.10).

8.3.9.2 A work area should be clearly defined and equipment reserved for the hazardous drug preparations (e.g. properly identified, dedicated counter):

- a Class 1 biological safety cabinet exhausted to the outdoors should be used when handling powders. If a separate hood is not available. the sterile hood may be used, provided that it is decontaminated following its use with non-sterile drugs;
- the equipment used (e.g. scale, pill counter, spatula, etc.) for the non-sterile preparations of hazardous drugs should not be used to prepare other drugs;
- the tray used to count solid oral forms of hazardous drugs should be cleaned following each use with a gauze pad soaked in detergent and water, and subsequently rinsed with water.

8.3.9.3 The preparation of creams, ointments and oral solutions, as well as the crushing of hazardous drug tablets, should be performed in a protected environment (Class 1 or Class II hood, glove box). Workers should be double-gloved and wear the same type of gown as for work in the hood. If topical preparations are prepared using injectable drugs (e.g. mechlorethamine cream), the measures used for an injectable drug should be adopted.

8.3.9.4 The bagging machines (or other automated equipment) should not be used to package unit doses of oral forms of hazardous drugs. Manual bagging devices (e.g. blister cards) should be used, as these prevent cross-contamination with other, non-hazardous drugs.

8.3.9.5 The Pharmacy Department should attempt to limit additional handling of hazardous drugs by other health professionals. Unit doses of hazardous drugs in liquid oral form should be prepared in the pharmacy and placed in an oral syringe, ready for administration. However, a Luer-Lock syringe must not be used for oral syringe preparations, to avoid accidental parenteral administration.

8.3.9.6 Any material used to prepare oral forms of hazardous drugs must be disposed of in the receptacles for cytotoxic waste. For practical purposes, a single type of waste receptacle should be used for all hazardous drugs prepared in or outside the oncology pharmacy. If a waste receptacle identified with the "Cytotoxic" hazard symbol is not used for the other hazardous drugs prepared outside the oncology pharmacy, the receptacle used should, at the very least, be marked "Pharmaceutical Waste – Incineration".

APES, p. 5-9, 5-10 ♦ ASHP, p. 1182-83, 1189 ♦ CSHP, Sections 8.7.1, 8.7.3 ♦ ONS, p. 22 ♦ OSHA, Section Vc1g

❶

Soak a gauze pad with cleaning solution (water or alcohol)

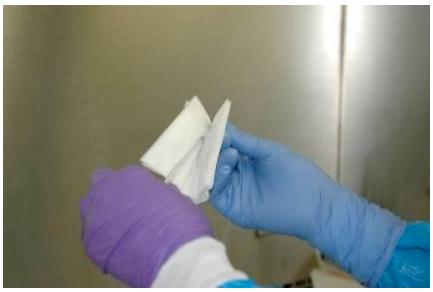
❷

Clean the tubing. Avoid touching the cleaned section with the gloves.

❸

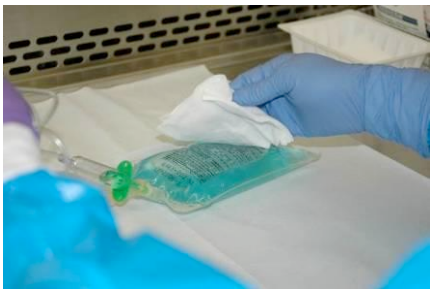
Remove one outer glove.

❹



Holding the cleaned section with the inner glove, clean the rest of the tubing.

❺



Clean one side of the infusion bag.

❻

Holding the cleaned side of the bag with the inner glove, clean the rest of the tubing.

❼

Clean the other side of the bag.

❽

Finish by cleaning the injection site.

❾

Remove the second outer glove, holding the infusion bag in the left hand.

FIGURE 13
Cleaning technique for drug bags prepared in the preparation cabinet

❶

Wearing both pairs of gloves, clean one part of the syringe. Avoid touching the cleaned section with the gloves.

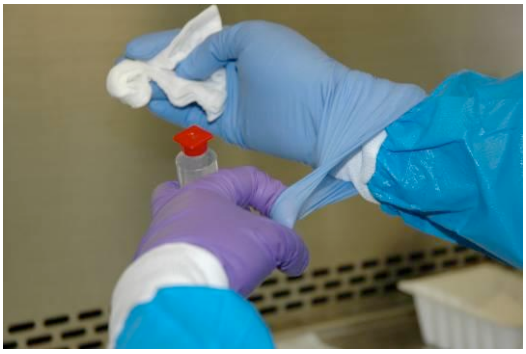
❷

Remove one outer glove.

❸

Holding the cleaned section with the inner glove, clean the rest of the syringe.

❹



Remove the second outer glove and dispose of the glove and the gauze pad.

FIGURE 14
Technique for cleaning a syringe in the preparation cabinet

The cleaning procedures described in Figures 13 and 14 were developed by Lucie Couture, Maryse Quirion et Marlène Thibeault, pharmacists and teachers at the Centre de formation professionnelle Fierbourg.

9 TRANSPORT AND STORAGE FOLLOWING PREPARATION

9.1 Issues and Risks

The breaking of a drug container through a fall or otherwise may expose the workers present and contaminate the environment through the spread of liquids, powders or aerosols or the diffusion of vapours.

Direct contact with a container (as the outside of the container may be contaminated if it was not properly *cleaned* following preparation).

9.2 Exposed Workers

- Pharmacy Department workers (e.g. pharmacist, clerk, pharmacy technician)
- Outpatient clinic and care unit workers (e.g. nurse, patient service associate, inhalation therapist)
- Transport workers (clerk, etc.)

9.3 Preventive Measures

9.3.1 Drug Transport

RATING: +++

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

RECOMMENDATIONS

9.3.1.1 Hazardous drugs should be placed in a closed, leakproof plastic bag (e.g. Ziploc® type).

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

9.3.1.3 The *transport container* must be identified with the "Cytotoxic" hazard symbol.

9.3.1.4 Mechanical transport systems which put stress on the contents should not be used to transport *antineoplastic* type hazardous drugs.

- Lifts may be used if the drugs are in rigid containers.
- Pneumatic conveyors should not be used unless:
  - the cartridges are sturdy and leakproof;
  - there is an effective system for *decontaminating* the tubes in the event a cartridge breaks or leaks;
  - there are dedicated cartridges for the transport of hazardous drugs which are identified as such, using a colour code or the "Cytotoxic" hazard symbol. The cartridges should allow the contents to be viewed prior to opening. The cartridges should be cleaned regularly to remove chemical contamination;
  - the drug tolerates the transport (the stability of certain drugs requires very gentle transport).

While it is generally agreed that antineoplastic hazardous drugs should not be transported via mechanical means (e.g. pneumatic conveyors), there is no consensus regarding the other, non-oncology, hazardous drugs. The members of the Committee feel that the proper labeling of these drugs with the word "Caution" on an appropriate container (e.g. leakproof Ziploc® type bag) is sufficient for sending these drugs with non-hazardous drugs via mechanical means.

9.3.1.5 The institution must avoid using these transport containers for other purposes. In addition, the containers should be cleaned once a week or as soon as visible traces of drugs (e.g. leaks) are observed.

APES, p. 5-35, 5-36 ♦ ASHP, p. 1175-76, 1188 ♦ CSA, Z317.10-01, Section 9.1 ♦ CSHP, Section 8.9 ♦ NIOSH, p. 12 ♦ OSHA, Section Vc6

9.3.2 Storage

RATING: ++

Store the hazardous drugs in the care units and outpatient clinics to avoid contaminating the premises.

RECOMMENDATIONS

9.3.2.1 Hazardous drugs should be stored on shelves in the storage units and refrigerators reserved for that purpose and identified with the "Cytotoxic" hazard symbol or "Caution", depending on the type of drug (i.e., antineoplastic or other).

9.3.2.2 Patient-specific storage systems should be cleaned periodically (e.g. every three months). *Disposable protective film* (i.e., patient-specific disposable container in a cassette drawer for daily unit dose distribution) may also be used, if applicable.

ASHP, p. 1175 ♦ NIOSH, p. 12

10 ADMINISTRATION OF DRUGS

10.1 Issues and Risks

The handling and administration of hazardous drugs may pose a risk of exposure to the drugs in a number of situations, i.e.:

- leaks or creation of aerosols when priming and removing air from tubing if this procedure was not performed in the preparation cabinet;
- leaks or creation of aerosols when syringes and tubing are connected to and disconnected from the injection ports;
- contamination through contact with drug bags, tubing or syringes which were improperly cleaned during the preparation stage. The drug preparation containers or transport trays may also be contaminated;
- inhalation of aerosols during administration via aerosolization (ribavirin, pentamidine) (see box below);
- contamination of surfaces (gloves, etc.) and inhalation of particles during the handling or crushing of pills;
- contamination through contact during the application of creams or ointments;
- accidents: needlesticks, broken containers, spills;
- direct contact via spraying or splashing or inhalation of vapours during special procedures, such as *hyperthermic intraoperative intraperitoneal chemotherapy (HIIC)* (operating room or intensive care unit). This procedure involves heating the drug solution (42-45° C), which increases toxicity and the risk of vaporization (Gonzalez-Bayon, 2006).

Studies performed in the administration areas have demonstrated the presence of contamination on various work surfaces. One study, conducted in six American and Canadian hospitals, revealed the presence of contamination on the arms of patient chairs, the floor around the chair or bed and on the administration preparation table or counter (Connor, 1999). Variable amounts of contamination were found around the infusion tubing (Kromhout, 2000).

10.2 Exposed Workers

- Care unit, outpatient clinic and home care workers: nurses, patient service associates, physicians, inhalation therapists
- Pharmacists
- Hygiene and Sanitation Department workers
- Other patients and families of patients

Administration via Aerosolization

Some drugs can be administered via aerosolization. Two of these are on the list of hazardous drugs:

- Pentamidine: used for the prevention and treatment of Pneumocystis carinii pneumonia, particularly in AIDS patients.
  - While no malformations or reproductive effects have been demonstrated in humans, these effects remain of concern, as pentamidine's mode of action is similar to that of certain drugs which increase the incidence of spontaneous abortions and malformations. Therefore, pregnant women should not be exposed to this drug.
  - To date, no chronic effects have been demonstrated in exposed workers. Animal studies have not revealed carcinogenicity. However, workers may experience immediate discomfort following exposure – throat irritation, burning eyes, bronchial spasms, headaches. These effects are short-lived and reversible, but, in some cases, were unpleasant enough to force the affected individual to leave work.
  - Finally, one of the risks to consider is the transmission of tuberculosis, due to the presence of patients who are potential carriers (often of resistant strains). The incidence of tuberculosis is higher in workers in contact with patients treated with pentamidine than in the general hospital staff population (ISSA, 2002).
- Ribavirin: used for the treatment of infections due to the respiratory syncytial virus, particularly in immunocompromised children or adults. The use of ribavarin is gradually decreasing.
  - Animal studies have shown a *mutagenic*, carcinogenic, teratogenic and embryotoxic potential. To date, such effects have not been reported in humans. Due to the uncertainty in this regard, pregnant women should not be exposed to ribavirin.
  - Moreover, as is the case with pentamidine, immediate effects have been reported –irritation of the eyes and upper respiratory tract, headaches. These effects are short-lived and reversible.

In the absence of control measures (local exhaust ventilation), some of the drug will spread into the air. Worker exposure is generally due to short peaks of exposure (for example, when the nebulizer is removed from the patient's mouth or if it disconnects during drug administration).

There is no exposure threshold for pentamidine in the air. For ribavirin, a provisional limit of 2.7 $\mu g/m^3$ has been established in the United States (California). As long as this limit is complied with, there should be no reproductive risks (ISSA, 2002). When the preventive measures are correctly applied, the concentrations measured range from 2 to 60 $\mu g/m^3$ (see Section 10.3.13 for the preventive measures).

10.3 Preventive Measures

10.3.1 Planning and Use of Treatment and Patient Rooms

RATING: +

Plan and use the treatment rooms such that exposure risks are limited.

RECOMMENDATIONS

10.3.1.1 Hazardous drugs should be administered in a controlled access environment:

- access to the treatment and patient rooms should be restricted to trained workers, patients and, if necessary, a limited number of family members (who should be informed of the risks involved). Pregnant visitors and children should not be allowed in the treatment room. If their presence is unavoidable, they should be informed of the risks involved and avoid coming into contact with potential sources of contamination (e.g. excreta, vomitus);
- treatment rooms should be under neutral or negative pressure. There are no universal recommendations regarding patient rooms (e.g. positive pressure rooms are preferred for patients with bone marrow transplants to reduce the risk of microbial contamination, rather than to ensure a reduction in the risk of environmental contamination);
- materials and surfaces should be chosen for ease of cleaning (non-porous surfaces, no carpets or cloth surfaces, reduction in the number of horizontal surfaces (which can collect dust), etc.); (+++)
- workers and family members must not eat, drink, chew gum, apply makeup or store food in the drug administration areas. The patients may eat and drink, if necessary (e.g. long treatments); (++)
- workers must have access to a washroom reserved exclusively for their use; similarly, the washrooms used by oncology patients should be reserved for their exclusive use;
- rest areas for workers and family members should be located outside the hazardous drug administration areas.

ASHP, p. 1176 ♦ CS, p. 66

10.3.2 Personal Protective Equipment

RATING: +++

Wear the proper *personal protective equipment* for administering hazardous drugs..

RECOMMENDATIONS

10.3.2.1 **Gloves**

Nurses must wear one (1) pair of gloves (see 4.1.7.7) to handle and administer hazardous drugs, from the time they remove the drugs from their Ziploc® type plastic bag.

- Nurses may wear two (2) pairs of gloves when handling hazardous drugs, as recommended by a number of organizations. The members of the Committee feel it is acceptable to wear only one pair of gloves, as these are changed between patients (i.e., frequently). Wearing only one pair of gloves requires greater care to avoid cross-contamination (e.g. telephone, doors, chair arms, etc.) and defective gloves. The gloves must cover the gown cuff.
- Nurses must wear two (2) pairs of gloves during procedures involving an increased exposure risk (e.g. topical application of a *hazardous drug*). The first pair of gloves must be worn under the gown cuff, while the second pair must be worn over the cuff
- Nurses must remove their gloves as soon as the procedure requiring the wearing of gloves is completed. They must wash their hands with soap and water every time they remove their gloves.

10.3.2.2 **Gown**

Nurses who administer hazardous drugs must wear one (1) protective gown (see 4.1.7.8) to handle and administer the drugs from the time they are removed from their Ziploc® type plastic bag.

- In the outpatient clinic, one gown may be worn for a series of patients treated over a period of no more than 3.5 hours, after which the gown is to be disposed of in a *cytotoxic waste* receptacle and replaced with a new one.
- On the care units, a different gown should be worn for each patient treated.
- If a gown is to be worn again (e.g. following a break), it should be hung outside traffic areas, after being folded such that the potentially contaminated area faces inward. Alternatively, the outside portion may be placed against the wall (provided that the wall is washed on a regular basis). (See 4.1.7.8.) (+)
- Avoid touching the outside of the gown without protection. The outside of the gown must not come into contact with the clothes worn by the workers or patients.

10.3.2.3 **Face Protection**

Nurses who administer the drugs must wear face protection (see 4.1.7.10) when there is a risk of splashing (e.g. bladder irrigation). Limit the risk of facial exposure by working at a level lower than the face.

10.3.2.4 Workers who administer hazardous drugs must wash their hands, put on the gown and then put on the gloves (making sure that the gloves cover the gown cuff), after which they should put on the face protection, if necessary. Where two pairs of gloves are required, put on the first pair before putting on the gown. For additional information regarding the sequence for putting on and removing PPE, see Table 5, Section 4.

10.3.2.5 The protective equipment must be removed before leaving the treatment area.

APES, p. 5-27, 5-31 ♦ ASHP, p. 1188-90 ♦ CSHP, Sections 8.2.4, 8.8.2 ♦ NIOSH, p. 14 ♦ ONS, p. 17-19 ♦ OSHA, Section Vc2

10.3.3 Preparation, Priming and Removing Air from the Tubing

RATING: +++

Determine the appropriate preparation areas, as well as the techniques for priming and removing air from the tubing for hazardous drugs.

RECOMMENDATIONS

10.3.3.1 Hazardous drugs must be prepared in the pharmacy only. The bags containing the drugs must not be overfilled or put under pressure due to an excess volume of fluid. Overfilling makes the techniques described below difficult to apply and increases the risk of leaking.

10.3.3.2 The techniques used for priming and removal of air should minimize the exposure risks. Air should never be removed from the tubing with a solution containing the drug.

The tubes should be primed and the air removed in the pharmacy, prior to adding the hazardous drug to the infusion solution (1st choice).

10.3.3.3 If the priming and air removal cannot be done in the pharmacy, the workers who administer the drugs may do so using one of two techniques:

Technique 1. Priming the drug bag, followed by removing air from the tubing using the retrograde technique:

- to prime, the workers administering the drugs (nurses) may proceed to a dedicated room, in order to limit contamination (only workers wearing protective clothing are to be admitted to the dedicated room). In the event that there is no dedicated room, this may be done at the patient's bedside.
- the priming is done:
  - by working at chest level, to limit splashing near the face;
  - by inverting the hazardous drug bag, in order to collect the air at the top of the bag (Figure 15);

FIGURE 15
Collecting the air at the top of the bag

  - by inserting the tip of the tubing into the drug bag (Figure 16).

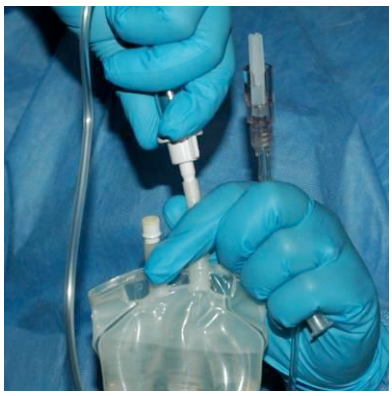


FIGURE 16
Priming the drug bag

- removing air from the tubing can be done at the patient's bedside, using the retrograde technique:
  - lower the hazardous drug bag to allow a sufficient amount of the compatible primary solution to reach the drug bag. Next, hang the bag of hazardous drug solution and proceed with the administration (Figure 17);

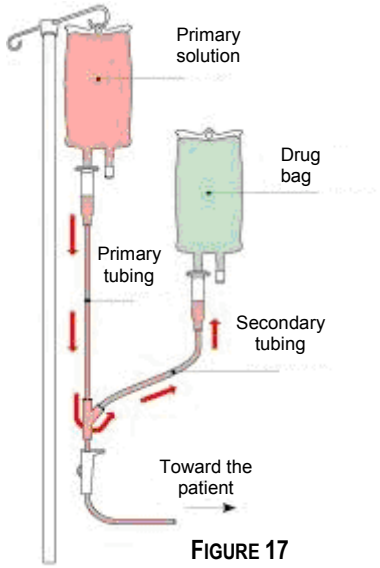


FIGURE 17
Air removal using the "retrograde" technique

Technique 2. Removing air from the tubing with a compatible solution, followed by priming:

- remove air from the tubing with a compatible solution. This technique may be used when the tubing does not allow retrograde filling or if the tubing is directly attached to the intravenous device (Figure 18)

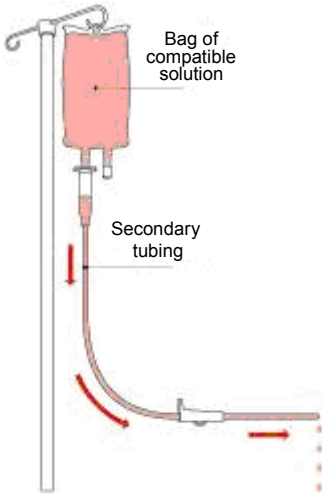


Figure 18
Removing air from the tubing before priming

- prime the drug bag with the tubing filled with compatible solution, following the instructions described for the priming step of technique 1.

ASHP, p. 1188 ♦ CS, p. 68 ♦ CSHP, Section 8.8.4 ♦ NIOSH, p. 14 ♦ ONS, p. 20, 21, 24 ♦ OSHA, Section Vc2

10.3.4 General Administration Measures

RATING: +++

Introduce general measures to reduce exposure risks related to the administration of hazardous drugs.

RECOMMENDATIONS

10.3.4.1 The caregiving staff should check the integrity of hazardous drug containers throughout the administration process.

10.3.4.2 The workers administering the drugs should use handling and administration techniques that minimize exposure risks:

- use syringes and other devices with a Luer-Lock tip with a proper connector;
- place a disposable, absorbent, plastic-backed pad for the containers, on the work table or under the patient's arm when applicable, and particularly during drug administration via the peripheral route (e.g. recommendation not applicable during central administration through an implantable chamber). This pad will also absorb any contamination;
- wrap the tubing connection site with a piece of gauze when removing the infusion tubing, to contain any potential leaks (Figure 19);

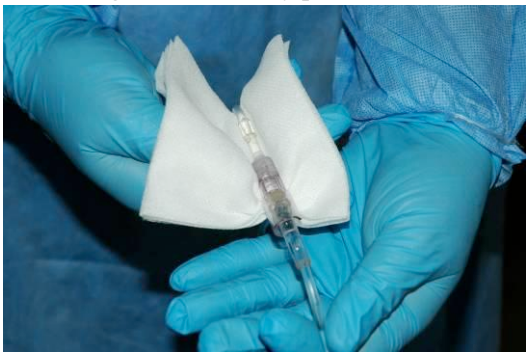


FIGURE 19
Wrap the tubing connection site with a piece of gauze when removing the infusion tubing

- in addition to the sanitary maintenance described, clean the arm of the chair when contamination is observed;
- as often as possible, use a needleless administration system, to reduce the risk of needlesticks with needles that have been in contact with hazardous drugs;
- a *closed-circuit administration system* (e.g. Phaseal®, Tevadaptor®, etc.) may be used, by connecting it to the devices used in the Pharmacy Department.

ASHP, p. 1189 ♦ CS, p. 68 ♦ CSHP, Section 8.8 ♦ NIOSH, p. 14 ♦ ONS, p. 24-26 ♦ OSHA, Section Vc2

10.3.5 Extravasation

RATING: +++

Establish a management protocol regarding *extravasation* of hazardous drugs.

RECOMMENDATIONS

10.3.5.1 Workers must wear a protective gown and one (1) pair of gloves (see 4.1.7.7) when managing an extravasation of hazardous drugs.

10.3.5.2 Face protection (see 4.1.7.10) must be worn when there is a risk of splashing; limit the risk of facial exposure by working at a level lower than the face.

10.3.5.3 A disposable, absorbent, plastic-backed pad for the containers should be placed on the work table or under the patient's arm when managing an extravasation of hazardous drugs. This pad will also absorb any contamination.

10.3.6 Intravenous Administration – direct injection (push)

RATING: +++

Use an administration technique that limits exposure risks.

RECOMMENDATIONS

NOTE The recommendations applicable to the General Administration Measures Section (i.e., Section 10.3.4) should be complied with.

10.3.6.1 When applicable, workers administering the drugs should place a disposable, absorbent, plastic-backed pad on the work table or under the patient's arm for the preparation containers (i.e., bag, syringe), when applicable, and particularly during administration via the peripheral route; this pad will also absorb any contamination. Avoiding pushing on the plunger, remove the protective cap from the syringe over the absorbent pad.

10.3.6.2 Insert the needleless device or the needle without removing the air.

10.3.6.3 Workers administering the drugs should use handling and administration techniques that minimize exposure risks:

- wrap the injection site with a *sterile* 10 x 10 cm gauze pad and inject the drug;
- withdraw a syringe from the primary tubing by wrapping the injection site with a sterile 10 x 10 cm gauze pad and gently withdrawing the tip; next, discard everything in a cytotoxic waste receptacle;
- if a needle is used, never remove it from the syringe; discard the syringe and the needle in a *cytotoxic waste* sharps container.

ASHP, p. 1189 ♦ CS, p. 68 ♦ CSHP, Section 8.8 ♦ NIOSH, p. 14 ♦ ONS, p. 24 ♦ OSHA, Section Vc2

10.3.7 Intravenous Administration (infusion)

RATING: +++

Use an administration technique that limits exposure risks.

RECOMMENDATIONS

NOTE The recommendations applicable to the General Administration Measures Section (i.e., Section 10.3.4), as well as the suggestions regarding the priming and air removal techniques (i.e., Section 10.3.3), should be complied with.

10.3.7.1 Workers administering the drugs should use handling and administration techniques that minimize exposure risks:

- once drug administration is complete, rinse the primary tubing with the primary solution;
- never remove the tubing, needle or tip from the hazardous drug bag; discard everything in a cytotoxic waste receptacle. If a needle is used, discard it in a cytotoxic waste sharps container;
- use separate tubing for each bag of hazardous drug;
- it is preferable to leave the secondary tubing attached to a hazardous drug bag and to discard the primary tubing and all of the secondary tubing when the treatment has been completed;
- if this is not possible, rinse the secondary tubing connection site before disconnecting it from the primary tubing:
  - using the retrograde technique, fill the secondary tubing containing the hazardous drug with the fluid from the primary tubing, in order to dilute the residual amount of hazardous drug (Figure 20); or

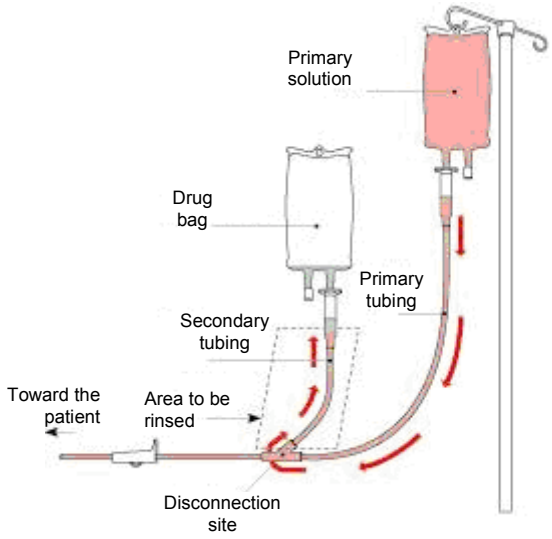


FIGURE 20
Rinsing the tubing using the retrograde technique

- ❖ if a one-way valve prevents the use of this technique, dilute the hazardous drug by using a syringe to inject 10 mL of compatible solution into the injection plug closest to the primary tubing (Figure 21). Do not withdraw the syringe and discard everything with the primary tubing.

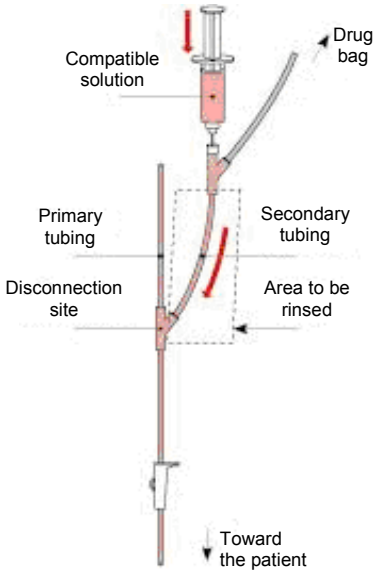


FIGURE 21
Rinsing the tubing with a syringe

APES, p. 5-28 ♦ ASHP, p. 1189 ♦ CS, p. 68 ♦ CSHP, Section 8.8 ♦ NIOSH, p. 14 ♦ ONS, p. 24 ♦ OSHA, Section Vc2

10.3.8 Subcutaneous or Intramuscular Administration

RATING: +++

Use an administration technique that limits exposure risks.

RECOMMENDATIONS

NOTE The recommendations applicable to the General Administration Measures Section (i.e., Section 10.3.4) should be complied with.

10.3.8.1 Workers administering the drugs should place a disposable, absorbent, plastic-backed pad on the work table for the containers; this pad will also absorb any contamination. Avoiding pushing on the plunger, remove the protective cap from the syringe over the absorbent pad.

10.3.8.2 Insert the needle without removing the air.

10.3.8.3 Workers administering the drugs should use handling and administration techniques that minimize exposure risks:

- ➢ a Z technique may be used for intramuscular administration of the drug (unless there is insufficient muscle mass – e.g. children), to reduce the risk of leaking. To use this technique, stretch the skin at the injection site at least 2 cm laterally, insert the needle at a 90° angle into the area where the skin is stretched and inject the drug at a rate of 1 mL every 10 seconds, in order to allow the muscle fibres to dilate and absorb the solution. Wait 10 seconds after completing the injection to allow the drug to diffuse into the muscle. Finally, quickly withdraw the needle and allow the skin to move back

into place;

- 0.2 mL of air may be injected at the end of the injection to reduce the possibility of a drug leak at the injection site (except in some cases, e.g. children);
- the needle must never be detached; discard the syringe and needle in a rigid cytotoxic waste container.

APES, p. 5-29 ♦ ASHP, p. 1189 ♦ Bélanger, 1985 ♦ CSHP, Section 8.8 ♦ ONS, p. 25

10.3.9 Oral Administration

RATING: ++

Use an administration technique that limits exposure risks.

RECOMMENDATIONS

NOTE The recommendations applicable to the General Administration Measures Section (i.e., Section 10.3.4) should be complied with.

10.3.9.1 Nursing staff must wear one (1) pair of gloves (see 4.1.7.7) (a gown is not necessary) when handling and administering solid form hazardous drugs - regardless of whether or not they are *antineoplastic* - from the time they remove the drugs from the plastic bag. For liquid formulations, both a gown and gloves must be worn.

10.3.9.2 Solid oral preparations (tablets) of hazardous drugs should not be crushed or cut outside the pharmacy. The pharmacy should provide these drugs in an oral syringe, in ready to administer, liquid oral form. (Do not use a Luer-lock syringe for oral preparations to avoid accidental parenteral administration.)

When the crushing of tablets cannot be planned in the pharmacy, the nursing staff should use a technique that limits the risk of contamination risk (e.g. use a disposable device to crush the tablets for each patient; the device is used to crush each dose of a hazardous drug; the device is kept safely in a plastic bag and disposed of with the hazardous drugs when the patient is discharged). In view of the risk related to transferring the crushed drug (e.g. into applesauce), the nurse must wear a N-95 type of *respirator*.

APES, p. 5-29 ♦ ASHP, p. 1189-90 ♦ ONS, p. 25

10.3.10 Topical Administration

RATING: +++

Use an administration technique that limits exposure risks.

RECOMMENDATIONS

NOTE The recommendations applicable to the General Administration Measures Section (i.e., Section 10.3.4) should be complied with.

10.3.10.1 The caregiving staff must wear two (2) pairs of gloves (see 4.1.7.7) and a gown when handling and administering topical hazardous drugs (creams, ointments, etc.).

10.3.10.2 Workers should place a disposable, absorbent, plastic-backed pad under the limb to which the hazardous drug is being applied.

10.3.10.3 Between applications, the hazardous drug container (i.e., tube, jar) should be placed in a clear, leakproof, plastic bag (e.g. Ziploc® type) identified with the "Cytotoxic" hazard symbol.

ONS, p. 25

10.3.11 Vesical Administration

RATING: ++

Use an administration technique that limits exposure risks.

RECOMMENDATIONS

NOTE The recommendations applicable to the General Administration Measures Section (i.e., Section 10.3.4) should be complied with.

10.3.11.1 Workers administering hazardous drugs via the vesical route must wear a protective gown and one pair of gloves (see 4.1.7.7), as well as face protection (see 4.1.7.10) if there is a risk of splashing during the procedure.

10.3.11.2 Workers should place a disposable, absorbent, plastic-backed pad under the patient's catheter for the containers; this pad will also absorb any contamination.

10.3.11.3 Workers administering the drugs should use handling and administration techniques that minimize exposure risks:

- over the absorbent pad, remove the protective cap from a syringe (avoiding pushing on the plunger) and insert the tip over the vesical catheter. If there is no Luer-Lock type connector between the syringe and the catheter, wrap the syringe/catheter connection with a sterile gauze pad to absorb any droplets, as well as any potential leaks;
- when a safe administration device (e.g. BCG) is supplied by the manufacturer, follow the manufacturer's instructions. Even when using a safe administration device, wear protective clothing and use an absorbent, plastic-backed pad;
- if a syringe is used to administer the drug, make sure some air (e.g. approximately 10 mL) is left in the syringe to empty the catheter of any hazardous drug and limit the risk of splashing during removal. A stopcock may also be used at the end of the administration tubing to inject air (e.g. approximately 10 mL) into the catheter upon completion of drug administration;
- use vesical syringes with a proper protective cap; contrary to the general rule (i.e., syringe filled ¾ full), a vesical syringe may be filled up to 50 mL, in view of the doses used and in order to limit the repeated handling of double syringes;
- upon completion of administration, gently withdraw the catheter without removing the syringe or the tubing attached to it. Place all of the items on the plastic-backed absorbent pad and fold the sides of the pad toward the middle. Place the pad and its contents in a Ziploc® type bag and discard it in a *cytotoxic waste* receptacle.

APES, p. 5-29, 5-31 ♦ ONS, p. 26

10.3.12 Intraperitoneal Administration

RATING: ++

Use an administration technique that limits exposure risks.

RECOMMENDATIONS

NOTE The recommendations applicable to the General Administration Measures Section (i.e., Section 10.3.4) should be complied with.

10.3.12.1 Workers administering hazardous drugs via the intraperitoneal route must wear a protective gown and one (1) pair of gloves (see 4.1.7.7), as well as face protection if there is a risk of splashing. (see 4.1.7.10).

10.3.12.2 The needle or needleless device should be inserted without removing air from the syringe.

10.3.12.3 Handling and administration techniques that minimize exposure risks should be used:

- if the administration is done through an intraperitoneal port, use tubing with a Luer-Lock tip; attach the needle to the port as securely as possible;
- if the administration is done through an external catheter, use an adaptor that will allow a locking connection (e.g. Luer-Lock); discard everything in a cytotoxic waste receptacle;
- after completing the administration, attach the drainage bag to the connection and lower it to collect the residual solution (which is considered cytotoxic waste).

10.3.12.4 *Hyperthermic Intraoperative Intraperitoneal Chemotherapy* (HIIC) Technique in the Operating Room:

- the closed-abdomen surgical technique reduces the risk of direct contact with and inhalation of drug vapours or aerosols when compared to other techniques (open-abdomen, etc.);
- only the workers strictly necessary should remain in the operating room during the procedure; a notice should be posted on the operating room door indicating that an operation using antineoplastic drugs is in progress;
- workers must wear an appropriate gown and gloves, face protection and a N100 type respirator during the procedure with the drug. Workers must wear two pairs of gloves (when possible). The gloves must be changed every 30 minutes during the drug handling and exposure phase. The surgeon's outer gloves must extend to the elbows;
- a disposable surgical drape and disposable sheets should be used;
- an extractor fan should be used throughout the procedure to reduce the risk of exposure to vapours and aerosols;
- biological fluids, as well as the drug following its use in the abdomen, are considered cytotoxic waste and handled according to the procedures applicable to such waste (see 12.3.1). As the fluid volumes can be fairly substantial, a solidifying product may be added to them to reduce the risk of leakage and facilitate their handling.

Gonzalez-Bayon, 2006 ♦ ONS, p. 26

10.3.13 Administration via Aerosolization

RATING: ++

Use an administration technique that limits the risk of exposure to pentamidine and ribavirin.

RECOMMENDATIONS

Pentamidine and Ribavirin

NOTE The risk is lower if the patient is intubated and ventilated. In this case, some of the containment measures described below do not apply (10.3.13.1, 10.3.13.2, 10.3.13.3) or apply only in part, (depending on the situation) (10.3.13.4, 10.3.13.5).

10.3.13.1 These drugs should be administered in a cubicle or tent specifically provided for this purpose in a negative-pressure chamber with at least 6 air changes per hour. There are various tent and cubicle systems on the market, for example, Demistifier (Figure 22). If this equipment is not available, the room should have 12 changes of air per hour. Do not administer these drugs in a positive-pressure room. Keep the door to the room closed at all times to ensure that the negative pressure is maintained. The room should continue to be ventilated for 30 minutes after the end of the treatment.

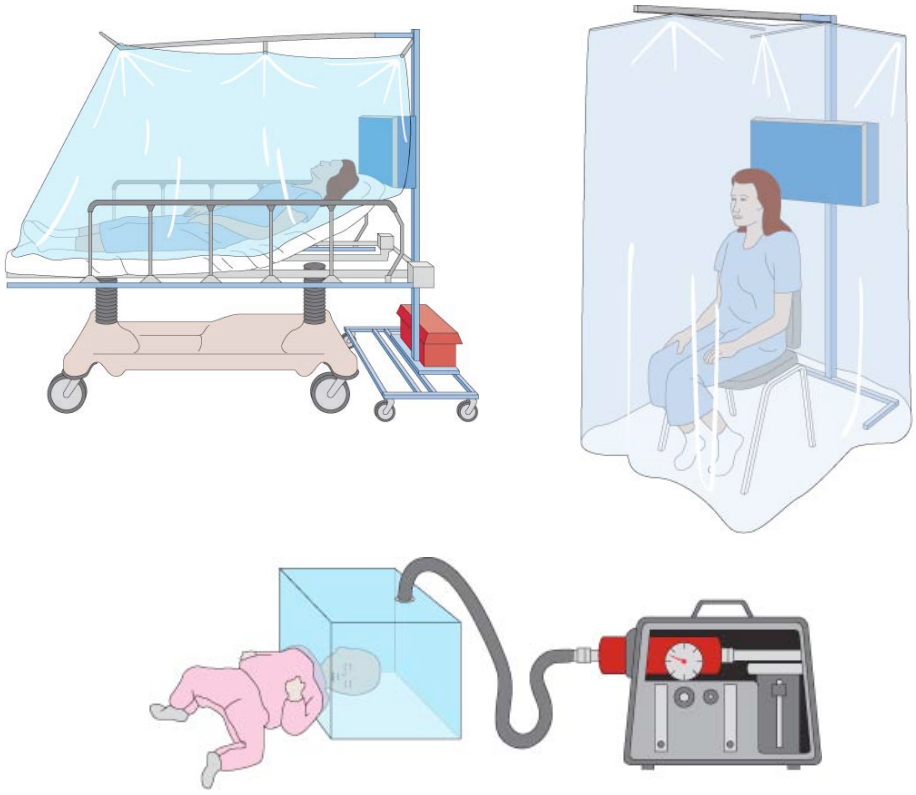


FIGURE 22
Various containment options for the administration of pentamidine or ribavirin

10.3.13.2 The air from the cubicle, tent or room should be exhausted to the outdoors; otherwise, it should be filtered through a *HEPA filter*.

10.3.13.3 The administration device should be equipped with a filter for patient exhalations and should automatically stop when the patient removes it from his mouth. Otherwise, it can be equipped with a patient interrupt mechanism. If the device does not stop automatically, when applicable, the patient can be given instructions regarding how to stop the nebulization. The patient should be encouraged to do so before calling the staff if he must remove the mask from his mouth to cough or if the mask becomes disconnected.

10.3.13.4 Unless it is an emergency situation, wait for at least five minutes following the end of the nebulization before interacting with the patient, to ensure that the air inside the cubicle or tent is free of drugs. Wait this length of time before entering the cubicle or lifting the sides of the isolation tent. In an emergency situation, workers should stop the nebulization as soon as possible. Protective equipment must be worn for any intervention inside the tent or cubicle.

10.3.13.5 Workers should not remain in the room during drug administration, except when the patient requires assistance. A visual (viewing window in the door) and/or vocal means of communication should allow remote monitoring of the patient.

10.3.13.6 If the drug is not administered in a cubicle or tent, workers must put on a N-95 respirator and goggles before entering the room.

10.3.13.7 Protective equipment (N-95 respirators, gloves, gowns and goggles) must be worn when handling the nebulizer and in situations where there is a high exposure risk (significant patient cough, accidental disconnection, uncooperative patient, lifting of the sides of the tent or entry into the cubicle).

10.3.13.8 The room should not be cleaned with dry equipment – mops and cleaning cloths should be damp. The room surfaces should be easy to clean and disinfect.

10.3.13.9 Pregnant workers should not work in areas where pentamidine and ribavirin are present.

10.3.13.10 Every precaution should be taken to limit the exposure of health care professionals to hazardous drugs. Thus, the Pharmacy Department should prepare the unit doses of hazardous drugs in aerosol form in a preparation cabinet (e.g. SPAG-2). In the event that this is not possible, the worker preparing the unit doses must wear protective equipment (N-95 respirator, gloves, gown, face shield or goggles (see 4.1.7.10)).

Pentamidine (additional measures)

10.3.13.11 Measures must be taken to prevent the transmission of tuberculosis.

ONS, p. 26 ♦ OSHA, Sections Vc2d, Appendix VI 2-2

10.3.14 *Intrathecal* Administration

RATING: ++

Use an administration technique that limits exposure risks.

RECOMMENDATIONS

NOTE The recommendations applicable to the General Administration Measures Section (i.e., Section 10.3.4) should be complied with.

10.3.14.1 Workers administering the drugs should use handling and administration techniques that minimize exposure risks:

- wear a gown, one pair of gloves (see 4.1.7.7) and face protection (see 4.1.7.10) ;
- use syringes and other devices with a Luer-Lock tip; fill the syringe no more than ¾ full;
- place a disposable, absorbent, plastic-backed pad under the injection site for the

containers; this pad will also absorb any contamination. Avoiding pushing on the plunger, the protective cap on the syringe should be removed over the absorbent pad;

- following the injection, discard the syringe in a rigid cytotoxic waste container and place the rest of the material in a Ziploc® type bag, which is to be discarded with the cytotoxic waste.

In the event that several consecutive intrathecal injections are required, the technique is the same for each syringe, i.e., the first syringe is placed on the absorbent pad, the contents of the second syringe are injected, etc. Everything is then discarded as described above.

10.3.15 Hazardous Drug Returns

RATING: ++

Use procedures that limit contamination to return unused hazardous drugs to the pharmacy.

RECOMMENDATIONS

10.3.15.1 Hazardous drug returns should be placed in a closed, leakproof, plastic bag (e.g. Ziploc® type), particularly if the treatment is postponed, refused or changed.

10.3.15.2 The closed, leakproof, plastic bag containing the unused hazardous drug returns should be taken from the care unit/clinic to the pharmacy in a rigid, shock-resistant, leakproof container made of a material which can be easily cleaned and decontaminated in the event of a leak. The *transport container* must be identified with the "Cytotoxic" hazard symbol.

10.3.15.3 Mechanical transport systems (such as pneumatic systems),which put stress on the contents, should not be used unless certain conditions are met (see 9.3.1.4).

10.3.15.4 Avoid using the transport containers for other purposes within the institution; in addition, the containers should be cleaned periodically (e.g. every three months).

CSHP, Section 8.9

10.3.16 Spill Kit

RATING: +++

Make sure a kit is available for the management of spills.

RECOMMENDATIONS

10.3.16.1 A spill management kit must be available in proximity to the care units/clinics where hazardous drugs are administered. In the event of a spill, see Section 12.3.4 and Appendix 4.

ASHP, p. 1176, 1183, 1189-90 ♦ CSHP, Section 8.15.3 ♦ NIOSH, p. 11, 12, 18 ♦ ONS, p. 31-32 ♦ OSHA, Section Vc5

10.3.17 Administration in the Home

RATING: +++

Establish policies and procedures to limit exposure risks.

RECOMMENDATIONS

NOTE All of the recommendations in this guide regarding administration also apply to administration in the home. For additional information, see also Section 11.3.3.

10.3.17.1 All hazardous drug preparations must be compounded in the pharmacy.

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

10.3.17.3 Make sure that the management of hazardous waste in the home complies with the recommendations in Section 12.3.2.

10.3.17.4 The nurse or inhalation therapist who administers hazardous drugs in the home must carry a spill kit. If the patient self-administers a hazardous drug, the institution should provide him with a spill kit, as well as the training necessary for its use. See Section 12.3.4 and Appendix 4.

ASHP, p. 1183 ♦ ONS, p. 32 ♦ OSHA, Section Vc2

11 PATIENT CARE

11.1 Issues and Risks

The biological fluids of patients who have received chemotherapy contain drug residues. Contact with patient excreta, bedpans, sheets or wash water may be a source of contamination (see Table 7). Tasks such as emptying bedpans, washing patients, changing sheets and *cleaning* toilets have been shown to cause contamination of the caregiver's gloves and hands and occasionally, of the caregiver's forehead and forearms. Wearing gloves reduces hand contamination by 4 when washing patients and by 1.6 when changing sheets (Fransman, 2005).

Table 7. Contamination of Objects in Contact with a Patient who has Received Cyclophosphamide (CP)

Parameter	*Average Amounts Measured**	*% of Samples Contaminated*
Outside of the bedpan	0.28 ng/cm^2	100%
Cloth used to wash the patient	10 ng/cm^2	100%
Towel used to dry the patient	13 ng/cm^2	89%
Patient's pillow	2.6 ng/cm^2	71%
Sheet (abdomen)	1.8 ng/cm^2	79%

* Measurements taken the day after the administration of CP. The maximum value proposed in the USA is 1 ng/cm^2.
Source: Fransman, 2005

The scientific literature reports that the bathrooms (floors, toilet bowls) and the environment (bedding, bedpans) of patients who have received *antineoplastic* drugs may be contaminated with traces of hazardous drugs (Fransman, 2005). It would be logical to think that this type of patient should be placed in a private room, to prevent the contamination of other patients in the room. Moreover, this would facilitate the implementation of adapted hygiene and sanitation measures (dedicated, disposable equipment, etc.). However, to date, no studies have been done that would support a recommendation in this regard.

Similarly, in view of the contamination of the bedding, sharing a bed with someone who has received antineoplastic type hazardous drugs during the previous 48 hours (or more, depending on the drug; see Table 8) may constitute an exposure risk. It should be remembered that the exposure varies with the frequency and duration of exposure and the amount of drug to which one is exposed (see 2.3.3). However, there are no studies evaluating the exposure of those sharing a bed with a patient who has received treatment with hazardous drugs. The Committee is thus unable to make a recommendation in this regard.

11.2 Exposed Workers

- Care unit / outpatient clinic / home care workers (e.g. nurses, physicians, inhalation therapists, patient service associates)
- Other patients, families of patients
- Hygiene and Sanitation Department workers
- Biomedical engineering workers

11.3 Preventive Measures

11.3.1 Personal Protective Equipment

RATING: +++

Wear personal protective equipment when handling bedding or handling/cleaning up excreta or vomitus.

RECOMMENDATIONS

11.3.1.1 Workers who handle the biological fluids, excreta, bedding and soiled equipment (e.g. bedpans) of patients who have received antineoplastic type hazardous drugs must wear one (1) pair of gloves (see 4.1.7.7) and a protective gown (see 4.1.7.8). These precautions should be taken for a minimum of 48 hours following the administration of the last dose of the drugs, with the exception of certain drugs with a half-life greater than 48 hours (Table 8 contains a representative list of the elimination time for certain drugs). In these cases, the period during which PPE must be worn must be increased accordingly. One pair of gloves must be worn when providing personal care to the patient and when changing the patient's clothes or sheets. A gown may be necessary if providing personal care to the patient involves a significant risk of splashing. Caregiving staff who are not providing direct patient care (e.g. physician, pharmacist talking with the patient) are not required to wear PPE.

11.3.1.2 Face protection (see 4.1.7.10) must be worn when there is a risk of splashing (e.g. when emptying and cleaning the bedpans of patients receiving antineoplastic type hazardous drugs).

APES, p. 5-28 ♦ ASHP, p. 1188 ♦ CSHP, Section 8.13 ♦ NIOSH, p. 17 ♦ ONS, p. 27 ♦ OSHA, Section Vc3

11.3.2 Organization of Work

RATING: ++

Use work methods that minimize exposure to hazardous products in the excreta.

RECOMMENDATIONS

11.3.2.1 The caregiving staff should use techniques for handling biological fluids and excreta that minimize exposure risks:

- limit, as much as possible, the measuring of biological fluids (i.e., excreta), in view of the risk of splashing when pouring. In some cases, weighing the patient may be used to assess the ingesta-excreta balance, rather than measuring the volume of fluids ingested and eliminated;
- encourage the patient to use the toilet, rather than a bedpan or urinal;
- encourage men to urinate while sitting, to reduce the risk of aerosol creation and droplet contamination;
- use disposable diapers. If they are soiled by a patient who has received chemotherapy treatment during the previous 48 hours or more (see 11.3.1.1), discard them in a *cytotoxic waste* receptacle;
- collect fluid from pleural drainage or ascites in a disposable, closed system and discard in a cytotoxic waste receptacle;
- rinse bedpans after every use and wash them with detergent and water once a day; store them such that they will not be used by another patient. Clean the storage areas regularly. When available, disposable bedpans or the use of closed-circuit bedpan washing machines may be considered. However, contamination must be minimized when transporting the bedpans from the patient's room to the bedpan washing machine on the care unit.
- use absorbent pads to cover the excreta of patients who have received antineoplastic type hazardous drugs during the previous 48 hours or more (see 11.3.1.1), e.g. vomitus, stools or urine, while waiting for the hygiene and sanitation workers to

arrive (see 13.3.1.3).

11.3.2.2 Workers who handle the bedding should be properly protected when doing so. The recommended Health Canada* procedures should be followed for every item of bedding soiled with blood, body fluids, secretions or excreta:

- as much as possible, avoid agitating or shaking the bedding, as this may release contaminated particles;
- roll or fold heavily soiled bedding such that the most heavily soiled parts are on the inside of the bundle;
- place the bedding in a single bag, unless there is fluid leaking from the bag, in which case a second bag must be used.

11.3.2.3 Make sure that the toilet flushes properly and that the water has been completely flushed away. Clean any droplets of biological fluids from the toilet rim and floor. In view of the flushing pressure of toilets in health care institutions and the absence of a lid, it is not necessary to flush more than once (contrary to what is the case for home toilets). (+)

CSHP, Section 8.13 ♦ ONS, p. 27-30

11.3.3 Home Care of Patients who have Received Hazardous Drugs

RATING: ++

Establish policies and procedures to reduce exposure risks

RECOMMENDATIONS

NOTE All of the recommendations in this guide regarding patient care also apply to home care.

11.3.3.1 Family members involved in the care of patients receiving antineoplastic drugs should be informed of the following, verbally and in writing:

- all hazardous drugs should be kept out of reach of children and animals;
- the hazardous drugs should be stored in rigid, sealed, properly-identified containers reserved exclusively for this purpose;
- pregnant or nursing women should avoid handling or administering hazardous drugs;
- patient linens and bedding may be washed with the regular laundry unless they are soiled by drugs or excreta up to 48 hours or more following the end of the treatment (see 11.3.1.1), in which case, they should be washed separately. The bedding should be agitated and shaken as little as possible, as this may release contaminated particles. Such laundry should be washed as quickly as possible. If a washing machine is not available, place the contaminated laundry in a plastic bag and close it securely, avoiding mixing it with the uncontaminated laundry. Heavily soiled clothing or bedding may be washed twice;
- exposed individuals must wear one (1) pair of gloves (see 4.1.7.7) to handle the excreta or the soiled clothing and bedding of a patient who received a *hazardous drug* during the first 48 hours or more following a chemotherapy treatment (see 11.3.1.1); they must always wash their hands after handling these items.

* Health Canada : Infection Control Guidelines : Handwashing, Cleaning, Disinfection and Sterilization in Health Care, December 1998, p. 34 to 36

- the lid of the toilet should be closed and the toilet flushed twice after being used to eliminate the contamination. Clean the toilet rim, as well as the floor around the toilet, daily. The toilet should be cleaned with the usual cleaning products; the cleaning cloths used for this purpose should not be used on other surfaces;
- patients receiving drugs via infusion over extended periods (e.g. 24 hours) should use a plasticized mattress cover to avoid contaminating their mattress in the event of accidental disconnection of the infusion;
- a spill kit should be available in the home if the patient receives drugs when the CLSC (Local community service centre) nurse is not present (e.g. pump, self-administration). Patients or their families should know how to use the spill kit.

APES, p. 5-29 ♦ CSHP, Section 8.2.4

11.3.4 Use of Pumps to Administer Hazardous Drugs

RATING: +

Establish policies for pump maintenance.

RECOMMENDATIONS

11.3.4.1 A portion of the pump inventory may be reserved for the patients receiving hazardous drugs via pump. Generally speaking, the pumps should be cleaned between patients and prior to being sent elsewhere in the institution. If pump management is centralized, a cleaning procedure can be established for potentially contaminated pumps before they are used by other patients (e.g. cleaning the outside of the pump with a towelette).

11.3.4.2 A policy should be established regarding the handling of potentially contaminated pumps by biomedical engineering workers, i.e., clean the pump before carrying out an intervention and wear a pair of gloves when performing preventive maintenance or repairs.

Table 8. Hazardous Drugs: Duration of the Presence of Detectable Residues in the Excreta

Drug	Duration of the Presence of Detectable Residues in the Urine	Duration of the Presence of Detectable Residues in the Stools
Bleomycin sulfate	72 hr; 50% excreted in the first 24 hr	--
Busulfan	12-24 hr	--
Capecitabine	24 hr	--
Carboplatin	24-48 hr; 60% in the first 24 hr	--
Carmustine	4 days	--
Cisplatin	7 days	--
Cyclophosphamide	72 hr	5 days after oral dose
Cytarabine	24 hr	--
Dacarbazine	6 hr	--
Dactinomycin	5 days; 20% in the first 24 hr	--
Daunorubicin	48 hr	7 days
Docetaxel	7 days	7 days; 80% in the first 48 hr
Doxorubicin	6 days	7 days
Epirubicin	7 days	5 days
Etoposide	4 days	7 days
Fludarabine	48 hr	--
Fluorouracil	48 hr	--
Gemcitabine	7 days	--
Hydroxyurea	12 hr	--
Ifosfamide	48 hr	--
Imatinib mesylate	7 days	7 days
Irinotecan	48 hr	--
Lomustine	24 hr	--
Mechlorethamine hydrochloride	48 hr	--
Melphalan	48 hr	7 days
Mercaptopurine	48-72 hr; 50% in the first 24 hr	--
Methotrexate	72 hr; major problem during the first 8 hr	7 days
Mitomycin	24 hr	--
Mitoxantrone hydrochloride	6 days	7 days
Paclitaxel	24 hr	5 days
Pegaspargase	Not detectable	--
Tamoxifen	--	2 weeks
Teniposide	5 days	48 hr
Thioguanine	24 hr	--
Thiotepa	24 hr	--
Vinblastine sulfate	4 days	7 days
Vincristine sulfate	4 days	7 days

Source: ONS – Safe handling of hazardous drugs, 2003, p. 28.

12 MANAGEMENT OF WASTE, ACCIDENTAL EXPOSURE, SPILLS AND RETURNS

12.1 Issues and Risks

The colour of waste receptacles used in institutions (plastic bags or rigid containers) is most often yellow, while white or red are also seen. There are currently no regulations or standards in Quebec prescribing a specific colour code for *cytotoxic waste*.

The *Guide de gestion des déchets comportant des risques en milieu de santé* (1989), one of the few documents that makes specific suggestions regarding cytotoxic waste, recommends using the colour YELLOW for plastic bags and receptacles designated to hold cytotoxic waste, while CSA Standard Z316.6-02 recommends using the colour RED for rigid cytotoxic waste containers. In addition, Med-Tech (Stericycle), which is the only company in Quebec licensed for the collection and final disposal of cytotoxic waste, requires that the waste either be identified as requiring incineration or be placed in a red plastic bag. Otherwise, the yellow bags must be placed in a leakproof cardboard box identified with the "Cytotoxic" hazard symbol. In Ontario, red is the colour required for waste which is to be incinerated.

In view of this, no colour code is recommended in this guide while we wait for new standards. The colours currently in use may continue to be used (which most often means the colour yellow). However, compliance with MedTech instructions is one way of ensuring the proper disposal of cytotoxic waste.

The major risks are:

- the transfer of *hazardous drugs* and contaminated supplies into waste receptacles, as well as the handling of these receptacles, may pose a risk of exposure (e.g. when closing the bags, during transport, etc.) ;
- while the waste receptacles to be used are relatively leakproof, leakage of contaminated fluids may occur if the receptacle tips over;
- if the receptacles are not closed, there is a risk of spreading as aerosols or through the diffusion of vapours (not documented);
- spills pose an exposure risk at every step of the medication circuit, due to potential direct contact with hazardous drugs or their spreading into the air as aerosols or vapours.

12.2 Exposed Workers

- Receiving or shipping clerks (e.g. stock-keeper, storeroom clerk)
- Waste collection workers
- Pharmacy Department workers (e.g. pharmacist, clerk, pharmacy technician)
- Care unit / outpatient clinic / home care workers (e.g. nurses, physicians, inhalation therapists, patient service associates)
- Other patients, families of patients
- Hygiene and Sanitation Department workers

12.3 Preventive Measures

12.3.1 Hazardous Drug Waste

RATING: +++

Establish polices and procedures regarding hazardous waste management.

RECOMMENDATIONS

NOTE The *Guide de gestion des déchets comportant des risques en milieu de santé* (1989) uses the term *Cytotoxic Pharmaceutical Waste* to identify the waste from *antineoplastic* drugs, including the residues from their preparation and use. This guide uses the term *Cytotoxic Waste*, which also includes items soiled by excreta (e.g. diapers).

12.3.1.1 The term "cytotoxic waste" includes any material that comes into contact with antineoplastic type hazardous drugs during their storage, handling, preparation, administration and disposal (e.g. packaging material, protective equipment, preparation supplies (such as syringes, tubing, drug bags), soiled diapers of patients who have received antineoplastic type hazardous drugs during the previous 48 hours, hood prefilters and *HEPA filters*, etc.). The production of cytotoxic waste should be minimized.

12.3.1.2 Cytotoxic waste must be placed in a waste container clearly identified with the "Cytotoxic" hazard symbol (see 4.1.5.3).
Cytotoxic waste must be disposed of in the appropriate containers;

- sharps must be placed in rigid containers with a leakproof lid; CSA standard Z316.6-02 specifies the use of the colour red for the rigid containers. If the containers are another colour, follow the instructions of the company ensuring the final disposal;
- other waste (soft items, such as tubing, protective equipment, etc.) must be placed in heavy-duty, double plastic bags, identified with the "Cytotoxic" hazard symbol, leakproof and tear-resistant under the anticipated conditions of use. For final disposal outside the institution, these bags must be placed in a rigid, leakproof , cardboard box identified with the "Cytotoxic" danger symbol and scheduled for transport outside the institution;
- any excess fluid from antineoplastic type hazardous drugs (e.g. drug loss) must be disposed of in a sealed container (e.g. jar with lid) 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;
- disposable diapers soiled by patients who have received antineoplastic type hazardous drugs during the previous 48 hours or more (see 11.3.1.1) must be considered cytotoxic waste and disposed of in a double bag identified with the "Cytotoxic" hazard symbol. (++)

12.3.1.3 Cytotoxic waste must be incinerated at a high temperature (i.e., 800 to 1200°C, depending on the product). Cytotoxic waste must not be disposed of in the receptacles used for infectious biomedical waste (which may be autoclaved and sent to a landfill site).

12.3.1.4 Every area where antineoplastic type drugs are handled (including patient rooms) must have cytotoxic waste receptacles. On care units, a receptacle on wheels, which can be moved into the rooms as needed during procedures generating cytotoxic waste (e.g. drug administration, etc.), may be used.

12.3.1.5 The lids of hazardous drug receptacles must remain closed, except when depositing waste. Pressure must never be placed on the waste to push it into the receptacle. Avoid overfilling receptacles (maximum ¾ full).

12.3.1.6 Workers must be careful to avoid contaminating the outside of the receptacle when depositing waste. Do not handle receptacles with contaminated gloves.

12.3.1.7 The transport of cytotoxic waste receptacles must be assigned to properly trained workers.

- Workers who handle cytotoxic waste receptacles must wear one pair of disposable gloves and a gown. They must avoid touching uncontaminated items with the gloves and must have a spill kit at their disposal;
- A route must be planned for the transport of the waste that goes through as few care units, public areas and areas containing food or linens as possible;
- The carts used to transport waste must be:
  - designed to prevent spills and leaks; open carts may be used to transport the plastic bags, provided that these are properly secured;
  - made of easily-cleaned materials;
  - designed to reduce to a minimum the mechanical stresses of loading and unloading the waste.

12.3.1.8 The sewer network must not be used to dispose of hazardous drugs, other than the urine and feces of patients who have received hazardous drugs.

12.3.1.9 The *final storage areas* for cytotoxic waste receptacles must be kept locked. The waste should be stored in a cool location. The ventilation of this area should prevent the spread of contamination to adjacent rooms. The air should be exhausted to the outdoors, without recirculation. This area should not be near areas accessible to patients.

12.3.1.10 The institution should agree to manage the cytotoxic waste receptacles used by patients in their homes. In some cases, depending on local agreements, cytotoxic waste from patient homes may also be directed elsewhere (specialized clinics, community pharmacies). The institution providing health care must take back the cytotoxic waste. In the event of self-care, the patient is responsible for returning the cytotoxic waste to the location where the drugs were dispensed.

12.3.1.11 For practical purposes, a single type of waste receptacle should be used to manage hazardous waste (antineoplastic or otherwise) for the oncology clientele, in view of the fact that the majority of the *pharmaceutical waste* comes from the antineoplastic type hazardous drugs for this clientele.

12.3.1.12 Other, non-antineoplastic, hazardous drugs used outside oncology may be disposed of in an appropriate container (i.e. rigid or soft, depending on the nature of the waste):

- pharmaceutical waste (i.e., drugs that are unusable, expired or contaminated) must be disposed of in a container marked “Pharmaceutical Waste – Incineration”;
- items contaminated by pharmaceutical products may be discarded in general or biomedical waste receptacles, as applicable.

APES, 5-39, 5-40 ♦ ASHP, p. 1175, 1179-80, 1183, 1188-90 ♦ CSA, Z317.10.01, Z321-96, Z316.6-02 ♦ CSHP, Sections 5.1, 5.2, 5.5, 5.6, 6.1, 6.2, 6.3, 7, 8.2, 8.4, 8.11, 8.12 ♦ NIOSH, p. 12, 13, 14, 17, 18 ♦ ONS, p. 30-31 ♦ OSHA, Section Vc4 ♦ RSST, Art. 92

12.3.2 Antineoplastic Type Hazardous Drug Waste in the Home

RATING: ++

Establish policies and procedures regarding the management of cytotoxic waste in the home.

RECOMMENDATIONS

12.3.2.1 Caregiving staff must provide the patients / caregivers involved in administering antineoplastic type hazardous drugs in the home with cytotoxic waste management receptacles.

12.3.2.2 The home care workers (or the patients / caregivers, as applicable) must return the cytotoxic waste receptacles to the institution for final disposal. There are two methods of doing so to avoid contaminating the worker's personal vehicle:

- a) soft items may be placed in a heavy-duty, leakproof, double plastic bag identified with the "Cytotoxic" hazard symbol. Sharps must be placed in a perforation-resistant, rigid container identified with the "Cytotoxic" hazard symbol. Any excess fluid (e.g. remaining drugs, etc.) must be placed in a sealed container (e.g. jar with lid) and placed in a rigid container, the bottom of which is to be covered with an absorbent pad.
  For transport by car, a double bag identified with the "Cytotoxic" hazard symbol should be placed in a reusable, rigid container (e.g. cooler). This container must be leakproof, rigid, washable with detergent and water and properly identified with the "Cytotoxic" hazard symbol; OR
- b) in accordance with the Regulation respecting Biomedical Waste (Art. 22), sharps must be placed in a rigid, sealed, leakproof, perforation-resistant container. A fairly large, rigid, non-reusable container (e.g. 8 to 10 litres) may be used to dispose of all contaminated items (needles, tubing, gowns, gloves, etc.). This container must be sturdy and leakproof. It must never be filled more than three-quarters full. The contents should not be touched with bare hands, nor should they be pushed down to compact the waste. The container must be sealable for transport and identified with the "Cytotoxic" hazard symbol;
- the cytotoxic waste container (scenario a or b) should be placed in the trunk of the car and secured to prevent it from tipping over while the vehicle is moving.

Pursuant to the *Code of Ethics of Pharmacists*, the pharmacist must, when someone makes a reasonable request of him, "participate in the safe collection of expired or unused medicines" as part of the administration of drugs. This provision applies in particular to hazardous drugs, regardless of whether or not they are antineoplastic.

CSHP, Sections 5.2, 7.2 ♦ R.Q. c. P-10, r.5, Art. 3.01.07

12.3.3 Accidental Exposure

RATING: +++

Establish policies and procedures regarding accidental worker exposure.

RECOMMENDATIONS

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

12.3.3.2 If a hazardous drug comes into contact with a worker's eyes, the worker should wash his eyes, preferably with an appropriate device installed on an easily accessible faucet / sink. Alternatively, a portable eye rinse system may be used. The worker must immediately rinse his eyes with water or an isotonic fluid (e.g. sterile NaCl 0.9%) for at

least 15 minutes.

Drug projections can be harmful to contact lens wearers, who must remove their lenses immediately in the event of accidental exposure. Contrary to popular belief, contact lenses do not provide protection.

12.3.3.3 In the event of a needlestick with a needle that has been in contact with a hazardous drug, massage in the direction of the wound to make it bleed and to limit absorption of the drug (avoid pinching, which causes suction and restricts the flow of blood). Next, thoroughly wash the affected area with water and contact the Occupational Health and Safety (OHS) Department. In the event of a needlestick with a needle that has been in contact with a hazardous drug AND a patient, apply the follow-up protocol for post-accidental exposure to blood and biological fluids within two hours or according to the policy of the institution.

12.3.3.4 Any accidental exposure to a hazardous drug through the skin or eyes or through blood or biological fluids must be declared on the accident or incident report form in use at the institution. This report must be filed with the Occupational Health and Safety (OHS) Department, which will provide medical follow-up when required and analyze the event.

This report is to be kept in the employee's file and/or in a record, in accordance with Article 280 of the *Act respecting Occupational Health and Safety*. In addition, according to the Recueil de règles de conservation des documents des établissements de santé et de services sociaux du Québec (Quebec Code regarding Document Retention in Health and Social Service Institutions), the reports must be kept for at least 20 years following the end of the worker's employment or for 40 years following the start of employment, whichever is longer. These records may not be destroyed. It is advisable to carry out a global analysis of these accidents for prevention purposes. It should thus be possible to trace these reports back for a given period.

APES, p. 5-42 ♦ ASHP, p. 1184 ♦ CSHP, Sections 8.3.3, 8.14 ♦ ONS, p. 33-35

12.3.4 Spill

RATING: +++

Establish policies and procedures regarding the management of a spill.

RECOMMENDATIONS

12.3.4.1 The institution should develop policies and procedures which take into account the various types of spills (i.e., limited amount vs substantial amount, location, etc.) and the workers who must be called upon (e.g. pharmacy workers, care unit/clinic workers, hygiene and sanitation workers). These policies and procedures should be incorporated into the institution's emergency measures planning process, the procedure for which is described in the *Manuel de planification des mesures d'urgence* (Emergency Preparedness Manual published by the MSSS (available, in French only, in the Publications section of the MSSS Web site).

12.3.4.2 A spill management team may be trained, if it is deemed necessary. Call criteria should be set for this team (e.g. spill of more than 1 litre, more than 1 spill kit required to manage the spill). A procedure is suggested in Appendix 4. A call code may be established for this team as suggested in the manual mentioned above. Code "brown" is often used in institutions for chemical spills.

12.3.4.3 A spill management kit must be available in the Pharmacy Department and near the care units/clinics where hazardous drugs are administered, as well as in the cytotoxic waste transport cart. In addition, nurses who administer hazardous drugs in the home must carry a spill kit.

12.3.4.4 Anyone noticing a spill should act quickly if they have been trained in spill management. Otherwise, they must quickly alert the individual responsible for handling spills. While waiting for the spill to be managed, they can ensure that no one comes into contact with the spill, cover it with absorbent material (absorbent, plastic-backed cloth or paper towels for liquid spills, wet towels for powder spills) and bring the spill management kit to the site. Appendix 4 lists the suggested contents of a spill kit.

12.3.4.5 The properly trained worker managing the spill should isolate and identify the spill zone to limit the contamination (cones, signs, tape, etc.) and ensure that no one comes into accidental contact with the hazardous drug.

12.3.4.6 The properly trained worker managing the spill must wear two (2) pairs of gloves (see 4.1.7.7), a protective gown, and an appropriate respirator, depending on the extent of the spill (see Appendix 4), face protection (see 4.1.7.10) and shoe covers (if the spill is on the floor) to *clean up* the spill. Once the clean-up is complete, the worker may remove the protective clothing, discard it with the cytotoxic waste and wash his hands.

12.3.4.7 All of the material used to clean up the spill must be disposed of in accordance with the recommendations in Section 12.3.1.

12.3.4.8 Damaged containers (e.g. cardboard box containing the drugs) should be handled like a spill. They should be opened in an isolated, ventilated area (the unpacking area may be used). To limit exposure, damaged containers should never be returned to the manufacturer or distributor. Instead, it is better to advise the manufacturer or distributor in writing and document the event (e.g. with supporting material, pictures). If the manufacturer requires the return of the damaged product to compensate the institution, the institution should discuss both the risks of contamination and the return procedures with the manufacturer, in order to prevent accidental exposure during shipping. (++)

12.3.4.9 The prevention program should include an annual spill simulation exercise.

APES, p. 5-41 to 5-43 ♦ ASHP, p. 1176, 1179-80, 1183, 1190-91 ♦ CSA, Z317.10-01 Section 5.11 ♦ CSHP, Sections 8.2.4, 8.3.2, 8.3.3, 8.15 ♦ NIOSH, p. 11, 12, 18 ♦ ONS, p. 31-32 ♦ OSHA, Sections Vc5 and 6

12.3.5 Shipping

RATING: ++

Establish policies and procedures regarding the shipping of hazardous drugs.

RECOMMENDATIONS

12.3.5.1 In the event that hazardous drugs are shipped off-site (e.g. from institution X to institution Y), they should be packed separately from other drugs, according to the recommendations for manufacturers and distributors (Section 5.3.2).

12.3.5.2 Antineoplastic drugs should be packed in a double plastic bag placed in a box which is properly identified with the "Cytotoxic" hazard symbol. If necessary, immobilize the drug with packing material. The "Cytotoxic" hazard symbol must be visible on the outside of the *delivery container*. Reusable delivery containers should be properly maintained on a regular basis.

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

CSHP, Sections 5.4, 8.10

13 HYGIENE AND SANITATION

13.1 Issues and Risks

The cleaning of premises and equipment should eliminate drug-related chemical contamination. The existing scientific literature is not clear regarding the products to be used and their action times. Studies in this regard are being sponsored by NIOSH.

The reference organizations (NIOSH, ASHP, etc.) suggest using sodium hypochlorite, which inactivates a number of (but not all) hazardous drugs; however, the concentration to be used and the action time are rarely specified. Studies documented in the scientific literature suggest various concentrations (generally, 2% to 5.25%) and action times ranging from 5 minutes to 1 hour. However, the use of sodium hypochlorite (bleach, Javel) is not without risk - splashing into eyes or on skin, inhalation of vapours, corrosion of surfaces (according to one manufacturer, the stainless steel of a number of *biological safety cabinets* would eventually rust if sodium hypochlorite were used), discoloration of surfaces or fabrics.

In the United States, a commercial product (SurfaceSafe) has been suggested to *decontaminate* surfaces. This product consists of two premoistened towelettes. The first is soaked in sodium hypochlorite (to decontaminate), while the second is soaked in sodium thiosulfate (to neutralize the corrosive effect of the sodium hypochlorite). This product is effective on a number of (but not all) *antineoplastic* drugs. Basically, there are no universally effective products. SurfaceSafe is not currently available in Canada.

In pharmacies, alcohol is often used for *cleaning*. However, it is used to ensure sterility, not for chemical decontamination. For example, one study compared alcohol and SurfaceSafe in the decontamination of a stainless steel surface contaminated with a known amount of cyclophosphamide or ifosfamide. With alcohol, 18% of the initial amount of cyclophosphamide remained on the surface vs 4.1% with SurfaceSafe; for ifosfamide, the figures are 100% with alcohol vs 3.6% with SurfaceSafe (Polovich *et al.*, 2002). In conclusion, alcohol does not appear to be very effective for chemical decontamination.

According to other studies, cleaning with a cloth and detergent appears to be effective in eliminating the majority of the chemical contamination through mechanical action (rubbing) and transfer to the cloth. One study (Roberts *et al.*, 2006) reported that 5-fluorouracil, cyclophosphamide and doxorubicin were effectively removed with an acidic or neutral detergent. Several wipings with a basic detergent were required to remove the doxorubicin. The authors suggested using a staged cleaning process, beginning with the use of water alone, followed by the use of a high pH (basic) detergent, subsequent cleaning with a low pH (acidic) detergent and finally, cleaning with alcohol. It is understood, however, that such a process may be difficult to implement in actual fact.

In view of the continuing uncertainty in the scientific literature regarding the optimal decontamination strategies, we recommend (in the majority of situations) the use of detergent and water, a microfibre cloth and a rubbing action. In some cases (for example, following a spill or for the periodic cleaning of the inside of the biological safety cabinets, when there is substantial residual contamination), decontamination with sodium hypochlorite 2.4% (action time: 10 minutes) would ensure a chemical breakdown of the molecules (Mateu, 1996). The corrosive action of the hypochlorite may be counteracted by the use of sodium thiosulfate or rinsing with water.

13.1.1 Risks

Sanitary maintenance can expose housekeeping workers to hazardous drugs. In addition, improper cleaning increases the exposure of everyone working in areas where hazardous drugs are handled.

Exposure may occur through contact with contaminated surfaces (e.g. counters, furniture, etc.), waste, excreta, soiled bedding or the cloths and mops used to clean contaminated areas (toilets or floors in the rooms of patients who have received hazardous drugs, preparation or administration areas, etc.).

Contamination is possible through ingestion, via contaminated hands or by eating or drinking in these areas.

Workers may also be exposed via the cleaning of hazardous drug spills or excreta and vomitus from patients who have received hazardous drugs.

13.2 Exposed Workers

- Hygiene and Sanitation Department workers

13.3 Preventive Measures

13.3.1 Hygiene and Sanitation Program

RATING: +++

Establish a Hygiene and Sanitation Program to limit exposure to hazardous drugs.

RECOMMENDATIONS

13.3.1.1 The Hazardous Drug Preventive Management Program should include a Hygiene and Sanitation Program to limit exposure to hazardous drugs, particularly in the Pharmacy Department, Oncology Division and the care units and outpatient clinics where hazardous drugs are administered.

13.3.1.2 The Hygiene and Sanitation Program in the Pharmacy Department should specify the nature and frequency of the cleaning, as well as the products used:

- the hygiene and sanitation workers should clean the work surfaces (e.g. counters, sinks, arms of patient chairs, nightstands, computer keyboards, door/refrigerator/cupboard handles, toilets, etc.) and traffic areas (e.g. floors) daily; cleaning of the inside of the hoods should be performed by pharmacy workers;
- the hygiene and sanitation workers should thoroughly clean all equipment (e.g. carts, racks) that enters or leaves the *sterile* preparation rooms;
- the hygiene and sanitation workers should clean the ceilings, walls, windows and the outside of equipment (e.g. refrigerators, hoods, shelves, chair legs) in the oncology pharmacy monthly. Cleaning of the inside of refrigerators and pumps should be performed by pharmacy workers; cleaning of the hazardous drug storage shelves may be done by hygiene and sanitation workers if the drugs are moved by the pharmacy workers beforehand;
- the purpose of cleaning the premises and equipment is to remove drug-related chemical contamination. In view of the vagueness of the scientific literature on the subject (see Issues, Section 13.1), we recommend using a detergent and water solution, following by rinsing with water. When more extensive surface contamination (e.g. spill, inside of the hoods, etc.) is suspected, we suggest following the cleaning with detergent and water with chemical decontamination using sodium hypochlorite 2.4% (which should be left to work for 10 minutes), followed by rinsing with water or neutralization with sodium thiosulfate. (++)
- when it is relevant to limit microbial contamination (e.g. sterile preparation room, biological preparation cabinets, etc.), it is important to follow the chemical decontamination with *disinfection* using a disinfectant, in accordance with the recommendations of the institution's Infection Control Committee.
- the cleaning activities should be documented to ensure that they are performed in compliance with the Hygiene and Sanitation Program (date/time, done/not done).

13.3.1.3 The Hygiene and Sanitation program in the care units/treatment rooms/patient rooms should specify the nature and frequency of the cleaning, as well as the products used:

- the hygiene and sanitation workers should clean the work surfaces and traffic areas (floors, counters, patient's chair, washroom and toilet bowl, section of the wall where the gowns may be hung, patient's table, etc.) daily. The patient washrooms should be cleaned twice a day.

- the excreta and vomitus from patients who have received antineoplastic type hazardous drugs during the previous 48 hours or more (see 11.3.1.1) must be covered with absorbent pads while awaiting the arrival of the hygiene and sanitation workers. They will remove the pads and dispose of them in the plastic bags provided for *cytotoxic waste*. They will then wipe and clean the contaminated

areas with detergent and water, moving from the least contaminated to the most contaminated, and rinse them three times with water.

13.3.1.4 Each area to be cleaned should have dedicated sanitary maintenance equipment, i.e., solely for use in the pharmacy or in the targeted units/clinics. The mops and cloths used in the room of a patient who has received chemotherapy treatment should not be used to clean another room.

13.3.1.5 The use of disposable equipment, to be discarded in the receptacles provided for cytotoxic waste, is recommended. The use of a flat mopping system with disposable cloths for the floors makes compliance with this recommendation easier. Microfibre cloths are a worthwhile, desirable solution when choosing wet mops and cloths. It is preferable to use a wet mop, rather than a dry mop.

13.3.1.6 All hygiene and sanitation workers assigned to clean an area exposed to hazardous drugs must have received proper training and documentation. The training must, at the very least, include knowledge of the "Cytotoxic" hazard symbol, the nature of the risks related to hazardous drugs, the importance of proper cleaning to limit the risks of exposure, the *personal protective equipment*, the cleaning equipment to be used and reserved for the areas of exposure, as well as the products to be used.

APES, p. 5-44 ♦ ASHP, p. 1175, 1183, 1188 ♦ NIOSH, p. 16, 17 ♦ OPQ, Section 7.3 ♦ OSHA, Section Vc3

13.3.2 Protective Equipment

RATING: ++

Wear proper protective equipment.

RECOMMENDATIONS

13.3.2.1 The housekeeping workers must wear a protective gown and one (1) pair of gloves (see 4.1.7.7) for the sanitary maintenance of the pharmacy and areas where hazardous drugs are administered. In addition, they must wear a cap and shoe covers for cleaning the airlock and the sterile preparation room.

13.3.2.2 Workers called upon to clean the excreta and vomitus of patients who have received antineoplastic drugs (see 11.3.1.1) must wear one pair of gloves (see 4.1.7.7) and an appropriate gown. The use of disposable material is recommended for these tasks; this material must be discarded with the cytotoxic waste. In the presence of a great deal of excreta and vomitus (copious diarrhea, incontinence, etc.), it may be useful to wear shoe covers, to avoid spreading the contamination to clean areas.

13.3.2.3 Cleaning of the inside of the preparation cabinets should be performed by pharmacy workers (see Section 8.3.8.1).

NIOSH, p. 16, 17 ♦ OSHA, Section Vc3

14 LAUNDRY

14.1 Issues and Risks

Management of the bedding of patients who have received *hazardous drugs* may expose workers to traces of hazardous drugs. According to studies conducted in Holland, contamination of laundry workers appears to occur primarily through inhalation of particles present on the sheets when these are sorted or moved about before being washed. There is no contamination left on the sheets following prewashing (Fransman, 2006).

Laundry facilities vary according to institutional size and mission. A number of institutions have washing tunnels, with no contact or sorting prior to prewashing. In these instances, the risk of exposure is very low, if not non-existent. Small institutions, however, may have machines that require manual loading and may sort the laundry prior to washing. Here, steps must be taken to prevent contact with the potentially contaminated sheets or clothing.

14.2 Exposed Workers

- Laundry workers

14.3 Preventive Measures

14.3.1 Protective Equipment

RATING: ++

Wear proper equipment for prewash handling.

RECOMMENDATIONS

14.3.1.1 Laundry workers in health care institutions must wear a protective gown and one (1) pair of disposable gloves for the prewash handling of the bedding or clothing of a patient who has received hazardous drugs during the previous 48 hours or more (see 11.3.1.1). The regular equipment used to handle linens is sufficient. The workers must remove the protective equipment following such handling to avoid contaminating themselves or the work environment.

ONS, p. 29 ♦ OSHA, Section Vc3

14.3.2 Bedding Management

RATING: ++

Reduce the risk of exposure for workers handling bedding exposed to hazardous drugs.

RECOMMENDATIONS

14.3.2.1 In health care institutions, bedding exposed to hazardous drugs may be washed with bedding which has not been exposed to hazardous drugs, since the amount of detergent is the same and is based on maximum soiling. The procedures recommended by Health Canada* for all linens soiled with blood, body fluids, secretions or excreta should be followed. The bedding should be moved and shaken as little as possible, as this may release contaminated particles.

For precautions in the home, see Section 11.3.3.1.

ONS, p. 29 ♦ OSHA, Section Vc3

* Health Canada: Infection Control Guidelines. Hand Washing, Cleaning, Disinfection and Sterilization in Health Care, December 1998, p. 34 to 36.

15 MEDICAL, BIOLOGICAL AND ENVIRONMENTAL MONITORING

15.1 Issues and Risks

Regarding evidence concerning the risks

Despite the adoption of safe practices in Pharmacy Departments with respect to the management and handling of hazardous drugs (particularly *antineoplastic* type hazardous drugs), workers may still be exposed. During the past decade, a number of investigators have demonstrated that concentrations of various hazardous drugs could be found in the urine of people who administered or prepared the drugs (NIOSH, 2004). However, the consequences of occupational exposure are difficult to document and the results of studies are inconsistent, as the work methods and facilities are constantly changing. The presence of hazardous drugs in the urine of workers does, however, indicate inadequacies in the preventive measures. The work done to date primarily focuses on the use and handling of and contamination by antineoplastic type hazardous drugs.

Genotoxic effects have been demonstrated. Those most often reported include such reproductive effects as fetal death, congenital anomalies and infertility. A recent systematic review (via meta-analysis) of the effect of antineoplastic drugs on health revealed a slight increase in the risk of spontaneous abortion (OR 1.46, CI 1.11-1.92) in exposed workers (Dranitsaris, 2005; Sessink, 1999). This study also indicated that occupational exposure to antineoplastic agents is associated with a slight increase in the number of malformations, stillbirths, cancers and acute health problems; however, the number of studies and their size are too limited for these observations to be statistically significant (see Section 2.3.2).

Medical monitoring

The toxic effects of occupational exposure to hazardous drugs are still not well known, occur late in a number of systems and are non-specific. The publication of the NIOSH Alert clearly illustrates, however, the concerns raised by the study results suggesting a cause and effect relationship between some types of occupational exposure and certain health effects. Despite this, the NIOSH recommendations regarding medical monitoring are not supported by the evidence, as no epidemiological studies have been performed based on the long-term follow-up of workers exposed to hazardous drugs.

There is no evidence to conclude that physical examination and the systematic search for symptoms allows the early detection of conditions resulting from occupational exposure to hazardous drugs. No conclusive assessments of the efficacy and usefulness of such monitoring have been performed. NIOSH particularly advocates the search for symptoms involving the skin or mucosa which reveal acute exposure. These traditional practices are not, *a priori*, valid tools with which to monitor health effects. They do not contribute to prevention or to the evaluation of the effectiveness of the measures implemented, particularly when there are only a small number of workers involved. In addition, medical monitoring cannot differentiate between problems (e.g. miscarriages, malformations, leukemias) related to occupational exposure and those which are not.

From a technical standpoint, medical monitoring can also be performed through the biological monitoring of genotoxicity (genes-chromosomes-DNA). Knowledge in this regard is progressing; however, the interpretation of the test results can be difficult. There remains a great deal of uncertainty regarding individual variability and the causal relationship between biomarker variation and the environment or the likelihood of developing pathology. Even today, this type of monitoring should only be done in a research setting.

Biological monitoring of exposure

It is now possible to measure the concentration of certain hazardous drugs in the blood or urine. Such measurement is sometimes done to adjust patient prescriptions (e.g. methotrexate, busulfan). However, in many instances, the analytical methods developed are only available in a research setting. It is reasonable to think that, over the next few years, once they have been validated and recognized, some of these methods will become more widely and commercially available.

A wide variety of hazardous drugs is handled in every pharmacy department, as well as in the care units and outpatient clinics. In the medium term, the assessment of worker exposure could be performed by identifying one or more of the most frequently used drugs and periodically measuring their concentrations in the blood or urine. Currently, however, there are no reference values in this regard. In addition, the finding of minute traces (in nanograms or picograms) must be interpreted with a great deal of caution.

In theory, this type of monitoring could probably provide a more accurate picture of actual occupational exposure than environmental monitoring and confirm the effectiveness of the corrective action being taken in the workplace. The results would take into account the actual effectiveness of both the protective measures for each worker and the work techniques. However, a biological monitoring protocol has yet to be validated and this type of monitoring may present drawbacks for the workers which are not yet well-documented. In particular, relatively little is known about the relationship between the level and duration of worker exposure and the likelihood of developing a health problem (Fransman, 2007). In addition, often not enough is known regarding how low doses of these drugs are metabolized in the body (Dranitsaris, 2005). The interpretation of the results in a group of workers may help circumvent the risk of adverse effects likely to result from analysis of a single individual and would, in all likelihood, be more reliable. Despite this, we are currently not recommending introducing this type of monitoring and these tests should only be used in a research setting.

Precautionary reassignment of pregnant or nursing workers

While improving preventive measures reduces exposure, the very importance of these measures and the necessity for periodic monitoring via environmental measurements and evaluation of work techniques confirm the existence of risk. Reducing contamination depends on many factors (facilities, the use of good techniques by the worker and her colleagues, protective equipment, thorough cleaning, etc.) and failures or disruptions can occur. Pregnant workers are entitled to be assigned to avoid any exposure – even accidental.

Precautionary reassignment prior to conception

Despite several requests in this regard, the working group is not issuing any formal recommendations in this guide regarding the reassignment of workers who are planning a pregnancy. In our opinion, such a measure will become less relevant as exposure control improves.

Exclusion of workers who have been treated for cancer

While it is true that the drugs used to treat a cancer can increase the risk of developing a new cancer, the level of occupational exposure is so marginal in comparison to the doses used during treatment that we do not feel it warranted to prohibit these individuals from resuming their work. However, the clinician should have the final word in this regard.

Environmental monitoring

Environmental monitoring allows the evaluation and measurement of chemical contamination by hazardous drugs. In view of the seriousness of the potential effects, the *Act respecting Occupational Health and Safety* and caution itself suggest reducing exposure as low as reasonably achievable (ALARA) (Turci, 2006). While an acceptable level has yet to be determined by occupational health and safety organizations, a scientific review of the publications in this regard should be carried out. For example, the August 15, 2006 update proposed by the United States Pharmacopoeia discusses a maximum acceptable threshold for cyclophosphamide of 1 ng/cm^2 (USP, 2006).

A number of organizations recommend keeping a record of environmental measurements. The ASSTSAS Hazardous Drug Committee supports this recommendation. To this end, the Committee has requested the help of the INSPQ Toxicology Laboratory in developing a technique for detecting and measuring traces of antineoplastic agents using samples taken from work surfaces. Tests have been developed to measure three agents. They are available from the INSPQ and are based on the procedures described in Appendix 5.

An Environmental Monitoring Program should provide for the periodic verification of the level of work surface contamination in institutions. An evaluation should be performed prior to implementing the preventive measures proposed in the ASSTSAS guide and repeated once they are in place. Thereafter, an evaluation should be performed annually or at the time of major changes in the facilities (e.g. change in preparation cabinets) or practices (e.g. new preparation or administration techniques, new hygiene and sanitation protocol). The guide suggests measurement sites in the Pharmacy Department, care units and outpatient clinics.

As there are currently no exposure standards (except for cyclophosphamide, for which a standard of 1 ng/cm^2 is proposed) and to help the institutions interpret their results, a compilation of the contamination values from 34 studies has been published in the INSPQ Bulletin **d'in**formation toxicologique (toxicology information newsletter) (Bussières *et al.*, 2006).

To summarize, the position of the Working Committee is as follows:

Type of follow-up	Working Committee Position
Medical monitoring	Not recommended
Biological monitoring of exposure	Not recommended
Environmental monitoring	Strongly recommended using the tests available
Recording of accidental exposure	Mandatory, in accordance with the LATMP legislation
Precautionary reassignment of pregnant or nursing workers	Immediate reassignment, to avoid exposure (even accidental)
Precautionary reassignment prior to conception	No recommendation
Exclusion of workers who have been treated for cancer	Not recommended, except on the advice of the attending physician

15.2 Exposed Workers

- Shipping and receiving clerks (e.g. stock-keeper, storeroom clerk)
- Hygiene and Sanitation Department workers
- Pharmacy Department workers (e.g. pharmacist, clerk, pharmacy technician)
- Care unit / outpatient clinic / home care workers (e.g. nurses, physicians, inhalation therapists, patient service associates)
- Laboratory workers (e.g. technicians performing tests on biological samples from exposed patients)

15.3 Preventive Measures

15.3.1 Monitoring of Exposure to Hazardous Drugs

RATING: +++

Be aware of and analyze worker exposure for preventive purposes.

RECOMMENDATIONS

15.3.1.1 Every institution should record the results of environmental monitoring measurements (see 15.3.2), as well the accidental exposures to hazardous drugs (see 12.3.3.4), in order to provide an overall analysis.

15.3.1.2 The Hazardous Drug Committee should periodically discuss the profile of the environmental contamination and the hazardous drug-related incidents and accidents, in order to establish their causes and effects, as well as the proper corrective measures. The workers involved in the use of hazardous drugs should be informed of the purposes, methods (and their limitations) and interpretation of the results of the environmental monitoring. The steps that will be taken to improve situations deemed critical should also be explained and understood.

ASHP, p. 1185 ♦ NIOSH, p. 18, 19

15.3.2 Environmental Monitoring

RATING: ++

Establish an Environmental Monitoring Program, based on the following procedures.

RECOMMENDATIONS

15.3.2.1 Every institution should plan regular monitoring activities with respect to both the work environment and work activities. An Environmental Monitoring Program would allow the periodic checking of contamination due to antineoplastic type hazardous drugs on work surfaces in the institution. The institution should contact the INSPQ Laboratoire de toxicologie (Toxicology Laboratory), which provides tests to measure surface contamination by three hazardous drugs (see Appendix 5).

15.3.2.2 An evaluation should be performed prior to implementing the preventive measures proposed in the ASSTSAS guide and repeated once they are in place. Thereafter, an evaluation should be performed annually or at the time of major changes in the facilities (e.g. change in preparation cabinets) or practices (e.g. new preparation or administration techniques, new cleaning protocol). The evaluations may also be used to validate the effectiveness of cleaning activities (e.g., following the *decontamination* of the safety cabinet, to validate the effectiveness of the decontamination).

15.3.2.3 Measurement of the degree of chemical contamination in the Pharmacy Department can be based on samples from the following suggested sites:

- receiving and unpacking areas (unpacking table, exterior surface of drug containers from manufacturers, floors, etc.);
- storage area (work table, storage shelves, cart, etc.);
- preparation area (preparation cabinet work surface, grille in front of the cabinet work surface, floor in front of the hood, outside window of the preparation cabinet, container/content verification counter, refrigerator door, floor under the technician's chair, exterior of drug bags, interior of *hazardous drug transport container*, etc.);

While there is no minimum recommended number of sites, we feel that samples from at least 12 sites per pharmacy are sufficient. The sampling sites and frequency of verification are determined according to the results obtained and how often the tasks are performed.

15.3.2.4 Measurement of the level of chemical contamination in the care units and outpatient clinics can be based on samples from the following suggested sites:

- in administration areas (tubing, floor near the administration areas, telephone, door handle, wall where the gowns (if reused) are hung, counter used to prime the hazardous drug tubing, arms of chairs, floor near the hazardous drug waste receptacles, pumps, etc.);
- in other areas (patient waiting room, patient rooms, cytotoxic waste storage area, storage area for sanitary maintenance equipment, etc.). The sampling sites and frequency of verification are determined according to the results obtained and how often the tasks are performed.

15.3.2.5 The institution should keep a record of the results of the environmental measurements. Based on Article 43 of the *Règlement sur la santé et la sécurité au travail* (Regulation respecting occupational health and safety), the records should be kept for at least 5 years. It may be useful to keep them longer for retrospective study purposes.

NIOSH, p. 19 ♦ OPQ, Section 12.4.1

15.3.3 Medical and Biological Monitoring

RATING: ++

Establish an accidental exposure record.

RECOMMENDATIONS

15.3.3.1 Medical monitoring of effects, using questionnaires and tests (including the biological monitoring of genotoxicity), should not be introduced as it does not allow the effective prevention of health problems related to exposure to hazardous drugs. (+)

15.3.3.2 We do not recommend undertaking biological monitoring of exposure at present, as its usefulness and effectiveness have not been demonstrated and as there are no validated protocols available.

15.3.3.3 Any significant accidental exposure (i.e., direct exposure of the skin or mucosa) to hazardous drugs should be reported to the OHS Department of the institution and recorded in the worker's file (see 12.3.3.4).

15.3.3.4 Every institution must keep the incident and accident reports sent to the OHS Department and/or keep a record of episodes of accidental exposure (see 12.3.3.4).

APES, p. 5-21 to 5-23 ♦ ASHP, p. 1185 ♦ CSHP, Section 8.1 ♦ NIOSH, p. 18 ♦ ONS, p. 35-42 ♦ OSHA, Section VI

15.3.4 Precautionary Reassignment

RATING: ++

Adopt rules regarding the reassignment of workers exposed to antineoplastic type hazardous drugs in certain situations.

RECOMMENDATIONS

15.3.4.1 Upon receipt of a precautionary reassignment request from a pregnant or nursing worker, the employer must comply with the recommendations, in accordance with Sections 40 *et seq* of the LSST. When the risk of handling hazardous drugs is indicated on the certificate presented by the worker, the employer should reassign the worker to an area which is not contaminated and where there is no risk of accidental contamination.

15.3.4.2 Reassigning a worker who has been treated for cancer is not recommended, except on the advice of the attending physician.

APES, p. 5-23 ♦ ASHP, p. 1185 ♦ CSHP, Section 8.17 ♦ NIOSH, p. 11 ♦ OSHA, Section VIf

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Appendices

APPENDIX 1- Glossary

TERMS	DEFINITIONS	COMMENTS
Antineoplastic Antineoplasic	Substance that destroys cancer cells or prevents their proliferation 📖 GDT (English /French database)	Anticancer agent is used as a synonym
Antineoplastic Drug	A drug that controls or kills the cancer cells. 📖 CSHP	
Aseptic Preparation Area	Room or area designated for the preparation of sterile products. 📖 OPQ	It includes the critical area and a clean room.
Aseptic Technique	Use of procedures that minimize or prevent contamination by micro-organisms during the preparation of sterile products. 📖 ASHP ♦ OPQ	
Batch Preparations	Preparation or repackaging of multidose units which will not be used immediately, in a single operation, by the same person, in accordance with preparation in standardized batches. 📖 OPQ	
Biological Safety Cabinets	Ventilated cabinets with an inflow of air to protect the worker and a downflow curtain of air (HEPA filtered) to protect the product. The exhaust is HEPA filtered to protect the environment. 📖 CSHP	The word "hood" is often used as a substitute for "cabinet". Also used is "laminar flow hood". In this guide, the term "preparation cabinet" is also used.
Chemotherapy Drug	Drug used for the treatment of cancer. 📖 ASHP	
Cleaning	Physical removal of dust, soil, blood, secretions, excretions and microorganisms, with water, detergents and mechanical action. 📖 CSHP	
Clean Room	Aseptic preparation area equipped to control environmental contamination due to particles or micro-organisms. 📖 OPQ	Grade C (ISO 7) or D (ISO 8) room, built and used in such a way as to limit the introduction, generation and retention of contaminants.
Closed System	A device which prevents the escape of contaminants or unfiltered air into the immediate environment. 📖 ASHP	

TERMS	DEFINITIONS	COMMENTS
Closed-system Drug-Transfer Device	Closed-system drug-transfer devices mechanically prevent the transfer of environmental contaminants into the system and the escape of hazardous drugs or vapours out of the system. ASHP	E.g.: PhaSeal® or Tevadaptor® systems
Critical Area	Grade A (ISO 5) area designed to protect the sterile products prepared in this area from secondary microbial contamination. OPQ	In a pharmacy, the critical area is usually the laminar flow hood or the biological hood located in the aseptic preparation area or the clean room..
Critical Surface	Surface that comes into contact with the sterile product or the packaging materials. OPQ	
Cytotoxic	Property of a substance or drug which has a toxic effect on a living cell. Which interferes with or prevents cell function. CSA ♦ GDT	Term describing pharmaceuticals used for the treatment of cancer and, in some cases, for the treatment of other conditions (e.g. psoriasis, arthritis)
Cytotoxic Pharmaceutical Waste Cytotoxic Waste	Antineoplastic drugs and residues from their preparation and use, as well as any material contaminated by these drugs. CSA, Z317.10-01 ♦ Guide gestion déchets	Any material that comes into contact with antineoplastic drugs during their storage, handling, preparation, administration and disposal (packaging material, protective equipment, syringes, tubing, drug bags, etc.).
Deactivation	Treating a chemical agent (such as a hazardous drug) with another chemical, heat, ultraviolet light or other agent to make it less hazardous. ASHP	
Decontamination	Inactivation, neutralization or removal of toxic agents, usually by chemical means. ASHP	
Disinfecting	Removing the viable organisms from a surface prior to the preparation of sterile products, using alcohol 70% or another effective disinfecting agent. ASHP	
Disposable Protective Film	Patient-specific disposable container in a cassette drawer for daily unit dose distribution.	

TERMS	DEFINITIONS	COMMENTS
Engineering Controls	Devices designed to eliminate or reduce the source of worker exposure to contaminants. Examples: hoods, retracting syringe needles, negative-pressure ventilation of an area where hazardous products are handled, etc. ASHP	
Extravasation	Leakage of a fluid outside its normal pathway and invasion of the adjacent tissues. GDT	
Final Storage Area	Area in the institution where waste is stored prior to its collection by the company specializing in its disposal. CSA, Z317.10-01	
Genotoxic	Substance capable of damaging the DNA and causing mutations as a result. ASHP	
Glove Box	Gas-tight cabinet equipped with gloves and designed for the handling, under visual control, of medical products, toxic substances and radioactive materials. ASHP ♦ GDT	Work is performed by inserting the hands into the gloves attached to the cabinet. Its purpose is to protect the worker, the product and the immediate environment.
Hazardous Drug	Any drug identified by at least one of the following six criteria: carcinogenicity, teratogenicity, reproductive toxicity, organ toxicity at low doses, genotoxicity, as well as new drugs that mimic existing hazardous drugs in structure or toxicity. ASHP	
Hazardous Drug Delivery Container	Bins or boxes from the manufacturer or distributor.	
Hazardous Drug Preparation Containers	Syringes, bags, bottles used for the preparation and administration of drugs.	
Hazardous Drug Storage Container	Bins, trays or other containers used to store hazardous drugs.	
Hazardous Drug Transport Container	Rigid containers for the transport of hazardous drugs within the institution. They must be shock-resistant, waterproof and made of a material which can be easily cleaned and decontaminated in the event of leakage.	
Hazardous Waste	Waste which, due to its nature or quantity, poses a risk to health or the environment and for which special disposal or neutralization procedures must be used. Environment Canada	Its characteristics, such as toxicity, inflammability, corrosive property and occasionally, its persistence, means that it can have many detrimental effects.

TERMS	DEFINITIONS	COMMENTS
HEPA Filter	High-efficiency filter to remove particulate from the air. 📖 ASHP	99.97% effective in filtering out particulate 0.3 microns in diameter.
HIIC or hyperthermic Intraoperative Intraperitoneal Chemotherapy	HIIC is an innovative technique for the local control of the dissemination of cancer cells in the abdominal cavity. It consists of lavage of the abdominal cavity with a highly concentrated chemotherapeutic agent (concentration twenty times higher than that administered intravenously), heated to 43°C to increase the toxic effect of the chemotherapy on the cancer cells. This lavage can be performed with an open or closed abdomen during the surgical procedure and extended following the procedure in the intensive care phase.	
Intrathecal	Administration via injection into the fluid contained between the thin layers of tissue covering the brain and spinal cord. 📖 National Cancer Institute (U.S.A.)	
ISO 5, 7, or 8	International Standard Level / particles/m^3 / American Standard particles/ft^3 ISO 5: 3520 / 100 ISO 7: 352 000 / 10 000 ISO 8: 3 520 000 / 100 000 📖 ISO Standard 14644-1	The clean rooms are classified according to the number of particles per unit of volume. The conventional standard, *US FED STD 209E*, used cubic feet, but has been replaced by *ISO Standard 14644-I*, expressed in cubic metres.
Lab Coat	Disposable or reusable, long-sleeved garment, buttoned in the back or front, worn over other clothing to avoid soiling it. 📖 ASHP	Usually made of permeable material.
Material Safety Data Sheet (MSDS)	Summary of the toxicological, physical and chemical properties of a chemical agent and the preventive measures required to handle it safely. This sheet is provided by the manufacturer. 📖 ASHP	
Mutagenic	Substance capable of producing genetic modifications in living organisms. 📖 ASHP	
Packaging Material	Packaging items in direct contact with the sterile product. 📖 OPQ	
Personal Protective Equipment (PPE)	Equipment that protects the worker from exposure to physical or chemical risks. 📖 ASHP	E.g. gloves, gowns, respirators, goggles or protective face shields, etc.

TERMS	DEFINITIONS	COMMENTS
Pharmaceutical Waste	Pharmaceuticals (drugs or medicinal chemical agents) which are no longer usable for care or which are expired or contaminated, have not been properly stored or are no longer required. CSA ♦ CSHP	If they have been contaminated by cytotoxic agents, they must be considered cytotoxic pharmaceutical waste.
Raw Material	Any substance of defined quality, with the exception of packaging materials, used for the preparation of sterile products. OPQ	
Respiratory Protection Apparatus (RPA) Respirator	Type of personal protective equipment that prevents hazardous products from reaching the respiratory system, usually via a filtration process or the flow of uncontaminated air. ASHP	Example: RPA N95 or N100 A surgical mask does not provide the worker with respiratory protection. It is not an approved RPA.
Sterile	Free of micro-organisms capable of multiplying. OPQ	
Sterile Preparation Cabinets	See *Biological Safety Cabinets*.	
Surface Decontamination	Transfer of a hazardous drug contaminant from a fixed surface (counter, solution bag, etc.) to a disposable surface (towels, cloths, etc.). ASHP	There is no established procedure for the decontamination of surfaces contaminated by hazardous drugs. Use of a gauze pad soaked in alcohol, sterile water, peroxide or sodium hypochlorite may be effective. There are no products universally effective against every hazardous drug.
USP 797	American standard for the preparation of sterile products. Issued in January 2004.	Under review in 2006.
Vesicant	Any agent that may lead to blister formation, severe tissue injury or tissue necrosis in the presence of extravasation. Mosby's Medical, Nursing and Allied Health Dictionary	

APPENDIX 2 - List of Hazardous Drugs (according to NIOSH) and According to the Classifications of the MSSS Liste de médicaments-établissements

This appendix contains the list of hazardous drugs in the NIOSH Alert published in 2004. The list includes labeling suggestions for health professionals and patients. It should be noted that the labeling corresponds closely to the preventive measures proposed in this guide.

However, during the summer of 2007, NIOSH began a consultation process with a view to adding other drugs to this list. As part of this consultation process, NIOSH published a list of drugs considered hazardous or non-hazardous, specifying for each the risks related to carcinogenicity, teratogenicity, mutagenicity, reproductive toxicity or organ toxicity. Unfortunately, the initial list (shown below) does not include a summary table showing each drug according to type of risk. The reader is strongly encouraged to check the progress of this update on the NIOSH Web site (http://www.cdc.gov/niosh/review/public/105/default.html).

HAZARDOUS DRUGS	AHFS	THERAPEUTIC CLASSIFICATION	SUGGESTED LABELING FOR HEALTH PROFESSIONALS AND PATIENTS	
			Cytotoxic / Cytotoxique	"CAUTION" Indication
Aldesleukin	10:00	Antineoplastic agents	✓	
Alemtuzumab	10:00	Antineoplastic agents	✓	
Alitretinoin	84:36	Others, skin and mucosa		✓
Altretamine	10:00	Antineoplastic agents	✓	
Amsacrine	10:00	Antineoplastic agents	✓	
Anastrozole	10:00	Antineoplastic agents	✓	
Arsenic trioxide	10:00	Antineoplastic agents	✓	
Asparaginase	10:00	Antineoplastic agents	✓	
Azacitidine	Not in AHFS	Antineoplastic agents	✓	
Azathioprine	92:00	Unclassified therapeutic agents (immunosuppressant)		✓
Bacillus Calmette-Guerin	80:12	Vaccines		✓
Bexarotene	10:00	Antineoplastic agents	✓	
Bicalutamide	10:00	Antineoplastic agents	✓	
Bleomycin	10:00	Antineoplastic agents	✓	
Busulfan	10:00	Antineoplastic agents	✓	
Capecitabine	10:00	Antineoplastic agents	✓	
Carboplatin	10:00	Antineoplastic agents	✓	
Carmustine	10:00	Antineoplastic agents	✓	
Cetrorelix acetate	92:00	Unclassified therapeutic agents (GnRH antagonist)		✓

HAZARDOUS DRUGS	AHFS	THERAPEUTIC CLASSIFICATION	SUGGESTED LABELING FOR HEALTH PROFESSIONALS AND PATIENTS	
			Cytotoxic Cytotoxique	"CAUTION" Indication
Chlorambucil	10:00	Antineoplastic agents	✓	
Chloramphenicol	8:12	Antibiotics		✓
Choriogonadotropin alfa	68.18	Gonadotropins		✓
Cidofovir	8:18	Antivirals		✓
Cisplatin	10:00	Antineoplastic agents	✓	
Cladribine	10:00	Antineoplastic agents	✓	
Colchicine	92:00	Unclassified therapeutic agents (mitotic inhibitor)		✓
Cyclophosphamide	10:00	Antineoplastic agents	✓	
Cyclosporin	92:00	Immunosuppressant		✓
Cytarabine	10:00	Antineoplastic agents	✓	
Dacarbazine	10:00	Antineoplastic agents	✓	
Dactinomycin	10:00	Antineoplastic agents	✓	
Daunorubicin HCl	10:00	Antineoplastic agents	✓	
Denileukin	10:00	Antineoplastic agents	✓	
Dienestrol	68:16.04	Estrogens		✓
Diethylstilbestrol	Not in AHFS	Nonsteroidal synthetic estrogen		✓
Dinoprostone	76:00	Oxytocics		✓
Docetaxel	10:00	Antineoplastic agents	✓	
Doxorubicin	10:00	Antineoplastic agents	✓	
Dutasteride	92:00	Unclassified therapeutic agents (5-alpha reductase inhibitor)		✓
Epirubicin	10:00	Antineoplastic agents	✓	
Ergonovine/methylergonovine	76:00	Oxytocics		✓
Estradiol	68:16.04	Estrogens		✓
Estramustine phosphate sodium	10:00	Antineoplastic agents	✓	
Estrogen-progestin combinations	68:12	Contraceptives		✓
Estrogens, conjugated	68:16.04	Estrogens		✓

HAZARDOUS DRUGS	AHFS	THERAPEUTIC CLASSIFICATION	SUGGESTED LABELING FOR HEALTH PROFESSIONALS AND PATIENTS	
			Cytotoxic Cytotoxique	"CAUTION" Indication
Estrogens, esterified	68:16.04	Estrogens		✓
Estrone	68:16.04	Estrogens		✓
Estropipate	68:16.04	Estrogens		✓
Etoposide	10:00	Antineoplastic agents	✓	
Exemestane	10:00	Antineoplastic agents	✓	
Finasteride	92:00	Unclassified therapeutic agents (5-alpha reductase inhibitor)		✓
Floxuridine	10:00	Antineoplastic agents	✓	
Fludarabine	10:00	Antineoplastic agents	✓	
Fluorouracil	10:00	Antineoplastic agents	✓	
Fluoxymesterone	68:08	Androgens		✓
Flutamide	10:00	Antineoplastic agents	✓	
Fulvestrant	10:00	Antineoplastic agents	✓	
Ganciclovir	8:18	Antivirals		✓
Ganirelix acetate	92:00	Unclassified therapeutic agents (GnRH antagonist)		✓
Gemcitabine	10:00	Antineoplastic agents	✓	
Gemtuzumab ozogamicin	10:00	Antineoplastic agents	✓	
Gonadotropin, chorionic	68.18	Gonadotropins		✓
Goserelin	10:00	Antineoplastic agents	✓	
Hydroxyurea	10:00	Antineoplastic agents	✓	
Ibritumomab tiuxetan	10:00	Antineoplastic agents (monoclonal antibodies bound to radioactive isotopes, thus risk of radioactivity)	✓	
Idarubicin	Not in AHFS	Antineoplastic agents	✓	
Ifosfamide	10:00	Antineoplastic agents	✓	
Imatinib mesylate	10:00	Antineoplastic agents	✓	
Interferon alfa-2a	10:00	Antineoplastic agents	✓	
Interferon alfa-2b	10:00	Antineoplastic agents	✓	
Interferon alfa-n1	10:00	Antineoplastic agents	✓	

HAZARDOUS DRUGS	AHFS	THERAPEUTIC CLASSIFICATION	SUGGESTED LABELING FOR HEALTH PROFESSIONALS AND PATIENTS	
			Cytotoxic Cytotoxique	"CAUTION" Indication
Interferon alfa-n3	10:00	Antineoplastic agents	✓	
Irinotecan HCl	10:00	Antineoplastic agents	✓	
Leflunomide	92:00	Unclassified therapeutic agents (antineoplastic agent)	✓	
Letrozole	10:00	Antineoplastic agents	✓	
Leuprolide acetate	10:00	Antineoplastic agents	✓	
Lomustine	10:00	Antineoplastic agents	✓	
Mechlorethamine	10:00	Antineoplastic agents	✓	
Megestrol	10:00	Antineoplastic agents	✓	
Melphalan	10:00	Antineoplastic agents	✓	
Menotropines	68.18	Gonadotropins		✓
Mercaptopurine	10:00	Antineoplastic agents	✓	
Methotrexate	10:00	Antineoplastic agents	✓	
Methyltestosterone	68:08	Androgens		✓
Mifepristone	76:00	Oxytocics		✓
Mitomycin	10:00	Antineoplastic agents	✓	
Mitotane	10:00	Antineoplastic agents	✓	
Mitoxantrone HCl	10:00	Antineoplastic agents	✓	
Mycophenolate mofetil	92:00	Immunosuppressants		✓
Nafarelin	68.18	Gonadotropins		✓
Nilutamide	10:00	Antineoplastic agents	✓	
Oxaliplatin	10:00	Antineoplastic agents	✓	
Oxytocin	76:00	Oxytocics		✓
Paclitaxel	10:00	Antineoplastic agents	✓	
Pegasparagase	10:00	Antineoplastic agents	✓	
Pentamidine isethionate	8:40	Miscellaneous anti-infectives		✓
Pentostatin	10:00	Antineoplastic agents	✓	
Perphosphamide	Not in AHFS	Antineoplastic agents	✓	
Pipobroman	Not in AHFS	Antineoplastic agents	✓	
Piritrexim isethionate	Not in AHFS	Antineoplastic agents	✓	

HAZARDOUS DRUGS	AHFS	THERAPEUTIC CLASSIFICATION	SUGGESTED LABELING FOR HEALTH PROFESSIONALS AND PATIENTS	
				"CAUTION" Indication
Plicamycin	Not in AHFS	Antineoplastic agents	✓	
Podoflilox	84:36	Others, skin and mucosa		✓
Podophyllum resin	84:36	Others, skin and mucosa		✓
Prednimustine	Not in AHFS	Antineoplastic agents	✓	
Procarbazine	10:00	Antineoplastic agents	✓	
Progesterone	68:32	Progestins		✓
Progestins	68:12	Contraceptives		✓
Raloxifen	68:16.12	Estrogen agonists-antagonists		✓
Raltitrexed	Not in AHFS	Antineoplastic agents	✓	
Ribavirin	8:18	Antivirals		✓
Streptozocin	10:00	Antineoplastic agents	✓	
Tacrolimus	92:00	Unclassified therapeutic agents (immunosuppressant)		✓
Tamoxifen	10:00	Antineoplastic agents	✓	
Temozolomide	10:00	Antineoplastic agents	✓	
Teniposide	10:00	Antineoplastic agents	✓	
Testolactone	10:00	Antineoplastic agents	✓	
Testosterone	68:08	Androgens		✓
Thalidomide	92:00	Unclassified therapeutic agents (immunomodulator)		✓
Thioguanine	10:00	Antineoplastic agents	✓	
Thiotepa	10:00	Antineoplastic agents	✓	
Topotecan	10:00	Antineoplastic agents	✓	
Toremifene citrate	10:00	Antineoplastic agents	✓	
Tositumomab	Not in AHFS	Antineoplastic agents (monoclonal antibodies bound to radioactive isotopes, thus risk of radioactivity)	✓	

HAZARDOUS DRUGS	AHFS	THERAPEUTIC CLASSIFICATION	SUGGESTED LABELING FOR HEALTH PROFESSIONALS AND PATIENTS	
				"CAUTION" Indication
Tretinoin	84:16	Cell stimulants and proliferants		✓
Trifluridine	52:04.06	Antivirals		✓
Trimetrexate glucuronate	8:40	Miscellaneous anti-infectives (folate antagonist)		✓
Triptorelin	10:00	Antineoplastic agents	✓	
Uracil mustard	Not in AHFS	Antineoplastic agent	✓	
Valganciclovir	8:18	Antivirals		✓
Valrubicin	10:00	Antineoplastic agents	✓	
Vidarabine	52:04.06	Antivirals		✓
Vinblastine sulfate	10:00	Antineoplastic agents	✓	
Vincristine sulfate	10:00	Antineoplastic agents	✓	
Vindesine	Not in AHFS	Antineoplastic agent	✓	
Vinorelbine tartrate	10:00	Antineoplastic agents	✓	
Zidovudine	8 :18	Antiretroviral agents		✓

APPENDIX 3 - Survey Regarding Practices in the Network

The Committee used a questionnaire to verify the preventive measures in use in Quebec on March 31, 2006 (in particular, compliance with the NIOSH recommendations). All of the Pharmacy Department Heads in institutions with more than 100 beds (at least 50 short-term care beds) received the questionnaire via email (61 questionnaires sent). The response rate was 87%. In 89% of cases, the questionnaire was completed with the help of the Nursing Department. Non-respondents received two email reminders and one telephone reminder. The results of the survey provide an overview of current practices in the network. This appendix describes the main findings, broken down according to the steps in the medication circuit. The findings were also reviewed in two articles – one, a brief overview (Bussières *et al.,* 2006), the other, a detailed description (Bussières *et al.*, 2007).

3.1 Overall Findings

It is interesting to note the following general findings of the survey.

- A significant proportion (more than 60%) of Pharmacy Department Heads and oncology pharmacists are familiar with the principal documents related to the normative framework regarding sterile preparations. A smaller proportion of the nursing staff is also familiar with this framework. It must be stressed that there are guidelines published by nursing associations which also use these principles of good practice. This tool was not included in the choices offered in the survey.
- From the publication of the NIOSH recommendations to March 31, 2006, only 33% of respondents (n = 16/49) had carried out an oncology practice compliance analysis.
- Policies and procedures are in place in proportions ranging from 0 to 87%, depending on the issue. The ten issues with fewer than 50% of policies and procedures primarily include the receiving and unpacking of inventory, the monitoring of preparation room controls, the training program for unit / clinic workers, medical, environmental and microbial monitoring, the cleaning of units / clinics and the administration of hazardous drugs in the home.
- 23% of the institutions (n = 53) have a Cytotoxic and Hazardous Drug Interdisciplinary Committee.
- 88% of the respondents (46/52) indicated having used training material to update their workers, including the APES video on sterile preparations (54%), the APES video on sterile preparations in oncology (96%), the ASHP video on sterile handling (9%), the work by Buchanan *et al.* for the ASHP (7%) or other tools (17%).
- The respondents were asked to describe their institution's action plan regarding hazardous drug preparation. Seventy-two per cent (36/50) are planning a self-assessment of their compliance. Sixteen institutions are planning to do so within one year, based on Ordre des pharmaciens du Québec Standard 95.01; twenty are planning to do so within one year based on the ASHP standard and eighteen are planning to do so within one year based on the NIOSH standard. The survey revealed that pharmacy facilities for hematology-oncology preparations often require updating; 57% of the respondents (29/52) are planning to update the satellite pharmacy (or rooms) dedicated to hematology-oncology (59% within 1 year, 21% within 2 years, 14% within 3 years and 5% within 5 years).
- The respondents were asked to rate, in descending order of priority (from the most important (1) to the least important (12)), the areas for which outside third parties, such as the OPQ, ASSTSAS, APES or CHQ (regarding space standards), should propose standards or programs. The findings are shown in the table below.

AREA	RATING, IN DESCENDING ORDER OF PRIORITY (from the most important (1) to the least important (12))				
	Average	Standard Deviation	Median	Interval	Number
Physical facilities	3.7	3.3	2	1 - 12	46
Drug preparation	4.3	3.4	3	1 - 12	46
Drug administration	5.3	3.4	4	1 - 12	46
Worker certification	5.4	3.0	5	1 - 12	46
Medical monitoring	6.2	3.0	6	1 - 12	47
Patient care	6.4	3.1	6	1 - 12	46
Environmental monitoring	6.7	3.5	7	1 - 12	46
Hygiene and sanitation	7.0	3.0	7	1 - 12	46
Waste, accidental exposure and spill management	7.2	2.7	7	1 - 12	47
Unpacking and storage	7.2	2.9	7	1 - 11	47
Receiving and transport	7.6	2.9	8	2 - 12	47
Laundry	10.5	2.1	11.5	4 - 12	46

3.2 Results Regarding Compliance By Medication Circuit Step

The practice compliance criteria were based on the NIOSH recommendations and ASHP guidelines to March 31, 2006. It must be stressed that these criteria were formulated in April 2006, before the Hazardous Drug Committee had made a final decision regarding the contents of this guide. A compliance rate was calculated for each statement, based on the assessment performed by the respondents, and contains the detailed information applicable to each step of the medication circuit.

3.2.1 Receiving and Transport of Drugs (Chapter 5)

COMPLIANCE CRITERIA	COMPLIANCE RATE (%)
Cytotoxic and hazardous drugs are delivered directly from the receiving dock to the Pharmacy Department. (n = 52)	85

3.2.2 Unpacking and Storage

COMPLIANCE CRITERIA	COMPLIANCE RATE (%)
Cytotoxic drugs are stored separately from other drugs, in a cupboard or location clearly identifying the special precautions to be taken during their handling. (n = 53)	55
The stocks of cytotoxic drugs are decontaminated (e.g. cleaned with water, not alcohol, to remove cytotoxic surface contamination) before being stored in the pharmacy. (n = 53)	4
Pharmacy workers wear gloves to unpack and handle cytotoxic drug containers. (n = 53)	17

3.2.3 Planning the Oncology Pharmacy

The survey revealed the following:

- 19% have a risk level of 1 (i.e., preparation based on a single ingredient for a single patient), 60% report a risk level of 2 (i.e., preparation based on one or more ingredients for one or more patients) and 21% have a risk level of 3 (i.e., preparation based on sterile or non-sterile ingredients with terminal sterilization).
- 72% of the respondents have premises (i.e., satellite pharmacy) separate from the main pharmacy for the preparation of cytotoxic drugs. The respondents were asked to identify every area for which the Pharmacy Department has a separate room for the preparations, i.e., room for the unpacking and receiving of inventory (5/53), dedicated storage room (14/53), airlock/access antechamber to the preparation room (12/53), clean or white rooms for sterile preparations (50/53), clean room for non-sterile preparations (7/53), room for inputting prescriptions (34/53), waste storage room (11/53), room for meeting with patients (24/53), records management room (12/53), room for the professionals (22/53). Of the 42 respondents who provided the dimensions of their oncology pharmacy, the average surface area was 25.9 ± 28.3 m^2 [3.5: 127.5]; median 17.6. On average, there were 3.6 ± 2.0 areas per respondent (interval of 0 to 9; median 3).
- Only 36 respondents were able to indicate the pressure in the sterile preparation room versus the adjacent rooms. It was under positive pressure in 7 cases, neutral in 8 and negative in 21. Only 12 respondents were able to indicate the number of air changes per hour or the value of the sterile preparation room pressure gradient.
- With respect to the number of preparation cabinets used for oncology, 53 respondents reported having 1 cabinet, 14 institutions have 2 cabinets, 4 have 3 cabinets and 1 institution has four. The distribution of Class II cabinets by type is illustrated in the table below.

Type	Number
A1	4
B1	4
A2	10
B2	47
Not specified	7
Total	72

- 29 preparation cabinets are 4 ft. wide , while 26 are 6 ft. wide; the others are of varying sizes (i.e., 3 or 5 ft.). 21 cabinets were purchased prior to 1990, 13 during the 1990s and the remainder since 2000.
- Only 6 respondents out of 53 report using a closed-circuit preparation device (i.e., PhaSeal®, Tevadaptor®) during the past year. Half of the respondents (26/52) used a needleless system for drugs administered by nurses. The oncology pharmacy produces an average of 8,615 ± 8,552 (median – 6,050; [100-43,680]) preparations annually. Seven respondents use a pump in their production.
- The practice compliance criteria were based on the NIOSH recommendations and ASHP guidelines to March 31, 2006. The following compliance rates were obtained based on the respondents' evaluations of the various statements:

COMPLIANCE CRITERIA	COMPLIANCE RATE (%)
The Pharmacy Department certifies the preparation cabinets (i.e., hoods, microenvironments) every 6 months. (n = 53)	81
The cytotoxic drug sterile preparation room in the pharmacy only contains the preparation cabinets and the equipment required on a daily basis (i.e., NO refrigerators, no computers/peripherals, no desks, etc.). (n = 53)	45
The Pharmacy Department has a dedicated area for the non-sterile handling of hazardous drugs (e.g. cyclosporin, tacrolimus) for the counting of solid oral forms. (n = 52)	12

3.2.4 Drug Preparation

COMPLIANCE CRITERIA	COMPLIANCE RATE (%)
All cytotoxic drugs (i.e., for oncology) for the patients treated by your institution are prepared in a preparation cabinet. No cytotoxic drugs for parenteral administration are prepared in the units or in the home by nurses. (n = 53)	94
Workers wash their hands before putting on and immediately after removing their gloves, to limit contact contamination. (n = 53)	92
No cytotoxic drugs are placed in an automatic packaging machine. (n = 53)	92
During the preparation of cytotoxic drugs in the pharmacy, the syringes are never filled more than ¾ full. (n = 52)	87
The Pharmacy Department provides its workers with protective equipment (i.e., chemotherapy gloves, impervious gowns, protective shields and goggles) in the event a shipment containing damaged goods is received and the receiving workers are trained and know how to respond should this occur. (n = 52)	58
Pharmacy Department workers wear protective goggles and a respirator (N-95 or better) at all times when cleaning the inside of the cabinet (e.g. when lifting the floor of the work surface). (n = 52)	56

COMPLIANCE CRITERIA	COMPLIANCE RATE (%)
The protective gloves are changed no less than every 30 minutes or when pierced, torn or contaminated or if the worker must leave the preparation cabinet. (n = 53)	51
Pharmacy workers wear two pairs of gloves recognized for use in chemotherapy preparation when handling cytotoxic drugs in preparation cabinets. (n = 53)	45
The Pharmacy Department installs the tubing required for the administration of cytotoxic drugs and primes it (i.e., purges it to remove any air) in the pharmacy. (n = 53)	40
Workers change their protective gown after 3.5 hours of use (i.e., half a day). (n = 52)	35
Pharmacy Department workers are certified (i.e., re-evaluated) each year with respect to the handling, preparation, transport and use of hazardous and cytotoxic drugs. (n = 53)	6

3.2.5 Transport and Storage Following Preparation

COMPLIANCE CRITERIA	COMPLIANCE RATE (%)
All of the cytotoxic drug sterile preparation containers (i.e., bags, syringes) are transported to the care units /clinics in a secure container. (n = 52)	83
The pharmacy workers use uncontaminated gloves to handle the finished product and the cytotoxic drug transport bag. (n = 53)	26

3.2.6 Drug Administration (Chapter 10)

COMPLIANCE CRITERIA	COMPLIANCE RATE (%)
The nurses never crush cytotoxic or hazardous drugs for oral administration. (n = 47)	89
There is a rinsing procedure following the administration of cytotoxic drugs that minimizes the risk of occupational exposure. (n = 37)	81
The nurses wear a protective gown and gloves during the handling of excreta from patients who have received cytotoxic drugs. (n = 51)	55
The nurses wear a protective gown and at least one pair of gloves throughout the entire period of cytotoxic drug administration. (n = 51)	54
The workers change the protective gown after 3.5 hours of use (i.e., half a day). (n = 52)	35
The nurses wear a protective shield/goggles when there is a risk of splashing. (n = 51)	31

3.2.7 Patient Care (Chapter 11)

COMPLIANCE CRITERIA	COMPLIANCE RATE (%)
The patient is given a comprehensive information sheet regarding cytotoxic drugs and the preventive measures to limit exposure, in order to reduce the risk of contamination during treatment (e.g. precautions regarding excreta, how to deal with family, etc.). (n = 3)	57

3.2.8 Management of Waste, Accidental Exposure, Spills and Returns (Chapter 12)

COMPLIANCE CRITERIA	COMPLIANCE RATE (%)
All disposable material used for the administration of *antineoplastic* drugs **is discarded in containers marked "cytotoxic products". (n** = 53)	98
There is a complete spill management kit (i.e., materials, procedure, protective equipment, etc.) in the Pharmacy Department. (n = 53)	94
There is a complete spill management kit (i.e., materials, procedure, protective equipment, etc.) in the targeted care units. (n = 52)	69
The bag containing the antineoplastic drug and the attached administration tubing are discarded as a unit (i.e., without being disconnected). (n = 52)	94

In a spring 2006 survey of Pharmacy Department Heads and Nursing Directors in Quebec health care institutions with a minimum of 50 short-term care beds and oncology activities, there were no particular findings regarding the laundry.

3.2.9 Hygiene and Sanitation (Chapter 13)

COMPLIANCE CRITERIA	COMPLIANCE RATE (%)
The equipment used by the housekeeping workers to clean the pharmacy areas dedicated to the handling/preparation of hazardous and cytotoxic drugs is not used to clean other areas of the hospital. (n = 52)	38

3.2.10 Laundry (Chapter 14)

The survey revealed no particular findings regarding the laundry.

3.2.11 Medical, Biological and Environmental Monitoring

COMPLIANCE CRITERIA	COMPLIANCE RATE (%)
The institution has known, defined criteria regarding the reassignment of a pregnant worker exposed to hazardous and cytotoxic drugs. (n = 51)	73
The Pharmacy Department uses a cytotoxic drug exposure record (i.e., is able to identify the workers exposed and the length of exposure per year). (n = 53)	26
The institution offers a medical monitoring program to pharmacy workers exposed to hazardous and cytotoxic drugs (e.g. annual hemogram, consultation with a physician, etc.). (n = 53)	21
The institution offers a medical monitoring program to the nursing staff exposed to hazardous and cytotoxic drugs (e.g. annual hemogram, consultation with a physician, etc.). (n = 52).	17
The Pharmacy Department checks the surface contamination in the pharmacy due to hazardous and cytotoxic drugs (i.e., measurement of trace residues) annually. (n = 53)	2
The Pharmacy Department carries out microbiological monitoring of its preparation cabinets at least once a week (i.e., using sedimentation with agar). (n = 53)	4

A study of practice compliance will be carried out in health care institutions in 2008, following the distribution of this guide. In addition, it should be noted that a Canadian survey regarding sterile drug preparations (in relation to Chapter 797 of the United States Pharmacopoeia*)*, including hazardous drugs, was conducted in the spring of 2007. The situation in Quebec was described in Pharmactuel 2007; 40(4): 228-31 (http://www.pharmactuel.com/sommaires/200704ge.pdf), while the situation in Canada will be described in 2008 in the Canadian Journal of Hospital Pharmacy.

APPENDIX 4 - Management of Hazardous Drug Spills

This appendix describes a procedure to be followed in the event of a spill, as well as the suggested contents of a spill kit.

The nature and extent of the spill can vary:

- larger or smaller amount;
- pure or diluted product;
- liquid or powder spill;
- spill in a hood or another area of the medication circuit or in the patient's home;
- spill on the floor, on equipment or on a bed, etc.

There are no universal criteria to differentiate a small spill (which can be managed locally) from a large spill (which may require a team that is specially trained and equipped). According to the literature, the criteria vary. To our knowledge, there are no established criteria based on scientifically-conducted studies regarding exposure.

Therefore, this procedure proposes criteria based on our subjective assessment of the risk and official sources such as ASHP:

small spill:	spill, outside a hood, of a diluted product which can be contained using a spill kit; spill, inside a hood, of less than 30 mL.
large spill:	spill of a concentrated drug (e.g. broken drug vial from the supplier); spill, outside the hood, which cannot be contained with a spill kit.

4.1 Spill Kit

The institution must provide a spill kit, at the very least, in every area where there is a possibility of a hazardous drug spill, i.e., receiving area for drugs from suppliers, the Pharmacy Department, every care unit and outpatient clinic where hazardous drugs are administered parenterally, for use by home care nurses. The kit should contain enough material to absorb approximately 1 litre (1000 mL) of fluid. It should also include the following:

- simple instructions to expedite the cleaning procedure;
- checklist of various measures, to document the event;
- material to identify and mark off the spill area (cones, yellow tape, etc.);
- enough absorbent material (towels or absorbent pads, absorbent powder, etc.) to absorb a spill of approximately 1000 mL (volume of a bag of solution);
- two or more pairs of gloves (latex, neoprene or nitrile);
- one pair of thick gloves (utility);
- one protective, splash-resistant gown (Section 4.1.7.8);
- a NIOSH-approved N95 or N100 *respirator*. Remember, the respirator must be chosen as part of a Respiratory Protection Program that takes the risk of spills into account.

  Note: larger spills can be managed by a team trained for this purpose and equipped with respirators for dust and vapours. (See 4.1.7.11)
- a face shield or protective goggles (See 4.1.7.10);
- ten disposable absorbent cloths;
- two plastic bags identified with the cytotoxic drug hazard symbol;
- a small disposable dustpan and broom to safely collect glass fragments/shards;
- a safe, rigid container to hold the glass fragments or shards;

- labels for cytotoxic products;
- an alkaline detergent to clean up the spill;
- conditions specifying when a shower or eye wash is required.

4.1.1 Home Kit:

Leave a spill kit with patients receiving home care. It will be smaller than the kit used in the hospital. Pack it in a bag to keep everything together. That way, if it is not used, it can be given to another patient.

4.1.2 Commercial Kits

The following commercial products have been available since December 1, 2006. The list is not exhaustive and other, comparable products may be available. The Hazardous Drug Committee does not recommend one commercial product over another. The names of these commercial products are provided to facilitate research by the institutions. The key words used to search the web for this type of product are (among others) *hazardous drug spill kit.*

JT Baker- http://www.jtbaker.com/safety/safe_Spill.html

Modern Lab Service – Chemo spill kit - http://www.modernlab.com/2/OverStock1.htm

Pharma System: spill kit for chemotherapy

Tyco: spill kit + several types of absorbent pads and cloths.

4.2 Spill Management Procedure

4.2.1 Spill Outside a Hood, on Hard Surfaces (Floor, Counter, etc.)

- Check the extent of the spill and request assistance from a trained team or worker, if necessary. Outside assistance should be requested (e.g. dedicated spill management team) for any spill that cannot be contained with a spill kit.
- Prohibit access to the contaminated area (using a sign, for example). In the event of a large spill, the area should be evacuated until the situation is brought under control. If this is not possible (e.g. patients undergoing treatment), move those not required for spill management as far away from the spill as possible.
- When possible, particularly in the event of a large spill, the ventilation in the room where the spill is located should be turned off if the air is recirculated to other rooms. If the air is exhausted directly to the outdoors, it is preferable not to turn off the ventilation.
- Locate the spill kit. Put the respiratory protection apparatus on first, followed by the remainder of the protective equipment, i.e., two pairs of gloves, gown, face protection. A mask with a high-efficiency filter (N95 or N-100 type) may be used for small spills. For large spills involving a risk of product inhalation (e.g. drug powder in the air), a respirator for organic dust and vapours or even a powered respirator (large spill) should be used.
- Cover a liquid spill with absorbent pads. Cover a powder spill with wet pads.
- Use the thick gloves contained in the kit to collect glass shards and place them in a rigid container.
- Pick up the pads or absorbent materials and discard them in the plastic bag provided for hazardous waste.
- Wipe and clean the contaminated area with detergent and water, starting with the least contaminated areas and working toward the most contaminated. Rinse three times with water.

  The cleaning described above can be followed by chemical decontamination with sodium hypochlorite 2.4 % left to work for 10 minutes, followed by neutralization with sodium thiosulfate or rinsing three times as described above.

- Discard all of the contaminated material in a thick plastic bag marked "Cytotoxic". Remove the gown, face protection and outer pair of gloves (being careful to avoid self-contamination) and place them in the plastic bag.
- Wearing the inner pair of gloves, close the bag and place it in another plastic bag. Remove the inner pair of gloves and the disposable respirator and place them in the bag before closing it. Dispose of the bag with the cytotoxic waste. If a powered respirator was used, it must be placed in a separate bag for future cleaning.
- Wash your hands with soap and water.
- Once the spill has been cleaned up, ask the Hygiene and Sanitation Department to clean the area.
- Complete a Spill Report Form (see sample). The Chemical Spill Report Form may also be used.

4.2.2 Spill Inside a Hood

- Immediately clean up any small spills (less than 30 mL) inside a hood.
- Use a spill kit if the spill is larger than 30 mL or if the contents of an ampoule or vial are involved. It should be noted that, in general, the workers on the scene are already protected by their *personal protective equipment*.
- Use the thick gloves contained in the kit to collect the glass shards. Place them in the rigid container in the hood.
- Clean and decontaminate the hood before using it again.
- Clean the drain placed under the grille of the hood if the spill reached it.
- If liquid has penetrated the HEPA filter or if the "clean" side of the filter was contaminated by powder particles, stop using the hood until it has been decontaminated and the filter replaced.

Sources:

- ASHP. ASHP Guidelines on Handling Hazardous Drugs, Prepublication copy, Dec. 2005. 33 pages
- Occupational and Health Administration. *OSHA Technical Manual*, Section 6, Chapter 2, 1999 [Web site: http://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html, accessed May 24, 2006]

4.3 Spill Report Form (sample)

Any spill of more than 5 mL should be reported by completing a Spill Report Form (see sample). The Chemical Spill Report Form provided as part of the institution's emergency measures planning process (see 12.3.4.1) may also be used.

Spill Report

DATE, TIME AND LOCATION

Date: _____ Location: _____

Time assistance requested (Housekeeping or dedicated team): _____

CIRCUMSTANCES SURROUNDING THE SPILL

Names of individuals in contact with the spill: _____

_____

_____

_____

Time of spill management: _____

CHECK OFF THE RECOMMENDED STEPS (COMMENTS, IF NECESSARY)

❒ Spill area isolated to prevent accidental contamination by workers or patients: _____

_____

❒ Spill kit availability: _____

_____

❒ Spill clean-up: _____

_____

COMPLETION OF THE REPORT

Submission to the Head of the Pharmacy Department or the Unit Head or his representative, confirming the end of the spill: _____

Spill management end time: _____

APPENDIX 5 - Measurement of Work Surface Contamination Caused by Antineoplastic Agents

Services Provided by the INSPQ Toxicology Laboratory

At the request of the Hazardous Drug Committee (which procured the necessary funding), the INSPQ Toxicology Laboratory has developed a method for estimating the work surface contamination in institutions caused by antineoplastic agents. The tests are performed in the INSPQ laboratory. However, the specimens are collected in the institutions (in the clinics and hospitals) by the on-site workers, using sampling kits provided by the INSPQ.

5.1 Products Tested

Cyclophosphamide, ifosfamide and methotrexate, with LOQ* = 0.01 ng/cm²

* LOQ = Limit of quantification

5.2 Cost

$50 per specimen collected. We recommend 12 specimens per pharmacy. Samples may also be taken in the care areas or at other steps of the medication circuit, depending on the client's objectives.

5.3 Method Summary

The analytical method is based on the recent article by Larson.[4] A standard-sized cloth, soaked in a special organic solution (10% acetonitrile, 25% methanol, buffered at pH 6), is used to wipe the work surfaces. Each specimen covers 600 cm² (20 cm x 30 cm), i.e., approximately the size of a piece of 8 ½ x 11 in. paper. The cloths are placed in a plastic tube and sent to the INSPQ laboratory. In the laboratory, 10 mL of the same solution are added and the cloth is agitated to release the products. An aliquot of the resulting solution is then analyzed using HPLC-MS-MS (an advanced spectrometry technique) to measure the concentration of antineoplastic agents present. The results are expressed in nanograms** per cm² (ng/cm²).

** 1 nanogram = 0.000 000 001 g, i.e., one billionth of a gram

[4] RR Larson, MB Khazaeli, HK Dillon. "Monitoring method for surface contamination caused by selected antineoplastic agents", *Am. J. Health-Syst Pharm* , 2002; 59(3): 270-7.

5.4 Auto-sampling In Health Care Institutions

The INSPQ Toxicology Laboratory provides all of the material required to measure the contamination in a ready-to-use kit. This kit includes the material necessary to collect 12 specimens and forward them to the laboratory for testing (Figure 23).

FIGURE 23.
INSPQ Auto-sampling Kit

The box also contains:

- a sampling protocol (PRC-041), which explains how to collect the specimens;
- a form (F11-91), on which to record the specimens collected;
- a form (F11-90), to identify the participating hospital, as well as the areas inspected.

5.5 Laboratory Contacts

The sampling kits may be ordered from the laboratory, via email (see below) or telephone (418) 650-5115:

- Michel Lefebvre: michel.lefebvre@inspq.qc.ca Tel.: extension 4025
- Alain Rodrigue: alain.rodrigue@inspq.qc.ca Tel.: extension 4028
- Jacinthe Larochelle: jacinthe.larochelle@inspq.qc.ca Tel.: extension 4023
- Secretariat Tel.: extension 4100