

**Model Standards for Pharmacy Compounding of Hazardous Sterile
Products**

DRAFT 2A

National Association of Pharmacy Regulatory Authorities
(adapted with permission from “Préparation de produits stériles dangereux
en pharmacie – Norme 2014.02,” Ordre des pharmaciens du Québec, 2014)

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1. INTRODUCTION

Parenteral therapies are becoming more complex, and patients may now receive continuous antibiotic therapy or chemotherapy, among other therapies, for several days at home. Consequently, attention must be paid to the environment in which these products are prepared, the training of personnel and quality assurance procedures to prevent complications and protect the public more generally¹.

Evolving practice and increased awareness of the inherent dangers of compounding sterile products for the health of both patients and compounding personnel^{2 3 4} led to the need to review the “Guidelines to Pharmacy Compounding” published by the National Association of Pharmacy Regulatory Authorities (NAPRA) in October 2006.

The new NAPRA Model Standards for Pharmacy Compounding of Sterile Products have been adapted from standards originally developed by the Ordre des pharmaciens du Quebec, which are in turn based on General Chapter <797> of the United States Pharmacopeia – National Formulary (USP–NF) in effect in the United States since 2004. Their preparation was led by the NAPRA ad hoc Committee on Pharmacy Compounding and involved extensive consultations with experts and stakeholders.

The Model Standards for Pharmacy Compounding of Sterile Products have been divided into two documents, one pertaining to non-hazardous and the other to hazardous (cytotoxic) compounded sterile preparations. Similar information is found in some sections of the two documents, but elsewhere the information differs according to the type of product (non-hazardous or hazardous). The creation of separate documents is intended for ease of reference by practitioners, according to the type of practice. The current document covers hazardous compounded sterile preparations. The companion document discusses non-hazardous compounded sterile preparations.

2. OBJECTIVES

The aim of these Model Standards is to provide pharmacists and pharmacy technicians who compound and pharmacists who dispense **hazardous** sterile preparations with the standards necessary to evaluate their practice, develop service-related procedures and implement appropriate quality controls for both patients and compounding personnel, with a view to guaranteeing the overall quality and safety of sterile preparations. The Model Standards will come into effect once they have been reviewed and approved by provincial pharmacy regulatory authorities.

The Model Standards represent the minimum requirements to be applied in compounding sterile preparations; however, it is always possible to exceed these standards. The use of other technologies, techniques, materials and procedures may be

¹ Dolan SA, Felizardo G, Barnes S, Cox TR, Patrick M, Ward KS, et al. APIC position paper: safe injection, infusion, and medication vial practices in health care. *Am J Infect Control*. 2010;38(3):167-72.

² Selenic D, Dodson DR, Jensen B, Arduino MJ, Panlilio A, Archibald LK. *Enterobacter cloacae* bloodstream infections in pediatric patients traced to a hospital pharmacy. *Am J Health Syst Pharm*. 2003;60(14):1440-6.

³ Patel PR, Larson AK, Castel AD, Ganova-Raeva LM, Myers RA, Roup BJ, et al. Hepatitis C virus infections from a contaminated radiopharmaceutical used in myocardial perfusion studies. *JAMA*. 2006;296(16):2005-11.

⁴ Kastango ES. The cost of quality in pharmacy. *Int J Pharm Compound*. 2002;6(6):404-7.

acceptable, so long as they are proven to be equivalent or superior to those described here. Such other technologies, techniques, materials and procedures require prior approval from the provincial/territorial regulatory authority.

3. REGULATORY FRAMEWORK



3.1 Pharmaceutical compounding

Many health care professionals prepare compounded sterile products, including nurses, physicians, pharmacists and pharmacy technicians. However, the majority of sterile compounding is performed by or under the supervision of pharmacists. Therefore, these standards pertain specifically to pharmacists, pharmacy technicians and pharmacies where compounded sterile products are prepared.

The preparation of medication has always been an integral part of the practice of pharmacy. It is essential to the delivery of health care and allows for personalized therapeutic solutions to improve patient care. However, it must always be carried out within an individual physician–patient–pharmacist relationship (i.e. from a prescription) or within a pharmacist–patient relationship for a specific need (e.g., with over-the-counter preparations). Provincial/territorial pharmacy regulatory authorities are responsible for verifying a pharmacy’s preparation services in these situations.

In situations involving requests to compound preparations outside an individual physician–patient–pharmacist relationship, without a prescription, the compounding activities fall under the federal legislative framework. The same federal legislative framework applies to bulk preparation of compounded products and to shipments across provincial/territorial borders.

Health Canada is the federal department responsible for the *Food and Drugs Act* and the *Controlled Drugs and Substances Act* and their associated regulations. In January 2009, Health Canada developed its “Policy on Manufacturing and Compounding Drug Products in Canada”⁵. At the time these Model Standards were prepared, Health Canada was examining this policy with a view to creating new standards for situations not covered within the practice of pharmacy or under the current federal licensing framework.

The NAPRA professional competencies for Canadian pharmacists and pharmacy technicians at entry to practice provide guidance for developing an ethical, legal and professional practice. One of these competencies specifies that a pharmacist or pharmacy technician must seek guidance when uncertain about his or her own knowledge, skills, abilities and scope of practice. Therefore, individuals who do not have the training, expertise, facilities or equipment required to compound sterile preparations must refer patients to a pharmacist who does offer this service or,

⁵ Health Canada, Health Products and Food Branch Inspectorate. Policy on manufacturing and compounding drug products in Canada. POL-051. Ottawa, ON: Health Canada; 2009. Available from: http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/docs/pol_0051-eng.php

where permitted by provincial/territorial legislation, ask a colleague to compound the preparation for them.

Compounded sterile preparations include the following types of medications:

- nasal sprays
- respiratory therapy solutions
- solutions for live organ and tissue or graft baths
- solutions for injection (e.g., intramuscular, intravenous, intrathecal, intradermal, subcutaneous)
- irrigation solutions for wounds and body cavities
- ophthalmic drops and ointments
- otic drops for intratympanic administration
- parenteral nutrition solutions
- dialysis solutions
- solutions for intradermal injection (allergens)
- topical preparations requiring sterility

Pursuant to these Model Standards, sterility is also required for reconstitution and certain manipulations (according to manufacturers' instructions) of sterile products approved by Health Canada and for the repackaging of approved sterile products, regardless of the route of administration.

3.2 Specific legislation and regulations on hazardous products

For the protection of workers, additional laws and regulations governing the compounding of hazardous sterile drugs and other hazardous materials may be in effect in Canadian jurisdictions. An example is presented below:

An Act Respecting Occupational Health and Safety Act (R.S.Q. S-2.1)

In the province of Quebec, the health and safety legislation includes several provisions pertinent to the compounding of hazardous products. Section 9 of the act sets out general workers' rights, and section 49 lists workers obligations. Section 50 sets out general employers' rights, and section 51 lists employers' general obligations. Appendix 1 quotes excerpts from these sections, but of most interest is section 51, concerning employers' obligations.

Section 51 stipulates that employers must take necessary measures to protect the health, safety and physical well-being of their workers. Employers must ensure that medication and the hazardous materials used for sterile preparations do not endanger the health and safety of any person in the workplace. It is also the responsibility of the employer (e.g., the health care establishment or the pharmacist owner), and ultimately that of the head of the pharmacy department, to ensure that employees use the required protective measures at their disposal.

Regulation Respecting Occupational Health and Safety (C.Q.L.R., S-2.1, r. 13)

This regulation sets out specific obligations on ventilation, personal protective equipment (PPE), air quality and storage of hazardous materials.

4. ABBREVIATIONS

The following abbreviations are used in this document.

Abbreviation	Name
ABHR	Alcohol-based hand rub
ACD	Automated compounding device
ACPH	Air changes per hour
ASSTSAS	Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales, a joint sector-based association dedicated to occupational health and safety in the health and social services sector within the province of Quebec
BUD	Beyond-use date
BSC	Biological safety cabinet
CACI	Compounding aseptic containment isolator
CFU	Colony-forming unit
GFTS	Gloved fingertip sampling
HEPA	High-efficiency particulate air
HVAC	Heating, ventilation and air conditioning
LAFW	Laminar airflow workbench
NF	National Formulary (United States)
NIOSH	National Institute for Occupational Safety and Health (United States)
PPE	Personal protective equipment
PTA	Pharmacy technical assistant
TSP	Technical support personnel
USP	United States Pharmacopeia

5. CORE REQUIREMENTS FOR A STERILE COMPOUNDING SERVICE

In addition to strict aseptic techniques, the compounding of hazardous sterile products requires the implementation of safety measures to protect personnel and the environment.

Hazardous products can penetrate the body through the skin, by ingestion, by accidental injection (needle-stick injury) or by inhalation. According to some studies, absorption through the skin is the primary known route of penetration⁶.

Absorption through the skin occurs by direct contact with contaminated surfaces or objects. Ingestion occurs by eating foods that might have been contaminated or by putting contaminated hands or objects, particularly pens, into the mouth^{7 8}. Inhalation of vapourized drugs can also be a source of contamination⁹.

References on the safe handling of hazardous products must be consulted before compounding services for such products are implemented.

5.1 Personnel

5.1.1 Roles and responsibilities

5.1.1.1 Pharmacist owner or pharmacy manager

The pharmacist owner or pharmacy manager is responsible for developing, organizing and supervising all activities related to pharmacy compounding of hazardous sterile preparations. This person may share or delegate these responsibilities to a pharmacist or pharmacy technician, who will be designated as the sterile compounding supervisor for these activities. If the designated pharmacist or pharmacy technician chooses not to perform these activities, the pharmacist owner or pharmacy manager must assume the responsibilities of sterile compounding supervisor and must prepare hazardous compounded sterile preparations in the pharmacy.

⁶ American Society of Health-System Pharmacists. ASHP guidelines on handling hazardous drugs. *Am J Health Syst Pharm.* 2006;63(12):1172-93.

⁷ American Society of Health-System Pharmacists. ASHP guidelines on handling hazardous drugs. *Am J Health Syst Pharm.* 2006;63(12):1172-93.

⁸ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs.* Montréal, QC: ASSTSAS; 2008. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

⁹ American Society of Health-System Pharmacists. ASHP guidelines on handling hazardous drugs. *Am J Health Syst Pharm.* 2006;63(12):1172-93.

If these responsibilities are delegated, the pharmacist owner or pharmacy manager must ensure that the sterile compounding supervisor fulfills them adequately.

In the pharmacy of a health care facility, a hazardous drugs committee¹⁰ should be established. The committee should comprise representatives of the employer, representatives of compounding and administration personnel, and representatives of cleaning and disinfecting personnel for the compounding areas. A pharmacist must be designated to support hazardous products management.

5.1.1.2 Sterile compounding supervisor

Definition

A pharmacist or pharmacy technician designated to supervise activities related to the compounding of hazardous sterile products. This person works with the pharmacy manager and with pharmacists and pharmacy technicians assigned to perform compounding duties.

The sterile compounding supervisor develops, organizes and oversees all activities related to compounding of hazardous sterile products. These responsibilities are delegated by the health facility's pharmacy department head, the pharmacist owner or the pharmacy manager.

The sterile compounding supervisor may, by writing a delegation policy and procedure and using appropriate quality control measures, delegate technical tasks related to sterile-product compounding and auditing, including the compounding of hazardous sterile products, to pharmacy technical support personnel (TSP). In jurisdictions allowing regulated pharmacy technicians, such delegation may be unnecessary if the technicians' scope of practice includes product preparation.

Responsibilities

The sterile compounding supervisor ensures that the following requirements are met:

- A personnel training and assessment program is implemented.
- Personnel know and fully comply with policies and procedures.
- Appropriate measures are taken to ensure the safety of personnel during each preparation.
- Policies and procedures covering all activities are developed, regularly updated and always followed (see Appendix 2).

¹⁰ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

- **Prevention measures are implemented, in collaboration with the pharmacist owner or pharmacy manager, to limit exposure of personnel to hazardous products.**
- The facilities and equipment used to compound hazardous sterile products meet requirements and are maintained, calibrated or certified according to specifications.
- The existing compounding process yields high-quality final preparations that are safe for patients.
- **The available recognized scientific literature is used to determine stability and to correctly establish the beyond-use date (BUD) for each hazardous sterile preparation.**
- A quality assurance program, designed to ensure that preparation activities are performed in accordance with standards of practice, scientific standards, existing data and relevant information, is implemented and followed.
- Mandatory and supplementary documentation is available and updated regularly. Appendix 3 lists required publications and suggestions for supplementary documentation.
- All records required by the Model Standards are completed.

5.1.1.3 Compounding pharmacist or pharmacy technician

Definition

A pharmacist or pharmacy technician who prepares or supervises the compounding of sterile products

- for patients of the facility or pharmacy where the pharmacist or pharmacy technician is employed;

OR

- for patients of another facility or pharmacy at the request of a pharmacist at that facility or pharmacy, where permitted by provincial/territorial legislation; in this case, responsibilities toward the patient are shared between the compounding pharmacist and the patient care (dispensing) pharmacist.

When the compounding pharmacist is also the patient care (dispensing) pharmacist, the compounding pharmacist assumes the responsibilities associated with both roles.

Responsibilities

The compounding pharmacist or pharmacy technician must

- perform or supervise compounding activities;
- **ensure compliance with policies and procedures related to the**

compounding of hazardous sterile products;

- enforce or ensure compliance with required aseptic, hygienic, cleanliness and safety rules;
- ensure that all records related to ongoing activities are completed and initialled;
- ensure that all data required for monitoring and reproducing the preparation are recorded or digitized;
- ensure that the equipment, instruments and space used are properly cleaned and maintained;
- ensure application of and compliance with existing compounding procedures;
- ensure that there is a compounding protocol for each preparation produced;
- ensure the accuracy of calculations and measurements;
- use appropriate equipment and instruments for the preparation to be produced;
- follow the compounding process defined in the compounding protocol;
- perform verification during the various stages of compounding and verify the final preparation, or delegate such verification in accordance with the appropriate delegation procedure;
- ensure that all required verification and quality control measures are performed to ensure quality and sterility of each preparation;
- ensure that preparations are packaged and labelled in accordance with provincial/territorial requirements and that a BUD is included on the label (see section 6.1);
- where appropriate, provide the patient care (dispensing) pharmacist, orally or in writing, the information required for storing and transporting any medication prepared at the dispensing pharmacist's request (storage method, precautions, suggested BUD, etc.);
- ensure that the final preparation is properly stored until delivery to the patient or to the pharmacist who ordered it (where compounding is undertaken by another pharmacy, as permitted by provincial/territorial legislation);
- where appropriate, notify the patient care (dispensing) pharmacist when a preparation must be recalled;
- if a sterile preparation has been compounded for an external patient care (dispensing) pharmacist (where permitted by provincial/territorial legislation), ensure that each patient management activity is performed by

the dispensing pharmacist and/or the compounding pharmacist or pharmacy technician, to ensure continuity of care¹¹;

- where appropriate, collaborate with the patient care (dispensing) pharmacist and share information on the preparation for the patient's benefit and to optimize treatment results;
- ensure that patient management is adequate and consistent with agreements among the various stakeholders.

5.1.1.4 Patient care (dispensing) pharmacist

Definition

The pharmacist who dispenses a sterile preparation to a patient or another health care professional. The dispensing pharmacist may be same person as the compounding pharmacist; alternatively, the dispensing pharmacist may ask another pharmacist or pharmacy technician to compound the preparation. The patient care (dispensing) pharmacist shares professional responsibilities with the compounding pharmacist or pharmacy technician.

When the patient care (dispensing) pharmacist is also the compounding pharmacist, the dispensing pharmacist assumes the responsibilities associated with both roles.

Responsibilities

When providing patient care that includes dispensing medications or medication therapies, the patient care (dispensing) pharmacist must follow the standards of practice for Canadian pharmacists¹².

5.1.1.5 Other employees

Employees must follow and comply with specific procedures for the compounding of hazardous sterile products.

5.1.2 Training and assessment

Compounding personnel and cleaning and disinfecting personnel have a major impact on the risks associated with contamination of preparations and with

¹¹ National Association of Pharmacy Regulatory Authorities (NAPRA). *Model standards of practice for Canadian pharmacists*. Ottawa, ON: NAPRA; 2009. Available from: http://napra.ca/Content_Files/Files/Model_Standards_of_Prac_for_Cdn_Pharm_March09_Final_b.pdf

¹² National Association of Pharmacy Regulatory Authorities (NAPRA). *Model standards of practice for Canadian pharmacists*. Ottawa, ON: NAPRA; 2009. Available from: http://napra.ca/Content_Files/Files/Model_Standards_of_Prac_for_Cdn_Pharm_March09_Final_b.pdf

chemical contamination of the environment. Stringent work methods^{13,14} are therefore required.

Integration and maintenance of required competencies is achievable only with adequate training and assessment.

Compounding personnel must keep their compounding knowledge up to date.

5.1.2.1 Conditions

Pharmacists and pharmacy technicians involved in the organization, training, compounding, supervision and quality control of hazardous sterile-product preparations must have the appropriate mix of education and experience.

Before compounding any hazardous sterile products, employees must receive specific training in the workplace and must undergo an assessment of their competency, as described in section 5.1.2.3. An annual competency assessment program must also be put into place.

All personnel (pharmacists, pharmacy technicians and TSP) must know and apply appropriate procedures for the receipt, storage, distribution and disposal of hazardous products and hazardous waste, as well as the procedures for dealing with accidental exposure and spills.

All new personnel involved in the compounding of hazardous sterile products must successfully complete a workplace training and competency assessment program pertinent to the type of preparations to be produced.

Compliance with operating procedures and use of techniques appropriate for the compounding of hazardous sterile products must be evaluated as part of the competency assessment program for personnel involved in hazardous sterile-product compounding.

The assessment results and any corrective measures imposed must be recorded, and these records must be retained.

The sterile compounding supervisor must ensure that all compounding personnel have the knowledge and competency required to perform quality work.

5.1.2.2 Initial training and assessment program

Personnel assigned to the compounding of hazardous sterile products

The initial training and assessment program for compounding personnel must have the following components:

- reading and understanding the policies and procedures related to the compounding of hazardous sterile products (see Appendix 2);

¹³ Thomas M, Sanborn M, Couldry R. I.V. admixture contamination rates: traditional practice site versus a class 1000 cleanroom. *Am J Health Syst Pharm.* 2005;62(22):2386-92.

¹⁴ Trissel LA, Gentempo JA, Saenz LM, Woodard MY, Angeles CH. Effect of two work practice changes on the microbial contamination rates of pharmacy-compounded sterile preparations. *Am J Health Syst Pharm.* 2007;64(8):837-41.

- theoretical training, with assessment covering various topics, including those in Appendix 4;
- individualized practical training and assessment in the workplace clean room (see section 7 and Appendix 4);
- assessment of aseptic techniques, based on gloved fingertip sampling (GFTS) and a media fill test, for the various types of hazardous sterile products to be compounded.

Any compounding employee who has successfully completed the initial workplace training and assessment program may begin work in the compounding of hazardous sterile products. In situations involving employees with limited experience, additional attention must be given to their supervision.

Cleaning and disinfecting personnel

The initial training and assessment program for cleaning and disinfecting personnel must have the following components:

- theoretical training and assessment covering the issues and particularities of cleaning and disinfecting the premises and equipment used for compounding hazardous sterile products (see Appendix 4 for a list of the competencies required for theoretical assessment of cleaning and disinfecting personnel);
- practical training and assessment in the areas reserved for the compounding of hazardous sterile products.

Any cleaning and disinfecting employee who has successfully completed theoretical and practical training in the workplace may perform cleaning duties in facilities where hazardous sterile products are compounded, in accordance with established procedures.

The sterile compounding supervisor must ensure appropriate training of all new cleaning and disinfecting personnel.

In health care facilities, the sterile compounding supervisor must work closely with the head of environmental services and the head of infection prevention and control to develop joint work and training procedures, which must be understood and followed by all cleaning and disinfecting personnel.

5.1.2.3 Competency assessment program

Sterile compounding supervisor

Training

- The sterile compounding supervisor must have undergone training (i.e., courses) in the compounding of hazardous sterile products and must have demonstrated the required qualifications.
- The sterile compounding supervisor must also have the competency required to manage a safe, high-quality hazardous sterile-product

compounding department.

Assessment

- The sterile compounding supervisor must be evaluated at least every 3 years by a third party (a peer external to the compounding environment, with expertise in the compounding of hazardous sterile products).
- The external evaluator (either a pharmacist or pharmacy technician) must meet the criteria set out in section 5.1.2.4 for external evaluators.

Pharmacist who never compounds sterile products but whose role includes supervising pharmacy technicians and TSP

A pharmacist whose activities are limited to supervising a pharmacy technician or TSP during the compounding of hazardous sterile products

- may be exempted from the practical section of the assessment of competency in aseptic compounding, the media fill test and GFTS;
- must possess demonstrated ability to determine whether the pharmacy technicians and TSP are complying with aseptic processes, in order to quickly detect any risk of error and possible contamination;
- must pass the practical section of the training program regarding assessment of the aseptic compounding process, the media fill test and GFTS, if there is a possibility that this pharmacist will compound hazardous sterile products on an occasional basis.

Duty pharmacist in a health care facility

A pharmacist on duty in a health care facility must receive the same training as a compounding pharmacist and must undergo annual assessment of competency in the compounding of hazardous sterile products.

Frequency of assessment

Compounding personnel

All personnel (pharmacists, pharmacy technicians and TSP) assigned to the compounding of hazardous sterile products must undergo assessment at the following frequencies:

- at least once a year in the workplace for preparations with low or medium risk level
- at least once a year in the workplace for hazardous products
- at least twice a year in the workplace for preparations with high risk level

The risk levels of various preparations are explained in section 6.1.3.

The results of these assessments should be noted in each employee's file.

Cleaning and disinfecting personnel

All cleaning and disinfecting personnel must be evaluated at least once a year in the workplace.

The results of these assessments must be retained for the period specified by the provincial/territorial regulatory authority.

Content of assessment

Compounding personnel

A competency assessment program for all compounding personnel (pharmacists, pharmacy technicians and TSP) must be implemented in the workplace. This program must include the following:

- a theoretical test measuring required knowledge of policies and procedures, the aseptic compounding process, and accidental exposure and spills (see Appendix 4);
- a practical test in the workplace clean room (including GFTS and a media fill test, with simulations involving a hazardous product) to evaluate compliance with operating procedures and knowledge of aseptic compounding processes.

Cleaning and disinfecting personnel

A competency assessment program for cleaning and disinfecting personnel must be implemented in the workplace (see Appendix 4 for more details on the training required).

Failures (all personnel)

Compounding personnel and cleaning and disinfecting personnel who fail the written or practical assessment must immediately stop work and redo their training. An individual may resume assigned duties after passing the elements previously failed.

In case of repeated failures, a decision must be made regarding permanent termination of sterile-product compounding or cleaning and disinfecting activities.

5.1.2.4 Management of the competency assessment program

Sterile compounding supervisor and delegation of employee training

The sterile compounding supervisor is responsible for the training of and competency assessment program for all employees involved in the compounding of hazardous sterile products. The supervisor may

- delegate the training portion of the program to a pharmacist, pharmacy technician or TSP on the supervisor's team, but must perform the assessment portion;

OR

- delegate both training and assessment of personnel to an external evaluator (a pharmacist or pharmacy technician with expertise in compounding sterile products, from a workplace external to the supervisor's environment).

External evaluator

If the sterile compounding supervisor delegates training and assessment of compounding personnel and cleaning and disinfecting personnel to a third party,

- the third party must be a professional peer (pharmacist or pharmacy technician) with expertise in the compounding of hazardous sterile products;
- the sterile compounding supervisor must ensure that the external evaluator is qualified to fulfill the mandate;
- the external evaluator must have training that covers the compounding of hazardous sterile products, certification that competencies in this area are being maintained and developed, and proof of passing the annual competency assessment;
- the external evaluator's annual competency assessment must include the same elements as the competency assessment program for the compounding personnel (pharmacists, pharmacy technicians and TSP) described above.

5.2 Policies and procedures^{15,16,17}

The quality, absence of contamination and efficacy of the final preparation depend upon, among other things, full compliance with compounding procedures.

- The sterile compounding supervisor must establish the content of policies and procedures, providing detailed descriptions of all activities in the pharmacy's compounding of hazardous sterile products (see Appendix 2). The supervisor must also ensure application of and compliance with these policies and procedures.
- Procedures must be clear, must follow a standard format and must include an index for easy access to information when it is needed. Appendix 5 may be used as a model for developing these procedures.
- The sterile compounding supervisor must ensure that all established policies and procedures are promptly updated whenever there is a change in practice. In addition, policies and procedures must be reviewed at least every 3 years.

¹⁵ United States Pharmacopeial Convention (USP). General chapter <1075>: good compounding practices. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008–2009. p. 867.

¹⁶ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 44, 47, 54, 55.

¹⁷ Pharmacy Compounding Accreditation Board (PCAB). Standard 1.40: Standard operating procedures compliance indicators. In: *PCAB accreditation manual*. Washington, DC: PCAB; 2011. p. 7. Available from: <http://www.pcab.org/cms/wp-content/themes/pcab/img/PCAB-Accreditation-Manual.pdf>

- The drafting and revision dates, the date of each change and the names of authors and reviewers must be included in each policy or procedure.
- Where compounding is undertaken by another pharmacy, as permitted by provincial/territorial legislation, pharmacists who dispense but do not compound medications should include in their general procedures information about acquiring hazardous compounded sterile preparations for their patients (choice of supplier, entry in the file, delivery, etc.).

5.3 Facilities and equipment¹⁸

Facility design (spaces, ventilation, materials, etc.), as well as the conduct and competency of personnel, helps to achieve the objectives of these Model Standards.

Facilities for the compounding of hazardous sterile products must be designed and built in accordance with these Model Standards, with provincial/territorial and local regulations and, for health system facilities, with other applicable standards regulating the construction of government buildings.

5.3.1 Useful references

5.3.1.1 ISO Standard 14644-1¹⁹

The ISO 14644-1 classification describes air cleanliness requirements in facilities and clean rooms. This standard specifies the allowable concentration of airborne particles for each class (Table 1). To achieve and maintain the ISO class for a clean room, all sources that generate particles must be controlled.

¹⁸ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

¹⁹ International Organization for Standardization (ISO). *ISO 14644-4 Cleanrooms and associated controlled environments — Part 4: Design, construction and start-up*. Geneva, Switzerland: ISO; 2001.

Table 1

Classes of air cleanliness for airborne particulates in clean rooms and clean areas, according to ISO 14644-1	
ISO Class Number	Maximum concentration of non-viable particles $\geq 0.5 \mu\text{m}$ diameter, measured under dynamic operating conditions (particles/m³ of air)
3	35.2
4	352
5	3 520
6	35 200
7	352 000
8	3 520 000

μm = micrometre; m³ = cubic metre; ISO = International Organization for Standardization

5.3.1.2 Prevention Guide — Safe Handling of Hazardous Drugs²⁰

In 2008, the Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS; a joint sector-based association for occupational health and safety in the health and social services sector in the province of Quebec) published a guide pertaining to the risks associated with handling hazardous drugs and the preventive measures to be applied in a health care facility at the various stages of the preparation, distribution and administration of hazardous drugs.

The guide explains that the principles of precaution “definitely apply to all antineoplastic drugs, whether used in oncology or to treat other illnesses (e.g. methotrexate for arthritis). However, certain precautions could be modulated for other categories depending on the specific risks of each category”²¹.

These Model Standards pertain mainly to hazardous compounded sterile preparations of antineoplastic drugs, since these drugs constitute the majority of hazardous compounded sterile preparations undertaken in pharmacy.

²⁰ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

²¹ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

5.3.1.3 NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings²²

The US Department of Health and Human Services, through its Centers for Disease Control and Prevention and the National Institute for Occupational Safety and Health (NIOSH), publishes and updates a list of hazardous products. This published list can be used by individual pharmacies to develop their own lists of hazardous products that require special handling precautions. A list of hazardous products used must be available at the pharmacy.

In addition, NIOSH published an alert on preventing occupational exposure to antineoplastic and other hazardous drugs in 2004²³.

5.3.2 Facilities reserved for the compounding of hazardous sterile products

The requirements for facilities vary, depending on whether the sterile products to be compounded are hazardous or non-hazardous, although several of these requirements are similar for the two types of products. The companion document, Model Standards for Pharmacy Compounding of Non-hazardous Sterile Products, describes the facilities required for the compounding of non-hazardous products.

5.3.2.1 Dimensions

Areas reserved for the compounding of **hazardous sterile products** must be large enough to

- facilitate compounding
- allow housekeeping without constraint
- ensure good flow of people and equipment

5.3.2.2 Lighting

The lighting must be sufficient and fixtures located so as to

- facilitate the sterile compounding process
- allow verification at all stages of compounding

5.3.2.3 Heating, ventilation and air conditioning system for controlled rooms (clean room and anteroom)

²² National Institute for Occupational Safety and Health (NIOSH). NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2012. Publ. No. 2012-150. Atlanta, GA: Department of Health and Human Services, Centers for Disease Control and Prevention, NIOSH; 2012 June. Available from: <http://www.cdc.gov/niosh/docs/2012-150/pdfs/2012-150.pdf>

²³ National Institute for Occupational Safety and Health (NIOSH). NIOSH alert: preventing occupational exposures to antineoplastic and other hazardous drugs in health care settings. Publ. No. 2004-165. Atlanta, GA: Department of Health and Human Services, Centers for Disease Control and Prevention, NIOSH; 2004 Sep. Available from: <http://www.cdc.gov/niosh/docs/2004-165/pdfs/2004-165.pdf>

The air in controlled rooms must be “clean,” and levels of airborne particulates must be controlled. Thus, the facility’s heating, ventilation and air conditioning (HVAC) system must be designed to minimize both the risk of airborne contamination in controlled rooms used for the compounding of hazardous sterile products and the propagation of hazardous products in the work environment. It must also be designed to achieve and maintain the appropriate ISO class for clean rooms and anterooms used for the compounding of hazardous sterile products²⁴ (see section 5.3.2.5, Table 2).

The air supplied to areas used for compounding **hazardous** sterile products must pass through a high-efficiency particulate air (HEPA) filter to ensure a very high level of cleanliness. The intake air must come from the ceiling via diffusers, each fitted with a terminal HEPA filter²⁵.

All sources that generate particles must be controlled to achieve and maintain the ISO class for clean rooms and anterooms used to compound **hazardous** sterile products²⁶.

The air quality in controlled rooms must comply with the ISO 14644-1, according to the specifications listed in Table 1, under dynamic operating conditions, as follows:

- The number of particles $\geq 0.5 \mu\text{m}$ diameter per cubic metre of air must be verified while compounding personnel perform or simulate a typical procedure for compounding hazardous sterile products.
- Simulation of a typical procedure for compounding **hazardous** sterile products is achieved by placing the drug in a syringe or bag, in accordance with the compounding procedure used in the pharmacy.

The particle count must be performed by trained, qualified personnel at least twice a year as part of an internal quality control program for facilities, biological safety cabinets (BSCs) or compounding aseptic containment isolators (CACIs). The particle count may also be measured by a qualified **certified** (see Appendices 6 and 7).



All of the air from the clean room and anteroom must be exhausted to the exterior of the building.



Exhaust air intakes must be installed at the bottom of the walls²⁷, forcing the particles to flow downward. In older facilities, an airflow analysis must be performed under dynamic operating conditions (using the air speed achieved at the front of the BSC) to ensure that the location of the **exhaust** air intake does not hinder the compounding process.

²⁴ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 372-3.

²⁵ Health Canada, Health Products and Food Branch Inspectorate. *Good manufacturing practices (GMP) guidelines – 2009 edition, Version 2*. GUI-0001. Ottawa, ON: Health Canada; 2009, revised 2011 Mar 4. p. 85. Available from: <http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/docs/gui-0001-eng.php>

²⁶ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 372-3.

²⁷ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 373.

An air conditioning system must be included in the HVAC system to help ensure the comfort of personnel wearing personal protective equipment (PPE).

5.3.2.4 Windows and openings

Controlled rooms should have no windows or doors leading directly to the exterior of the building. If any windows are present, they must be sealed. If any doors lead to the outside or to a non-controlled area (other than the doors designated for accessing the room), they must be sealed. An environmental control procedure and a housekeeping procedure, including the cleaning of sealed windows and doors, must be implemented by cleaning and disinfecting personnel.

5.3.2.5 Compounding areas

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

Clean room

The clean room is a room in which the atmospheric properties (temperature, content of particles and microorganisms, air pressure, airflow, etc.) are controlled. The functional parameters of the clean room are maintained at a specific level (Table 2). The room is designed to minimize the introduction, generation and retention of particles **within the room and the spread of hazardous products outside the room.**

The clean room must be isolated from the rest of the pharmacy and from other non-controlled areas, to reduce the risk of introducing viable and non-viable contaminants into the room²⁸ **and the spread of hazardous products outside the room.** It must be physically separated from contiguous areas by walls, doors and pass-throughs.

Use

The clean room is used only for the compounding of **hazardous** sterile products.

Contents

The primary engineering control is installed in the clean room. **For hazardous compounding, the primary engineering controls may be BSCs or CACIs²⁹.**

Many hazardous drugs can volatilize at room temperature. Therefore, they must be stored within a negative pressure room. The storage area should have at least 12 air changes per hour (ACPH), with the air being completely exhausted to the

²⁸ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 372.

²⁹ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 372.

exterior. Given these requirements, a facility may choose to construct a separate storage area for hazardous drugs. (See also subsection below, "Area for storing hazardous products".)

Alternatively, hazardous sterile drugs and the refrigerator in which they are stored may be placed in the clean room for hazardous drugs. This approach ensures that the drugs are stored in a negative pressure room with sufficient ACPH (since the clean room has at least 30 ACPH, with the air being completely exhausted to the exterior). The facility must ensure that air exhausts are placed so that they will remove particles generated within the storage area and the refrigerator and must also ensure that there are sufficient ACPHs to maintain an ISO class 7 clean room.

Anteroom³⁰

The anteroom is located between the clean room and the non-controlled areas of the pharmacy, acting as a transition space. The anteroom has two doors with a locking system that allows users to open only one door at a time for moving from one area to another, thus keeping the areas isolated from one another.

The anteroom helps to maintain pressure differentials. It must therefore be adjacent to the clean room, separate from the rest of the pharmacy and fully enclosed, to provide the required seal and to meet and maintain the desired specifications. Users usually enter the anteroom from the pharmacy.

The anteroom is separated into two spaces by a demarcation line:

- The first space or area, referred to as "microbiologically dirty," is located at the entrance to the anteroom, in the section adjacent to the pharmacy. Even though this area is referred to as "dirty," it is considered to be chemically clean when hazardous products are being compounded in the clean room.
- The second space or area, referred to as "microbiologically clean," is adjacent to the microbiologically dirty area on one side and the clean room on the other. Even though this area is referred to as "clean," it is considered to be chemically contaminated when hazardous products are being compounded in the clean room.

It is important to take these "clean" and "dirty" areas into account when traversing the anteroom and when removing PPE.

Use

The anteroom is the location for activities with higher generation of particulates, such as garbing, hand hygiene, labelling and staging of components.

Activity in the anteroom shall be kept to a minimum and shall be limited to those activities that are essential to or that directly support the work undertaken in the clean room.

Access of supplies, equipment and personnel into the clean room shall be through the anteroom. No supplies, equipment or personnel shall enter the clean room from a non-controlled area.

³⁰ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 372-3.

Contents

The contents of the anteroom must be limited to facilitate maintenance and to maintain the target ISO air quality classification.

The anteroom must contain the following items:

- PPE accessories and storage space for hair covers and shoe covers, placed in the correct order to allow users to follow the correct garbing sequence;
- easy-to-clean wall sink, ideally made of stainless steel or other material not harmed by cleaning products and large enough to allow users to wash their hands and forearms without touching the sides of the sink, with minimal splashing;
- soap dispenser (cartridge or disposable, non-refillable unit);
- long-acting alcohol-based hand gel dispenser;
- hand-drying system:
 - lint-free paper towels with a dispenser (preferred)
 - air hand dryer designed specifically for use in a controlled area (i.e., the anteroom)
- mirror or other means to verify garbing;
- **cytotoxic waste bin;**
- eyewash station³¹, if available (if not located in the anteroom, the eyewash station must be installed nearby).
- cart reserved for use in the “clean” area of the anteroom and the clean room.

Supplies

In principle, supplies are not kept in the clean room. The supplies, drugs, labels and other items required for each preparation or batch are gathered and assembled in the anteroom and placed in a bin or tray for entry into the clean room at the time of compounding.

A balance must be established between the need for supplies in the anteroom and the need to leave the anteroom to obtain supplies not available there. A maximum 1-day supply of compounding equipment and materials may be stored in the anteroom. If applicable, steps must be taken to maintain the anteroom’s ISO air quality classification.

Requirements applying to both clean room and anteroom

Doors between the anteroom and the clean room and between the pharmacy and anteroom must have windows to prevent accidents involving personnel entering

³¹ Canadian Centre for Occupational Health and Safety (CCOHS). Emergency showers and eyewash stations. Hamilton, ON: CCOHS; 2010. Available from: http://www.ccohs.ca/oshanswers/safety_haz/emerg_showers.html

or leaving through the doors. A window covering half the door may be sufficient. Doors between the anteroom, the clean room and the pharmacy must be easy to open without using the hands or must have an automatic opening device; the doors should be interlocking. If there is no interlocking system, a procedure must be developed and implemented to prevent both doors from begin open at once.

Because horizontal surfaces require daily cleaning, their presence in the anteroom must be kept to a minimum, to avoid unduly increasing the workload for cleaning and disinfecting personnel.

Table 2 and Figure 1 illustrate the functional parameters of the clean room and the anteroom for hazardous sterile products.

Table 2

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

General principles:

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

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

- The clean room must be kept under negative pressure relative to the anteroom³².
- The pressure of the clean room must be -2.5 Pa relative to surrounding areas (pharmacy or other)³³.
- The pressure differential between the anteroom and the clean room ($P_B - P_C$) must be at least 2.5 Pa to maintain unidirectional airflow from the anteroom to the clean room.
- The pressure in the anteroom must be positive. The pressure differential must be at least 5.0 Pa relative to the pharmacy adjacent to the anteroom.
- ISO Class 7 air quality must be maintained in the clean room and the anteroom under dynamic operating conditions³⁴.
- There must be at least 30 or more air changes per hour (ACPH)³⁵ in the clean room and the anteroom. Depending on the size of the rooms and the number of people working in them, a greater number of ACPH may be required.
- The temperature in the controlled rooms must be less than or equal to 20°C ³⁶, taking into account employees' comfort once all clean room garb (including PPE) has been donned. Medication storage temperatures must not exceed 25°C .

Note: There is no requirement for relative humidity; refer to the recommendations of the Canadian Society of Hospital Pharmacists³⁷. See also the pressure diagram for the anteroom and the clean room (Figure 1, page 27).

³² United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 368.

³³ United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings [draft]. Rockville, MD: USP; 2014 Mar.

³⁴ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 368.

³⁵ International Organization for Standardization (ISO). *ISO 14644-4 Cleanrooms and associated controlled environments — Part 4: Design, construction and start-up*. Geneva, Switzerland: ISO; 2001.

³⁶ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. <<Should a specific page be indicated for this reference?>>

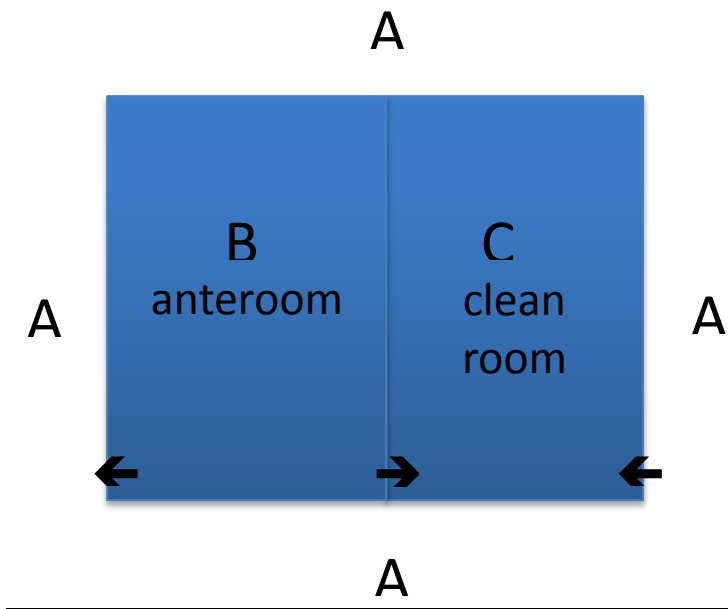
³⁷ Canadian Society of Hospital Pharmacists (CSHP). *Sterile preparation of medicines: guidelines for pharmacists*. Ottawa, ON: CSHP; 1996.

Given the PPE that compounding personnel are required to wear, the clean room must be maintained at a temperature that will ensure their comfort and allow them to do their work conscientiously. These conditions increase the safety of the aseptic compounding process and minimize skin desquamation.

Access to the clean room must be restricted to compounding personnel and cleaning and disinfecting personnel.

To enable supervision and verification activities, one or more observation windows must be installed. Such windows reduce the number of times individuals need to enter and exit the clean room, especially visitors or observers. They also ensure the safety of compounding and other personnel.

Figure 1: Pressure diagram



Pressure differentials:	
Pressure differentials to be maintained at all times:	<ol style="list-style-type: none"> 1) $(P_B - P_A) \geq 5.0 \text{ Pa}$ 2) $(P_B - P_C) > 2.5 \text{ Pa}$ 3) $-2.5 \text{ Pa} < (P_C - P_A)$
Legend:	
	<ul style="list-style-type: none"> A = facilities environment B, C = compounding room P = pressure Pa = pascal (SI unit of measure for pressure)

Area for unpacking hazardous products

If a hazardous product arrives from the manufacturer in an undamaged state, sealed in impermeable plastic, then no special precautions are necessary³⁸.

If a hazardous drug arrives in a damaged state and unpacking is required, a Class I BSC will be needed. The Class I BSC may be used just for unpacking the damaged product, or it could also be used for the compounding of non-sterile hazardous drugs³⁹.

Area for storing hazardous products

Hazardous products must be grouped and stored in a properly ventilated room with all air exhausted to the exterior⁴⁰. The storage area must have negative pressure relative to the adjacent rooms and must have at least 12 ACPH. It must be properly identified with the appropriate “cytotoxic” symbol to indicate the presence of hazardous products⁴¹.

Additional requirements for a hazardous products storage area are listed in Table 3.

³⁸ United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings [draft]. Rockville, MD: USP; 2014 Mar.

³⁹ United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings [draft]. Rockville, MD: USP; 2014 Mar.

⁴⁰ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 6-4. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

⁴¹ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). Chapter 4: General Preventive Measures. *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. pp. 4-4. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

Table 3

Required conditions for a hazardous products storage area

- Area separate from the unpacking area
- Dedicated room
- Negative pressure relative to adjacent rooms
- At least 12 air changes per hour (ACPH) with all air exhausted to the exterior
- Presence of shelves with lips to prevent drug containers from falling off and breaking⁴²
- Storage spaces for hazardous products and preparations identified with the “cytotoxic” danger symbol⁴³
- Sufficient ventilation to prevent contamination from spreading to adjoining rooms⁴⁴

A facility may choose to construct a separate room for the storage of hazardous drugs. However, the storage of sterile hazardous drugs is permitted in the clean room (see the section on clean rooms, above, for more information).

5.3.2.6 Shared facilities

Compounding of hazardous and non-hazardous sterile products

Facilities in community pharmacies or health care facilities that compound both hazardous and non-hazardous sterile products must have two clean rooms: one for the compounding of sterile hazardous products and another for the compounding of sterile non-hazardous products, as well an anteroom for each type of compounding.

In some community pharmacies and smaller health care facilities, space may be limited. Although separate clean rooms are still required for each type of preparation (i.e., one for hazardous sterile products and another for non-hazardous sterile products), there may be only one (shared) anteroom.

⁴² Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 6-4. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

⁴³ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). Chapter 4: General Preventive Measures. *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. pp. 4-4. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

⁴⁴ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 7-9. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

This layout is not recommended, but if space constraints dictate that facilities for compounding hazardous and non-hazardous sterile products share an anteroom, the conditions described in the following subsections must be met.

Clean room for the compounding of non-hazardous sterile products

The functional parameters of the clean room for this type of facility are the same as those required for the compounding clean room described in the Model Standards for Pharmacy Compounding of Non-hazardous Sterile Products (section 5.3.2.5).

Clean room for the compounding of hazardous sterile products

The functional parameters of the clean room for this type of facility are the same as those required for the compounding clean room described in section 5.3.2.5 of the current document.

Shared anteroom

The sole anteroom is connected to both clean rooms for the compounding of sterile products (hazardous and non-hazardous) and is shared for hand hygiene and garbing activities of personnel working in both clean rooms. The functional parameters of the shared anteroom for the compounding of hazardous and non-hazardous sterile products are explained in Table 4.

In this case, the anteroom is separated into two spaces by a demarcation line:

- a space or area referred to as “dirty,” located adjacent to the pharmacy, at the entrance to the anteroom;
- a space or area referred to as “microbiologically clean but possibly chemically contaminated,” located adjacent to the clean room for the compounding of hazardous sterile products and the clean room for the compounding of non-hazardous sterile products.

If there is enough space, the clean area of the anteroom may be further divided into two areas:

- a “microbiologically clean but chemically contaminated” space or area *adjacent to the clean room for the compounding of hazardous sterile products*;
- a “microbiologically and chemically clean” space or area *adjacent to the clean room for the compounding of non-hazardous sterile products*.

It is important to take these “clean” and “dirty” areas into account when traversing the anteroom and when removing PPE. If the anteroom is shared, this area is limited to hand hygiene and donning of PPE. No drugs are stored in the shared anteroom.

Table 4

Functional parameters of a shared anteroom for the compounding of hazardous and non-hazardous sterile products

The following functional parameters must be met:

- The anteroom must be kept under positive pressure relative to the adjacent areas.*
- The pressure differential must be at least 5.0 Pa⁴⁵ (equivalent to 0.02 inches water column) relative to the adjacent area.
- ISO Class 7 air quality must be maintained in the anteroom under dynamic operating conditions⁴⁶ ;
- There must be at least 30 air changes per hour (ACPH)⁴⁷. Depending on the size of the room and the number of people working in it, a greater number of ACPH may be required;
- The temperature of the anteroom must be less than or equal to 20°C, taking into account employees' comfort once all clean room garb (including PPE) has been donned. Medication storage temperature must not exceed 25°C.

* Excluding the clean room for the compounding of non-hazardous sterile products.

The air diffusers must be positioned so that the particle stream is directed toward the “dirty” area of the anteroom.

All air flowing within the shared anteroom must be exhausted to the exterior of the building. The air flowing into the anteroom must not be recycled.

5.3.2.7 All other facilities

The specifications recommended in the previous sections are similar to the recommendations for facilities laid out in General Chapter <797> of the United States Pharmacopeia – National Formulary (USP–NF)⁴⁸ for hazardous and non-hazardous sterile-product compounding rooms. Other approaches could also be suitable. For facilities where the functional parameters must differ in some respect, explanations and justifications must be provided. Other technologies, techniques, materials and procedures require prior approval from the provincial/territorial regulatory authority.

5.3.2.8 Materials and finishes

⁴⁵ United States Pharmacopeial Convention (USP). Response provided by USP for a shared anteroom, March 21, 2012.

⁴⁶ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 368

⁴⁷ International Organization for Standardization (ISO). *ISO 14644-4 Cleanrooms and associated controlled environments – Part 4: Design, construction and start-up*. Geneva, Switzerland: ISO; 2001.

⁴⁸ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding – sterile preparations. In: *USP pharmacists' pharmacopeia*. 2nd ed., Suppl. 2. Rockville, MD: USP; 2008. pp. 372 and 373.

The surfaces of ceilings, walls, floors, doors, door frames, shelves, counters and cabinets in controlled areas must be smooth, impermeable, free from cracks and crevices, non-porous and resistant to damage from cleaning products. These characteristics make them easy to clean and prevent microorganisms and non-viable contaminants from accumulating.

Dust-collecting overhangs, such as door sills, utility pipes and windowsills, must be avoided. There must be no curtains or paintings.

Ceilings

In controlled areas (clean room and anteroom), ceilings must have the following characteristics.

Ceilings must be constructed of smooth, non-friable, impermeable, non-porous, waterproof materials resistant to damage from cleaning products. All joints must be sealed.

In the clean room and the anteroom, joints between the ceiling and walls should be free of sharp corners where foreign substances could accumulate⁴⁹. Instead, the corners should be rounded.

If a recessed panel ceiling must be installed, the panels must be specifically designed for use in a clean room.

If a conventional recessed panel ceiling is installed⁵⁰, the panels must be impregnated with polymer to make them impermeable and hydrophobic, and the edges must be coated with clean room silicone to seal them to the support frame⁵¹. The tiles on this type of ceiling require periodic preventive sealing because the sealer eventually dries. When facilities undergo certification, this type of ceiling must be tested for tightness. Also, this type of ceiling is not recommended for new facilities.

In all rooms reserved for the compounding of sterile products, any holes, cracks or breakage in ceilings must be repaired and sealed.

Walls

In controlled areas (clean room and anteroom), the walls must have the following characteristics.

The walls must be constructed of smooth, non-friable, impermeable, non-porous, waterproof materials resistant to damage from cleaning products, such as gypsum board coated with epoxy paint, thick polymer panels or glass panels. All joints must be sealed. In locations at higher risk of breakage, stainless steel

⁴⁹ Health Canada, Health Products and Food Branch Inspectorate. *Good manufacturing practices (GMP) guidelines – 2009 edition, Version 2*. GUI-0001. Ottawa, ON: Health Canada; 2009, revised 2011 Mar 4. p. 10. Available from: <http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/docs/gui-0001-eng.php>

⁵⁰ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 373.

⁵¹ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p.373.

plates should be installed to prevent walls from being damaged when furniture is moved.

In the clean room and anteroom, the joints between walls should be rounded.

In all rooms reserved for the compounding of sterile products, any holes, cracks or breakage in walls must be repaired and sealed.

Floors

In controlled areas (clean room and anteroom), the floors must have the following characteristics.

Flooring must be non-porous, non-friable, flat, smooth, sealed and resistant to damage from cleaning products. Any breakage must be repaired and sealed immediately.

In the clean room and anteroom, the floor must be coved to the side wall.

There must be no mats or rugs. Anti-fatigue mats must be avoided they are typically made of porous materials⁵².

5.3.2.9 Accessories

Ceiling fixtures

In controlled areas (clean room and anteroom), ceiling fixtures must be recessed and flush-mounted. Their external surfaces, whether made of glass or other material, must be washable, smooth and sealed.

Plumbing

Water sources, sinks and drains must not be located in a clean room but are permitted in the anteroom.

Functional parameter control systems

Control systems indicating the temperature and differential pressure between controlled areas should be positioned together. Functional parameters require constant monitoring, so the controls should be installed where it is easy for personnel to take frequent readings.

Control systems must be connected to a notification system to alert personnel when operating parameters are outside preset limits. This allows personnel to make the necessary adjustments quickly while avoiding contamination of controlled areas and the problems that may result, including service interruption.

BSCs and CACIs must be connected to a notification system⁵³ to alert personnel to any unscheduled interruption or any alert related to the operation of the device outside compounding periods.

⁵² Canadian Centre for Occupational Health and Safety (CCOHS). Anti-fatigue mats. Hamilton, ON: CCOHS; 1997, confirmed current 2006. Available from: <http://www.ccohs.ca/oshanswers/ergonomics/mats.html>

Instruments for measuring differential pressure between controlled areas must be calibrated at least once a year or as recommended by the manufacturer.

5.3.2.10 Work surfaces and furniture

Work surfaces

Work surfaces and furniture must be constructed of smooth, non-porous, non-friable and impermeable materials, preferably stainless steel. Any material used for work surfaces must be able to withstand repeated cleaning and be resistant to damage from cleaning products. Any breakage must be repaired and sealed.

A horizontal surface for donning gloves should be installed in the clean room.

Furniture

Furniture in the clean room and anteroom must be designed and placed to facilitate cleaning and disinfecting, including disinfecting all floor and wall surfaces.

All movable furniture must be cleaned and disinfected before being placed in the clean room.

A locked cabinet dedicated to storage of cleaning and disinfecting equipment may be installed in the pharmacy (*also see section 5.3.4*).

Chairs used in controlled areas must be made of smooth, non-porous, non-friable, washable materials resistant to damage from cleaning products. Some chairs are specifically designed for use in clean rooms, and these should be the preferred choice.

Pass-through

A pass-through, with or without ventilation, should be installed for transferring products into and out of the clean room. The pass-through should be sealed and made of stainless steel or a smooth, non-porous, antistatic material resistant to damage from cleaning products.

The pass-through must be airtight. It is also recommended that the pass-through be equipped with an interlocking system that prevents both doors from being open at once. Otherwise, a door-opening procedure must be implemented.

If there is no pass-through, the clean room cart may be used to transport materials from the “clean” area of the anteroom into the clean room.

Interlocking door system

⁵³ Occupational Safety and Health Administration (OSHA). *OSHA technical manual (OTM): controlling occupational exposure to hazardous drugs*. Section VI, Chapter 2. Washington, DC: US Department of Labor; 1999. Available from: https://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html

Access doors to controlled areas should be equipped with an interlocking system. Such a system, which allows only one door to be open at a time, helps to maintain the pressure differential.

If this type of system is not installed, a door-opening procedure must be implemented and followed by compounding personnel and by cleaning and disinfecting personnel.

5.3.2.11 Signage

Each room must be identified with appropriate and informative signs (usually pictograms indicating cytotoxicity, the need for special care, hazards, restricted access, dress code, etc.).

5.3.2.12 Facility maintenance

Facility maintenance involves keeping the areas for compounding of hazardous sterile products operational within established specifications or bringing facility systems, including HVAC, back to satisfactory operating condition after an interruption. Maintenance must also be performed on equipment within the facility.

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

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

Filters and pre-filters

Existing clean room and anteroom pre-filters must be inspected regularly and replaced as recommended by the manufacturer.

The efficiency of HEPA filters in the ventilation system must be tested during facility certification (at least twice a year) and replaced as recommended by the manufacturer.

Filters used to exhaust air from rooms, BSCs or CACIs must be considered contaminated and must be handled with care appropriate to protect personnel and the environment. Where applicable, "bag in/bag out" containment systems can be used to enhance the safety of such operations.

5.3.3 Equipment

5.3.3.1 Biological safety cabinet and compounding aseptic containment isolator

Hazardous sterile products must be compounded inside a Class II or Class III BSC or CACI. Class II BSC types A2, B1 and B2 are all acceptable⁵⁴. Oncology support treatments can also be prepared in these devices, if they are being compounded for the same patient.

The BSC or CACI is located in the clean room. The device's ventilation system and its HEPA filter serve to filter the air in the compounding environment. The air quality must comply with ISO Class 5. The HEPA air filter of a BSC or CACI must be fully exhausted to the exterior of the building.

Before a BSC or CACI is used,

- personnel must read and understand the user's manual;
- the BSC or CACI must be installed according to the manufacturer's recommendations and certified by a qualified certifier (see Appendix 6);
- cleaning and disinfection must be performed.

The sterile compounding supervisor must ensure that the certification is completed according to certification standards currently in force (see Appendix 7).

A BSC or CACI must operate continuously, 24 hours a day⁵⁵. If the BSC or CACI has been turned off, it must be allowed to run for at least 30 minutes or as recommended by the manufacturer, before cleaning, disinfection and compounding of hazardous sterile products is undertaken⁵⁶.

The BSC or CACI must provide a work area with air quality meeting ISO Class 5 or better under dynamic operating conditions.

The floor of the enclosure must be resistant to damage from cleaning products and must be changed if it is damaged.

If a CACI is in use, the recovery time recommended by the manufacturer (i.e., the waiting time required to achieve ISO Class 5 air quality after materials have been transferred, before aseptic processing is started) must be observed when transferring products from the clean room to the manipulation area.

Location of BSC, CACI and other furniture

The BSC, CACI and other pieces of furniture should be positioned to avoid interfering with facility ventilation systems^{57 58 59}.

⁵⁴ United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings [draft]. Rockville, MD: USP; 2014 Mar.

⁵⁵ Occupational Safety and Health Administration (OSHA). *OSHA technical manual (OTM): controlling occupational exposure to hazardous drugs*. Section VI, Chapter 2. Washington, DC: US Department of Labor; 1999. Available from: https://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html

⁵⁶ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 380.

⁵⁷ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

⁵⁸ Peters GF, McKeon MR, Weiss WT. Potentials for airborne contamination in turbulent- and unidirectional-airflow compounding aseptic isolators. *Am J Health Syst Pharm* 2007;64(6):622-31.

⁵⁹ Controlled Environment Testing Association (CETA). *CETA compounding isolator testing guide: CAG-002-2006*. Raleigh, NC: CETA; 2006, revised 2008 Dec 8. Available from:

<http://www.cetainternational.org/reference/CETACompoundingIsolatorTestingGuide2006.pdf>

To facilitate cleaning and disinfecting activities, such as cleaning the floor and exterior of the **BSC or CACI**, and to avoid interfering with the operation of the BSC or CACI, there must be sufficient clearance around the **BSC or CACI** (usually 0.3 m⁶⁰). Some types of BSC can be built into the wall and sealed or wall-mounted and sealed, but this is not possible with other types. When positioning a **BSC or CACI**, the manufacturer's recommendations must be strictly followed to avoid interfering with normal operation. A smoke test may be used to validate proper operation during certification.

BSC⁶¹

The **BSC** must be positioned in an ISO Class 7 clean room or better, under negative pressure, and must not be placed near doors or other sources of drafts that might adversely affect unidirectional airflow.

If multiple **BSCs** are used, they must be positioned to prevent interference with one another.

CACI⁶²

The **CACI** must be positioned in an ISO Class 7 clean room or better, under negative pressure and adjoining an ISO Class 7 anteroom.

However, ISO Class 8 air quality in a negative-pressure room may be acceptable if all of the following conditions are met:

1. **The room has negative pressure (at least 2.5 Pa negative pressure relative to adjacent spaces)**⁶³.
2. The room has at least 12 ACPH⁶⁴.
3. The **CACI** maintains an ISO Class 5 environment (see Table 1) at all times during compounding, including during the transfer of ingredients, equipment and devices into and out of the CACI.
4. Particulate sampling from 15 to 30 cm upstream of the critical exposure site within the **CACI used for hazardous sterile products** shows ISO Class 5 air quality during compounding.
5. Particulate sampling conducted as close as possible to the doors when materials are being transferred, without obstructing the passageway, shows no more than 3520 particles (0.5 µm diameter or larger) per cubic metre of air (ISO Class 5) in the **CACI**.

⁶⁰ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 7-9. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

⁶¹ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

⁶² United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

⁶³ United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings [draft]. Rockville, MD: USP; 2014 Mar.

⁶⁴ United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings [draft]. Rockville, MD: USP; 2014 Mar.

The sterile compounding supervisor must obtain the following information from the manufacturer:

- documentation indicating that the **CACI** meets established standards when installed in an environment where the number of particles meets ISO Class 8 specifications;
- the waiting time required to achieve ISO Class 5 air quality after materials have been transferred, before aseptic processing is started (recovery time).

Compounding personnel working in a **CACI** must comply with the garbing procedure for compounding of **hazardous preparations in a BSC to maintain air quality and to protect themselves from spills.**

Maintenance of BSC and CACI

BSCs and CACIs must be maintained in accordance with the manufacturer's recommendations.

BSCs and CACIs must be certified⁶⁵

- twice a year
- when relocated
- after major repairs
- when sterility controls show that the **BSC or CACI** may not be in compliance with specifications

BSC and CACI pre-filters must be accessible. They should be inspected every 6 months and replaced if necessary or as recommended by the manufacturer. Washable pre-filters must not be used.

HEPA filters should be verified during installation and certification to ensure there are no leaks or damage to the filters after they have been transported or installed.

Preventive equipment maintenance (for **BSCs, CACIs**, etc.) must be performed when no compounding is in progress, before cleaning and disinfection operations.

All **BSC and CACI** maintenance, including maintenance of filters and pre-filters, must be noted on a form and entered in the general maintenance log (paper-based or computerized).

The sterile compounding supervisor must ensure that **BSC or CACI** maintenance has been performed. The supervisor must review the results or ensure that the results have been reviewed and corrective measures taken, as appropriate. The supervisor must sign the maintenance form or log.

5.3.3.2 Other devices, instruments or accessories related to the compounding of hazardous sterile products

⁶⁵ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 374.

Equipment used to compound **hazardous** sterile products must be clean and made of materials resistant to damage from cleaning products.

The decision to place equipment, instruments or accessories not directly related to the compounding of **hazardous** sterile products (carts, cabinets, computer monitors, etc.) in the clean room depends on whether such placement will have an impact on maintaining environmental conditions in the clean room (air quality control and surface sampling, etc.)⁶⁶.

All necessary devices, instruments and accessories must be cleaned and disinfected before being placed in a controlled area⁶⁷. Devices, instruments and accessories to be used in controlled areas should not be removed without good reason. **If they must be removed, they must be decontaminated.**

Maintenance of devices, instruments and accessories must be recorded in the general maintenance log.

Automated compounding device and balance

The automated compounding device (ACD) and the balance, if required for manipulations, must be positioned in the **BSC**. However, the ACD may be positioned outside the **BSC** if this allows compounding to be performed while maintaining critical sites within the **BSC**.

If the ACD is a peristaltic pump, this device must be calibrated several times during compounding of each batch. The ACD must also be calibrated between batches.

The ACD must be calibrated at least once a day (after cleaning), then as needed, according to the manufacturer's recommendations. The balance must be calibrated before each use, after it is moved, after cleaning and as needed, according to the manufacturer's recommendations.

The ACD and the balance are to be maintained according to the manufacturer's recommendations.

The results of calibration must be entered in the preparation log or general maintenance log for each batch, at a minimum.

Carts

If carts are used, one cart must be reserved for the "dirty" area of the anteroom and must remain there⁶⁸.

A second cart must be reserved for use in the "clean" area of the anteroom and in the clean room⁶⁹.

⁶⁶ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 373.

⁶⁷ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 373.

⁶⁸ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 379.

If the anteroom is shared, one cart must be reserved for the “microbiologically clean but chemically dirty” area and another for the “microbiologically and chemically clean” area.

Carts used to bring supplies into the anteroom from outside the controlled area shall not cross the demarcation line. Likewise, carts taken into the anteroom from the clean room shall not be moved beyond the clean side of the demarcation line.

Carts should be made of stainless steel or very good quality plastic, should be smooth, non-friable, non-porous and resistant to cleaning products, and should have easy-to-clean casters.

Carts should be cleaned and disinfected on a regular basis.

Refrigerator and freezer

Choice

Refrigerators and freezers used to store medications must be commercial, biomedical-grade units.^{70, 71, 72} Domestic refrigerators and freezers must not be used.

Use and placement

Refrigerators and freezers must be used only for storing hazardous drugs. They must not be used to store food.

Refrigerators and freezers used to store hazardous drugs may be placed in the clean room, to allow for containment of the drug in case of a spill. An air exhaust must be placed behind the refrigerator or freezer to remove any particles generated by the unit. There must be sufficient ACPH in the clean room to maintain the ISO Class 7 air quality classification.

Temperature and temperature control

The tested storage temperature in these units must meet the following parameters:

- controlled refrigeration temperature: 2°C to 8°C
- controlled freezing temperature: –25°C to –10°C

Accurate temperature probes (gauges or sensors) must be installed to indicate the actual temperature. A continuous recorder built into each unit is the preferred option, because it will record the temperature history.

⁶⁹ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 379.

⁷⁰ Public Health Agency of Canada (PHAC). *National vaccine storage and handling guidelines for immunization providers*. Ottawa, ON: PHAC; 2007. p. 22. Available from: <http://www.phac-aspc.gc.ca/publicat/2007/nvshgllp-ldemv/pdf/nvshgllp-ldemv-eng.pdf>

⁷¹ Health Canada, Health Products and Food Branch Inspectorate. Guidelines for temperature control of drug products during storage and transportation. GUI-0069. Ottawa, ON: Health Canada; 2011. Available from: <http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/docs/gui-0069-eng.php>

⁷² *Drug and Pharmacies Regulation Act*, R.S.O. 1990, c. H.4. Available from: http://www.e-laws.gov.on.ca/html/statutes/english/elaws_statutes_90h04_e.htm

A notification system must be installed in each refrigerator and freezer to alert pharmacy personnel when temperatures deviate from specifications.

Refrigerator and freezer temperature readings must be recorded on a form stored in the general maintenance log, unless the units are equipped with a continuous temperature recorder. In the latter situation, the data recorded by this device must also be verified and stored.

Temperature probes must be maintained and calibrated at least once a year or in accordance with the manufacturer's instructions. Calibration of these instruments must be noted in the general maintenance log.

Incubator

An incubator is a device used in microbiology laboratories to maintain a constant temperature for the culture of microorganisms.

The incubation temperature must be controlled (20°C to 25°C or 30°C to 35°C, depending on the culture medium and incubation period).

When the incubator is in operation, the incubator temperature must be read and recorded in the general maintenance log at least once a day.

The incubator must be calibrated and maintained according to the manufacturer's recommendations.

The incubator must not be placed in the clean room or the anteroom. It may be located in the pharmacy or another room nearby.

Cameras and computer equipment

Audio-visual and computer equipment used for verification during compounding (camera, monitor, pedal system) is allowed in the clean room under certain conditions. Preference must be given to audio-visual and computer equipment that features "hands-free" operation and that is made of smooth, non-porous, cleanable materials with low particulate emission and resistance to damage from cleaning products.

The use and installation of accessories (monitor, camera) that can be maintained and repaired outside the controlled areas is preferred.

Equipment cables must be covered to facilitate cleaning.

Communication system

A functional communication system (intercom, telephone or other) may be installed to allow verbal communication between the various controlled areas and the pharmacy.

These devices should be used in "hands-free" mode, must be easy to clean and must be resistant to damage from cleaning and decontamination products.

Waste containers

A sufficient number of easy-to-clean waste containers of suitable size and made of materials resistant to damage from cleaning and decontamination products must be available. Waste containers must be closable, to limit the spread of vapours. The exterior of each waste container must be decontaminated before it is removed from the controlled area.

The waste containers must be emptied and cleaned at least once a day, outside compounding hours. Waste containers must be identified with appropriate hazardous materials symbols (e.g., pictogram indicating cytotoxicity).

5.3.3.3 Personal protective equipment and clothing⁷³

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

Gloves

Gloves used in the clean room, in the clean area of the anteroom and during aseptic processes must be

- sterile
- non-powdered
- made of latex or (preferably) nitrile or neoprene
- compliant with the standard for chemotherapy gloves, standard D-6978-05 of ASTM International (formerly the American Society for Testing and Materials)

Non-sterile gloves that meet the ASTM International standard should be kept for use in unpacking areas, the “dirty” area of the anteroom and storage areas.

Personnel entering the clean room to perform tasks other than the compounding of hazardous sterile products, including verification of final compounded sterile preparations, may wear non-sterile gloves donned after aseptic hand hygiene. The gloves must then be disinfected with sterile 70% isopropyl alcohol before the person enters the clean room.

For the following activities, personnel must wear *two pairs of gloves* meeting the ASTM International standard:

- unpacking and cleaning
- compounding and disinfecting in the BSC
- compounding of hazardous drugs in the clean room
- cleaning procedures after a spill

Glove changes

Outer gloves must be changed in the event of contamination, breakage or spill.

Both pairs of gloves must be changed every 30 minutes⁷⁴ ⁷⁵ ⁷⁶, unless indicated otherwise by the manufacturer or unless there is breakage or contamination.

⁷³ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 4-5 to 4-11. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

The manufacturer's recommendations regarding product permeability must also be considered in determining the appropriate frequency of changing gloves.

Hands must be washed thoroughly each time gloves are changed. If hands are not dirty or sweaty, a long-lasting sterile 70% isopropyl alcohol gel, such as Sterigel+® or equivalent, may be applied in the clean room, before gloves are donned.

Gown

A chemotherapy gown worn during compounding of hazardous sterile products must be disposable^{77, 78}, made of a waterproof, non-shedding material, such as polyethylene or vinyl-coated polypropylene. It must have long sleeves and a tight-fitting rounded collar and must be adjustable at the wrists.

The gown must be discarded and replaced according to the manufacturer's time limit for permeation of the material. A gown must also be discarded and replaced after each removal or after 2–3 hours of consecutive^{79, 80} compounding work or after a spill or splash, whichever occurs first.

A protective gown is required if the employee is unpacking a damaged hazardous drug or if a spill has occurred⁸¹.

Hair cover

A disposable hair cover must be worn during the compounding of hazardous sterile products. It must be changed after each removal, after 3.5 hours of consecutive work or if it becomes contaminated⁸².

⁷⁴ Buchanan EC, Schneider PJ. *Compounding sterile preparations*. 3rd ed. Bethesda, MD: American Society of Health-System Pharmacists; 2009. p. 85.

⁷⁵ Wallemacq PE, Capron A, Vanbinst R, Boeckmans E, Gillard J, Favier B, Permeability of 13 gloves to 13 cytotoxic agents under controlled dynamic conditions. *Am J Health Syst Pharm*. 2006;63(6):547-56.

⁷⁶ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. pp. 4-5. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

⁷⁷ National Institute for Occupational Safety and Health (NIOSH). NIOSH alert: preventing occupational exposures to antineoplastic and other hazardous drugs in health care settings. Publ. No. 2004-165. Atlanta, GA: Department of Health and Human Services, Centers for Disease Control and Prevention, NIOSH; 2004 Sep. p. 13. Available from: <http://www.cdc.gov/niosh/docs/2004-165/pdfs/2004-165.pdf>

⁷⁸ Buchanan EC, Schneider PJ. *Compounding sterile preparations*. 3rd ed. Bethesda, MD: American Society of Health-System Pharmacists; 2009. p. 87.

⁷⁹ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 4-6. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

⁸⁰ United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings [draft]. Rockville, MD: USP; 2014 Mar.

⁸¹ United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings [draft]. Rockville, MD: USP; 2014 Mar.

⁸² Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 4.6. Available from:

Mask

Table 5 outlines the uses for and limitations of different types of masks.

Surgical masks do not provide respiratory protection against drug exposure and therefore should not be used during compounding of hazardous drugs.

For most activities, an N95 or N100 mask (NIOSH approved) will protect against airborne particles. An N95 or N100 mask must be used during decontamination procedures.

No mask is necessary for unpacking hazardous drugs that have been received from the supplier in impervious plastic. However, if hazardous drugs have been damaged before receipt, an N95 mask is required during unpacking⁸³.

Chemical cartridge respirators are preferred, as they provide protection against vapours and gases from medications. A cartridge with a pre-filter (for protection from dust) should be used, because there may be solid particles (medication dust) and organic vapours in the air when the BSC is cleaned.

A chemical-cartridge respirator with a pre-filter must be worn in the presence of vapours, gas and particles (e.g., dust) or if there has been a spill. A cartridge that protects against the chlorine found in chlorinated disinfectants used for cleaning the BSC or for chemical decontamination after a spill can also be considered, to help prevent irritation of airways.

Any mask (including N95 or N100 masks and chemical-cartridge respirators) must first be fit-tested and approved by the employer's respiratory protection program.

The mask must be changed after each removal, after 3.5 hours of consecutive work or if it becomes contaminated.

<http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

⁸³ United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings [draft]. Rockville, MD: USP; 2014 Mar.

Table 5

Masks and chemical-cartridge respirators				
Type of mask	Activity	Operating conditions	Filters	Notes
N95 or N100 (NIOSH approved)	Compounding of hazardous sterile products	ISO Class 7 compounding room under negative pressure BSC with front window closed Compounding in a CACI	N/A	Must be a mask specific for health care workers (not for construction workers) Dust protection required
	Receipt of goods or decontamination of materials	Unpacking area with wall air return	N/A	
Chemical-cartridge respirator	Receipt of goods or decontamination of materials	Unpacking area without wall air return Well-aerated room	For organic vapour, gas and dust	Will filter chlorine Frequency of filter change depends on saturation, so frequency will vary
Chemical-cartridge respirator plus shield or eye protection	Manipulation with splash risk Attending to spills Cleaning of BSC or CACI	ISO Class 7 compounding room under negative pressure BSC with front window open	For organic vapour, gas and dust	

BSC = biological safety cabinet, CACI = compounding aseptic containment isolator, N/A = not applicable, NIOSH = National Institute for Occupational Safety and Health (United States).

Safety shield or eye protection

A safety shield that covers the face (or eye protection combined with a chemical-cartridge respirator) must be worn when cleaning the BSC or CACI or when cleaning up after a spill.

Shoe covers

Disposable shoe covers must be worn in controlled rooms (clean room and anteroom), even if dedicated shoes are worn. The shoe covers must be changed after each removal, after 3.5 hours of consecutive work or in the event of contamination, spill or breakage⁸⁴. Shoe covers prevent the contamination of shoes and subsequent spread of contamination to other areas of the facility⁸⁵.

Beard cover

If the compounding personnel has facial hair, a disposable beard cover must be worn while compounding hazardous sterile products.

The beard cover must be changed after each removal, after 3.5 hours of consecutive work or if the cover becomes contaminated.

Uniform

Compounding personnel should wear a uniform (of the style worn in operating rooms) instead of street clothes. Use of a uniform reduces the risk of contaminating the environment by means of clothing; uniforms can also be used as a change of clothes in the event of a spill.

5.3.4 Cleaning and disinfecting in areas reserved for the compounding of hazardous sterile products

5.3.4.1 General

Cleaning and disinfecting (housekeeping) in areas reserved for the compounding of hazardous sterile products must be performed to ensure the cleanliness required for the quality and integrity of final compounded sterile preparations⁸⁶.

Policies and procedures for cleaning and disinfecting tasks must be developed, and cleaning and disinfecting personnel must be trained and assessed on correct application of these policies and procedures. In particular, cleaning and disinfecting procedures must be strictly enforced in the clean room and the anteroom.

Only trained and qualified cleaning and disinfecting personnel may be allowed to clean areas reserved for the compounding of hazardous sterile products⁸⁷.

⁸⁴ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 4.6. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

⁸⁵ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 4.8. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

⁸⁶ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 376.

Surface decontamination, deactivation and disinfection

When hazardous sterile products are compounded, cleaning of the premises and equipment must also eliminate chemical contamination from the hazardous products used. Methods used include decontamination, deactivation and disinfection.

Decontamination

Decontamination is the inactivation, neutralization or removal of a toxic product, usually through the application of chemical compounds.

Surface decontamination

Surface decontamination involves the transfer of a hazardous drug contaminant from a fixed surface (e.g., counter, bag of solution) to a disposable surface (e.g., towel, cloth).

A mixture of water and detergent, followed by rinsing water, is used to decontaminate surfaces. (See sections 5.3.4.5 and 6.6.4.3 for frequency of surface decontamination.)

Deactivation

Deactivation involves making a chemical compound (such as a hazardous drug) less hazardous by treating it with another chemical product. For example, the material safety data sheets for several hazardous drugs recommend 2.4% sodium hypochlorite for deactivation, followed by neutralization with 1% sodium thiosulfate to reduce the corrosive effect of the sodium hypochlorite on stainless steel surfaces. Surface Safe™ (Hospira) is a commercially available system of wipes containing both of these substances⁸⁸. Sodium hypochlorite also has an additional germicidal effect for disinfection⁸⁹.

These products (2.4% sodium hypochlorite followed by 1% sodium thiosulfate for neutralization) must be used for deactivation of a BSC and CACI (see section 6.6.4.3) or if there has been a significant spill or suspected contamination.

Disinfection

Disinfection is the removal of viable organisms from a surface with sterile 70% isopropyl alcohol or another effective disinfecting agent. Disinfection with sterile 70% isopropyl alcohol must always be preceded by cleaning, deactivation or decontamination of the surface (see sections 5.3.4.5 and 6.6.4.3).

5.3.4.2 Disinfectant

⁸⁷ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 376.

⁸⁸ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 13-2. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

⁸⁹ Kastango ES, Douglass K. Quality assurance for sterile products. *Int J Pharm Compound*. 2001;5(4):246.

Use of a germicidal disinfectant detergent is required to disinfect all surfaces in a clean room and anteroom. Many types of germicidal disinfectant detergents are acceptable.

The sterile compounding supervisor must

- initially choose an appropriate disinfecting agent for controlled areas, considering mainly its effectiveness and compatibility with materials used for facilities and equipment;
- in health care facilities, take into account the organization's disinfection policies and procedures, following the manufacturer's directions to dilute the disinfectant properly;
- follow the manufacturer's directions regarding required contact time between the disinfectant and the surface to be cleaned.

Use of an alternative disinfectant in the rotation is unnecessary. However, the daily use of a germicidal disinfectant should be augmented with weekly (or monthly) use of a sporicidal agent⁹⁰.

The use of sterile water is strongly recommended for diluting disinfectant solutions used inside ISO Class 5 areas.

The material safety data sheets for disinfectants used in the facility must be available on site and easily accessible.

5.3.4.3 Equipment used for cleaning and disinfection and its storage

Equipment used for cleaning and disinfecting must be accessible.

To avoid cross-contamination and to protect cleaning and disinfecting personnel, cleaning equipment (mop heads, towels, etc.) must be reserved exclusively for cleaning areas used for the compounding of **hazardous** sterile products^{91, 92}.

Non-shedding (lint-free)⁹³ equipment (mop heads, towels), preferably made of cellulose or microfibre, must be used for cleaning controlled areas.

This equipment (mop heads, towels, etc.) should preferably be disposable. If reusable accessories are used, they must be reserved for cleaning and disinfecting within the facility, must be washed and dried after each use and must be stored in a clean cabinet dedicated to storing this equipment⁹⁴.

The outside of containers for detergent and other cleaners must be kept clean. Small formats are preferred, and smaller containers filled from bulk containers must be disposable.

⁹⁰ United States Pharmacopeial Convention (USP). General chapter <1072>: disinfectants and antisepsis. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008–2009.

⁹¹ Okeke CC, Allen LV Jr. Considerations for implementing United States Pharmacopeia chapter <797> pharmaceutical compounding – sterile preparations. Part 4: Considerations in selection and uses of disinfectants and antiseptics. *Int J Pharm Compound*. 2007;11(6):492-9.

⁹² United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 376.

⁹³ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 376.

⁹⁴ McAteer F. Points to consider for developing a USP-797 compliant cleaning and sanitization program. *Clean Rooms*. 2007;21(8):44-48. Available from: <http://electroiq.com/issue/?issue=2302>

Cleaning equipment (mop handle, outside of bucket, etc.) must be disinfected before each entry into a controlled area. A closed, dedicated cabinet located in the anteroom or nearby must be provided for storing equipment (mop handle, etc.), refills (mop heads, towels) and cleaning products used for cleaning and disinfecting. Cleaning and disinfecting personnel must have access to a water supply and a place to dispose of waste water in the pharmacy.

5.3.4.4 Garbing of cleaning and disinfecting personnel

Cleaning and disinfecting personnel must comply with the pharmacy's hand hygiene and garbing procedure before entering sterile compounding areas and performing housekeeping duties. Personnel must also don **ASTM International–approved** sterile or non-sterile disposable gloves disinfected with sterile 70% isopropyl alcohol before starting work.

5.3.4.5 Cleaning frequency

Cleaning and disinfecting procedures must include surface decontamination followed by disinfection at regular intervals and at the following locations.

The minimum frequency of cleaning and disinfecting in clean rooms and anterooms will be either daily or monthly.⁹⁵

Daily cleaning is required for the following surfaces and areas:

- counters
- other easy-to-clean surfaces
- floors
- surfaces that are touched frequently (e.g., doorknobs, switches, chairs)

Monthly cleaning is required for the following surfaces and areas:

- walls
- ceiling
- shelves
- area outside the laminar airflow workbench

Cleaning should be done from the “cleanest” area to the “dirtiest” area: i.e. the end of the clean room toward the anteroom exit.

Forms or schedules used to record cleaning and disinfecting activities, as per established policy, must be retained in the general maintenance log.

5.4 General maintenance log

The general maintenance log (paper-based or computerized) includes all records or forms regarding

⁹⁵ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding – sterile preparations. In: *USP pharmacists' pharmacopeia*. 2nd ed., Suppl. 2. Rockville, MD: USP; 2008. p. S2/47.

- cleaning and disinfecting, facility certification and maintenance, BSCs, CACIs and other equipment used;
- verification of proper operation of equipment and instruments (calibration, refrigerator temperatures, etc.).

All records must be retained as per standards of practices of the respective provincial/territorial regulatory authority and in accordance with the principles of confidentiality.

6. PRODUCT AND PREPARATION REQUIREMENTS

6.1 Beyond-use date and dating methods

6.1.1 Beyond-use date of preparations

For the purposes of these Model Standards, the BUD is the date and time after which the hazardous compounded sterile preparation cannot be used or administered to a patient. It is based on the date and time when the hazardous sterile preparation was compounded⁹⁶.

The BUD also specifies the storage time and temperature conditions that must be in effect before administration.

The method used to establish the BUD depends on the type of commercial container (with or without preservative) used for the preparation and/or the preparation's risk of microbial contamination.

Where no specific sterility test is performed for a preparation or batch, the sterile compounding supervisor must assign a BUD based on the following criteria:

The BUD must not exceed the earliest of the dates established by the following two criteria:

- expiration date based on chemical and physical stability^{97,98,99} according to reference texts;
- storage time related to risk of microbial contamination ("microbiological stability"¹⁰⁰ related to the compounding process).

⁹⁶ United States Pharmacopeial Convention (USP). General chapter <795>: pharmaceutical compounding — nonsterile preparations. USP 36. Rockville, MD: USP; 2011.

⁹⁷ Trissel LA. *Handbook on injectable drugs*. 17th ed. Bethesda, MD: American Society of Health-System Pharmacists; 2013.

⁹⁸ King JC. *King guide to parenteral admixtures* [electronic version]. Napa, CA: King Guide Publications Inc.; [updated quarterly].

⁹⁹ Trissel LA. *Trissel's 2 clinical pharmaceuticals database* [electronic database]. Cashiers, NC: TriPharma Communications; [updated regularly].

To establish a longer BUD, specific sterility tests must be performed for a given preparation or batch.

The pharmacy's operating procedures must describe the method used to establish the BUD and the storage conditions.

6.1.2 Beyond-use dates for commercial products according to type of container (with or without preservative)

During compounding, the use of commercially available products must have priority. More specifically, if a sterile product is commercially available, compounding personnel must not use non-sterile ingredients to compound a sterile preparation.

The BUDs for commercial products used for compounding of hazardous sterile preparations specified in the following three sections (6.1.2.1, 6.1.2.2 and 6.1.2.3) apply when the products are stored in the original package and container.

6.1.2.1 Preservative-free sterile product, including "bulk" packaging

- BUD: up to 6 hours (controlled room temperature or refrigerator temperature)¹⁰¹ (see Table 6).
- The contents of a bulk vial cannot be divided for the sole purpose of extending stability.

Table 6

Beyond-use dates (BUDs) for hazardous compounded sterile preparations when a preservative-free vial is used¹⁰²			
BUD without any additional sterility testing	BUD for compounded (final) preparation at controlled room temperature (calculated from time of initial needle puncture)	BUD for compounded (final) preparation stored in refrigerator (calculated from time of initial needle puncture)	BUD for (final) compounded preparation stored in freezer
Vial used within 6 hours of initial needle puncture	Low risk = 48 hours Medium risk = 30 hours High risk = 24 hours	Low risk = 14 days Medium risk = 9 days High risk = 3 days	Low, medium and high risk = 45 days
*See Table 7 in section 6.1.3, below, for information about risk levels.			

¹⁰⁰ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 365-7.

¹⁰¹ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 365-7.

¹⁰² United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

- Administration of the compounded sterile preparation must start before the BUD has been exceeded.
- To properly manage risk, a label must be affixed to the vial indicating the time of initial needle puncture. The vial must be punctured in a **BSC** that maintains ISO Class 5 air quality or a **CACI** that meets the requirements of these Model Standards.

6.1.2.2 Open ampoule

- BUD: immediate use

6.1.2.3 Multiple-dose vial containing a preservative

- BUD: 28 days, unless otherwise specified by the manufacturer.

6.1.3 Beyond-use date according to risk of microbial contamination

After a stationary phase (phase 1), which varies by species, bacteria replicate within 20 to 30 minutes (phase 2 growth). Once contamination occurs, bacterial growth increases rapidly starting 6 hours after onset of contamination¹⁰³. For example, contamination of 10 colony-forming units per millilitre (CFU/mL) at 6 hours will increase to 640 CFU/mL by 9 hours, to 41 000 CFU/mL by 12 hours, and to 6.9×10^9 CFU/mL by 24 hours.

The BUD is based on the risk that a preparation may be contaminated (Tables 7 and 8).

Levels of risk for microbial contamination (Table 7) assume that preparations are compounded in a compliant, certified **BSC** that maintains ISO Class 5 air quality or better and that is located in an ISO Class 7 clean room. When the preparation is compounded in an isolator that meets the location criteria specified in section 5.3.3.1, the isolator must be installed in an ISO Class 8 environment or better.

Sterile unit

The concept of a “sterile unit” is used to specify certain criteria for determining the risk level and establishing the BUD.

A sterile unit is a vial, ampoule or bag of drug or diluent. The following examples illustrate the concept:

- 1 bag of solute represents 1 “sterile unit.”
- 2 vials of cefazolin represent 2 “sterile units.”

¹⁰³ Cundell AM. USP Committee on Analytical Microbiology — stimuli to the revision process. *Pharmaceutical Forum*. 2002;28(6).

- 1 vial of sterile water for injection represents 1 “sterile unit.”

Table 7

Contamination risk levels ^{104,105}		
Low	Medium	High
<ul style="list-style-type: none"> • Final product compounded using up to 3 “sterile units” • No more than 2 septum punctures at the injection site for each sterile unit • Simple aseptic transfer technique • Drug prepared for one patient (patient-specific dose) 	<ul style="list-style-type: none"> • Final product compounded using 4 or more “sterile units” • Complex manipulations • Prolonged preparation time • Batch preparations (for more than one patient) 	<ul style="list-style-type: none"> • Non-sterile ingredients or equipment used for preparation • Exposure, for more than 1 hour, of sterile material or content of sterile commercial products to an environment with air quality below ISO Class 5 requirements • Non-sterile preparations containing water, stored for more than 6 hours before sterilization

Table 8

Beyond-use dates (BUDs) for hazardous compounded sterile preparations, according to risk of microbial contamination ¹⁰⁶			
	BUD without additional sterility testing		
Risk of contamination	At controlled room temperature	With storage in refrigerator	With storage in freezer
Low	48 hours	14 days	45 days
Medium	30 hours	9 days	45 days
High	24 hours	3 days	45 days

¹⁰⁴ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

¹⁰⁵ American Society of Health-System Pharmacists (ASHP). *The ASHP discussion guide on USP chapter <797> for compounding sterile preparations. Summary of revisions to USP chapter <797>*. Bethesda, MD: ASHP with Baxter Healthcare Corporation; 2008. Available from: http://www.ashp.org/s_ashp/docs/files/discguide797-2008.pdf

¹⁰⁶ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 365-7.

Administration of the compounded sterile preparation must start before the BUD has been exceeded.

High-risk preparations must always be sterilized (the BUDs in Table 8 apply to high-risk *sterile* preparations).

Sterility and control test¹⁰⁷

A bacterial endotoxin sterility and control test must be performed for high-risk hazardous compounded sterile preparations (see Table 7) in the following situations:

- when hazardous sterile preparations are compounded in batches of over 25 identical units;
- when there has been more than 12 hours of exposure time at a temperature between 2°C and 8°C before sterilization;
- when there has been more than 6 hours of exposure time at a temperature above 8°C before sterilization.

6.1.4 Beyond-use dates for preparations in short-term critical situations

Pharmacy departments and community pharmacies that provide hazardous compounded sterile preparation services must meet the requirements specified in these Model Standards, specifically, adequate facilities and equipment, compliance with garbing requirements, application of stringent housekeeping and impeccable aseptic technique.

6.1.4.1 Beyond-use dates for immediate-use preparations

BUDs are not applicable to the compounding of hazardous sterile preparations for immediate use.

6.1.4.2 Preparations with beyond-use dates of 12 hours or less¹⁰⁸

For compounded sterile preparations made in a **BSC** that maintains the requirement for ISO Class 5 air quality or better, but is not located in an environment in compliance with ISO Class 7 air quality, the following conditions must be met:

- **The room has a minimum of 12 ACPH.**
- **The room maintains negative pressure of at least 2.5 Pa relative to adjacent spaces.**
- **Preparations are low or medium risk.**

¹⁰⁷ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 361.

¹⁰⁸ United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings [draft]. Rockville, MD: USP; 2014 Mar.

- One preparation is compounded at a time.
- The preparations are compounded in an area that is reserved for the compounding of sterile products and that minimizes contamination.
- There is no sink in the preparation area, and there are no unsealed windows and no doors to the exterior of the building. Furthermore, the preparation area is not in a high-traffic area or adjacent to construction sites, warehouses or food preparation sites.

The microbial contamination risks associated with compounding such products under these conditions remain high, even if there is full compliance with hand hygiene, asepsis, garbing and maintenance rules.

Given the associated risks, the compounding of sterile products under these conditions must be only a temporary measure, and administration must start within 12 hours after the start of compounding; otherwise, the preparation must be discarded.

6.2 Compounded sterile preparation protocols



Protocols for the compounding of **hazardous** sterile preparations must include all information required to prepare the compound:

- name
- pharmaceutical form
- all required ingredients
- quantity and source of ingredients
- necessary equipment
- instructions for compounding the preparation
- storage method
- BUD
- references
- draft and revision date
- pharmacist's signature

Appendix 8 presents a model for writing compounded sterile preparation protocols for each drug.

All protocols for **hazardous** pharmacy compounded sterile preparations must be stored together and readily available for quick consultation. The protocols must be reviewed and approved by the sterile compounding supervisor or delegate.

6.3 Compounded sterile preparation log



A **hazardous** compounded sterile preparation log (**either paper-based or computerized**) must be completed during the compounding process.

The pharmacy must keep such a log for individual patients, as well as a log for **hazardous** sterile preparations made in batches.

Computerized information and information recorded with cameras may be used as a record, if all the required information is present and easy to track.

6.3.1 Hazardous compounded sterile preparation log for one patient (individual preparations)

The **hazardous** compounded sterile preparation log for an individual patient must contain the following information:

- patient's name
- prescription number (if compounded in a community pharmacy)
- patient identification number (if compounded in a health care facility)
- preparation identification (name and concentration)
- compounding procedure
- for each ingredient (including primary and secondary diluents),
 - name
 - quantity/volume measured
 - batch number
 - expiration date
- compounding date
- preparation BUD
- compounder and verifier at each stage of the process

The log (paper-based or computerized) must be filed and retained for future reference.

6.3.2 Hazardous compounded sterile preparation log for products made in batches

The log of **hazardous** sterile products prepared in batches must contain the following information:

- preparation identification (name and concentration)
- compounding procedure
- for each ingredient (including primary and secondary diluents),

- name
- quantity/volume
- batch number
- expiration date
- quantity prepared
- prepared batch number
- compounding date
- preparation BUD
- compounder and verifier at each stage of the process

The log (paper-based or computerized) must be filed and retained for future reference.

6.4 Patient file

For any **hazardous** compounded sterile preparation that has been dispensed, all information required for review and assessment of the patient's file by pharmacists and for subsequent treatment of the patient must be recorded in the patient's file.

In community pharmacies, information recorded in the patient's file must allow users to accurately reproduce the prescribed preparation at a later date or identify the compounding pharmacist, if necessary.

The patient care (dispensing) pharmacist must record in the patient's file the origin of the hazardous compounded sterile preparation that is being dispensed, if the dispensing pharmacist did not compound the preparation (where compounding is undertaken by another pharmacy, as permitted by provincial/territorial legislation).

In health care facilities, the pharmacist must keep track of preparations compounded externally (by a community pharmacy, etc.).

In addition, the patient care (dispensing) pharmacist must be able to track information related to preparations made by another pharmacist.

6.5 Conduct of personnel in areas reserved for the compounding of **hazardous** sterile products

Compounding personnel must behave in a professional manner, following policies and procedures.

6.5.1 Conditions that may affect preparation quality

The sterile compounding supervisor or delegate must assess the possibility of temporarily removing any compounding personnel with a condition that may affect preparation quality¹⁰⁹, including

- uncontrolled weeping skin condition affecting face, neck or arms or that might cause significant skin desquamation or contamination;
- burns to the skin, including sunburns;
- cold sores (active herpes simplex viral infection);
- conjunctivitis (viral or bacterial);
- active respiratory infection with coughing, repeated sneezing or runny nose;
- fresh piercings;
- other fresh wounds.

A person with permanent tattoos may compound sterile products. However, a recent tattoo on the face, neck or arms is considered a fresh skin wound, and the individual must cease sterile compounding activities and wait until the skin is completely healed before resuming such activities. Tattoos transferred from paper to the skin of the face, neck or arms by wetting and henna tattoos are not acceptable and must be completely removed before the person resumes sterile compounding activities.

6.5.2 Conduct before entering the anteroom

Before entering the anteroom, compounding personnel must take the following steps¹¹⁰:

- remove personal outerwear (e.g., coat, hat, jacket, scarf, sweater, vest, boots and dirty outdoor shoes), which tends to shed particles or squamous cells;
- remove jewelry, studs and other accessories from fingers, wrists, forearms, neck and other body parts if they might interfere with the effectiveness of the PPE (e.g., for adjusting gloves and sleeves and for antiseptic washing of hands and forearms);
- remove all cosmetics (makeup, false eyelashes, perfume and hair products such as hairspray), which can produce particles that are possible sources of contamination;
- tie back long hair;

¹⁰⁹ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 376-7.

¹¹⁰ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 376-7.

- remove nail polish¹¹¹ or any nail application, extensions or other synthetic nail-lengthening products;
- ensure that nails are short and that skin around the nails is undamaged;
- ensure that skin of hands and forearms is undamaged;
- change into dedicated, low-shedding apparel suitable for the controlled area (e.g., scrubs);
- fully cover legs and feet, and wear closed shoes and socks;
- wash hands.

6.5.3 Conduct in controlled areas (clean room and anteroom)

In controlled areas, the following measures should be taken:

- Food items, drinks, chewing gum, candy and smoking are prohibited¹¹².
- Food items or drinks must not be stored in refrigerators reserved for storing compounded sterile preparations.
- All access doors to controlled areas must be kept closed.
- Anyone who enters the anteroom or a clean room must be authorized and follow all hand hygiene and garbing procedures.
- Only essential conversations are allowed, to minimize the risk of particulate contamination. Coughing, sneezing and talking in the direction of the **BSC** should also be avoided.

6.6 Aseptic compounding of hazardous sterile products^{113,114}

6.6.1 General

The aseptic compounding process includes all activities leading to completion of the final sterile preparation, including

- performing hand and forearm hygiene;
- garbing of personnel;

¹¹¹ Boyce JM, Pittet D. Guideline for hand hygiene in health-care settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. *MMWR Recomm Rep.* 2002;51(RR-16):1-45.

¹¹² United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 380.

¹¹³ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). Chaper 8 : [Drug Preparation. *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. pp. xx-yy. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

¹¹⁴ American Society of Health-System Pharmacists. ASHP guidelines on handling hazardous drugs. *Am J Health Syst Pharm.* 2006;63(12):1172-93.

- disinfecting and introducing products and equipment into the clean room;
- disinfecting the **BSC or CACI**;
- disinfecting and introducing products and equipment into the **BSC or CACI**;
- using aseptic techniques to compound **hazardous** sterile products in the **BSC or CACI**;
- **decontaminating final hazardous compounded sterile preparations**;
- verifying, labelling and packaging final hazardous compounded sterile preparations.

Personnel must develop work techniques to minimize the risk of cross-contamination, to avoid errors and to maximize performance of the BSC or CACI. The pharmacist or pharmacy technician must apply professional judgment at all times.

The number of people in the clean room and anteroom must be limited to the minimum number required to perform aseptic compounding activities¹¹⁵.

Before the compounding of sterile products begins, the pharmacist on duty must ensure that calculations are accurate and that the appropriate drugs, equipment and devices have been selected. The pharmacist must also ensure that compounding personnel follow the protocol for compounding the hazardous sterile product and must validate the preparations log.

All stages of compounding hazardous sterile products must be performed in a BSC or CACI that maintains ISO Class 5 air quality requirements.

6.6.2 Hand and forearm hygiene and garbing

Hand and forearm hygiene and garbing are the first important steps in preventing contamination of sterile products.

6.6.2.1 Hand and forearm hygiene

After donning dedicated shoes or shoe covers, head and facial hair covers and face masks, personnel must wash and disinfect hands and forearms in the following sequence:

- Under running water, use a nail cleaner to remove debris from underneath fingernails.
- Wash hands and forearms to the elbows with soap and water, for a period of 30 to 60 seconds.
- Rinse with water.
- Dry hands and forearms with disposable, lint-free paper towel.
- Dispense alcohol-based hand rub (ABHR) onto one palm.
- Immerse fingertips of the other hand into the ABHR.
- Cover the forearm of the other hand with ABHR until the ABHR evaporates.

¹¹⁵ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 380.

- Repeat with other hand and other forearm.
- Don non-shedding gown.
- Enter the clean room.
- Dispense ABHR onto palm of one hand. Rub both hands with ABHR, making sure that all surfaces of the hands are covered. Continue to rub until the ABHR has evaporated.
- Allow hands to dry.
- Don sterile gloves.

The selected sequence must be documented in the policies and procedures and updated as appropriate¹¹⁶.

6.6.2.2 Garbing

Personnel must wear the PPE required for compounding hazardous sterile products, whether compounding is performed in a BSC or a CACI¹¹⁷.

When using CACIs, compounding personnel must comply with the garbing procedure to preserve air quality.

Compounding personnel must don and remove garb in the sequence described in the policies and procedures. The selected sequence must be documented and reviewed regularly.

Any compounder must wear two pairs of gloves. The first (inner) pair of gloves goes under the sleeves of the person's gown, while the second (outer) pair must be pulled up over the gown sleeves just before entering the clean room. For compounding personnel, the outer glove must be sterile. Any person entering the clean room for a purpose other than the compounding of hazardous sterile products must wear a single pair of gloves. These gloves may be non-sterile but must be disinfected with sterile 70% isopropyl alcohol before entry.

Shoe covers are required at all times in the clean area of the anteroom and the clean room. All shoes worn must be closed, dry, clean and easy to maintain. These shoes should preferably be used only for walking about in the "clean" area of the anteroom and the clean room. Shoe covers should be worn even on shoes reserved for use in controlled areas.

After finishing the compounding of hazardous sterile products, personnel must remove their PPE in the anteroom following an established technique and sequence, to minimize the risk of chemical contamination, as set out in a detailed procedure developed by the facility. If a CACI is used for compounding, the PPE may be removed in the clean room. Personnel must dispose of soiled PPE in a

¹¹⁶ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 376-7.

¹¹⁷ Buchanan EC, Schneider PJ. *Compounding sterile preparations*. 3rd ed. Bethesda, MD: American Society of Health-System Pharmacists; 2009. Personnel cleansing and garbing.

container for cytotoxic waste and must then wash their hands before exiting and performing any other activity.

6.6.3 Introducing products and equipment into the clean room

Before a product enters the anteroom, it must be removed from cardboard shipping boxes. The product must be wiped with a sporicidal agent (since cardboard has been found to harbour mould spores). Any remaining packaging must be removed after the product enters the clean room from the anteroom. At this point, only packaging required for maintenance of sterility is retained.

Where packaging allows, compounding equipment and products must be disinfected with sterile 70% isopropyl alcohol just before being introduced into the clean room for the compounding of sterile products¹¹⁸.

Non-shedding sterile wipes or swabs must be used for disinfection. The wipes or swabs must be changed regularly during disinfection of products and equipment.

For introduction of compounding equipment and products into the clean room, the items must be placed in a plastic or stainless steel bin to prevent errors. The bin is then placed in the pass-through for transfer to the clean room. Bins used for this purpose must be disinfected before use.

If there is no pass-through, the equipment and products are transferred from the “dirty” cart or bin to the “clean” cart or bin at the demarcation line in the anteroom and then introduced into the clean room.

6.6.4 Surface decontamination, deactivation and disinfection of the biological safety cabinet or compounding aseptic containment isolator

Only compounding personnel are allowed to clean, decontaminate and disinfect the **BSC or CACI**. They must take the following steps:

- Follow hand and forearm hygiene and garbing procedures.
- Follow the cleaning, decontamination, deactivation and disinfection methods described in the pharmacy's procedures (respecting specified equipment, sequence, movements, frequency, etc.).

Only the person performing this maintenance should be present in the clean room¹¹⁹.

Cleaning, decontamination, deactivation and disinfection tasks performed must be recorded in the general maintenance log.

¹¹⁸ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 376, 379.

¹¹⁹ BC Cancer Agency (BCCA). Module 1: Safe handling of hazardous drugs. In: *BC Cancer Agency pharmacy practice standards for hazardous drugs*. Vancouver, BC: BCCA; 2012.

6.6.4.1 Requirements for cleaning and disinfecting

Personnel must comply with the following requirements for cleaning and disinfecting:

- Disinfect non-powdered sterile gloves with sterile 70% isopropyl alcohol and allow to dry before starting to clean and disinfect the **BSC or CACI**.
- Ensure that the head and upper body do not enter the **BSC or CACI**.
- Use non-shedding, disposable swabs.
- Avoid contaminating the surface of swabs used for cleaning and disinfecting.
- Change swabs after completing disinfection of each section of the **BSC or CACI**.
- **Clean the BSC or CACI** with clean swabs and sterile water at the start or end of the day or shift (minimum once per day).
- Follow the cleaning method described in the pharmacy's procedures (with regard to equipment, sequence, movements).
- **Fully disinfect the BSC or CACI with sterile 70% isopropyl alcohol or another disinfecting agent, using sterile swabs, at the start and end of the day or shift (minimum twice per day).**
- Follow the disinfecting method described in the pharmacy's procedures.
- Wait until the disinfectant has dried before compounding the first preparation in the BSC or CACI¹²⁰.
- Record cleaning and disinfecting activities in the maintenance log.

6.6.4.2 Daily maintenance of the BSC and CACI

On its own, sterile 70% isopropyl alcohol does not deactivate hazardous drugs and may, on the contrary, spread any chemical contamination that is present to other surfaces.^{121,122,123} Therefore, for daily activities such as cleaning the inside of the BSC, a surface decontamination step using a mixture of water and germicidal disinfectant detergent, followed by rinsing with water¹²⁴, must precede the usual disinfection step performed with sterile 70% isopropyl alcohol.

6.6.4.3 Frequency of surface decontamination, deactivation and disinfection for BSCs and CACIs

¹²⁰ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 391.

¹²¹ Sessink PJM, Boer KA, Scheefhals APH, Anzion RB, Box RP. Occupational exposure to antineoplastic agents at several departments in a hospital. Environmental contamination and excretion of cyclophosphamide and ifosfamide in urine of exposed workers. *Int Arch Occup Environ Health*. 1992;64(2):105-12.

¹²² Dorr RT, Alberts DS. Topical absorption and inactivation of cytotoxic anticancer agents in vitro. *Cancer*. 1992;70(4 Suppl):983-7.

¹²³ American Society of Health-System Pharmacists. ASHP guidelines on handling hazardous drugs. *Am J Health Syst Pharm*. 2006;63(12):1172-93.

¹²⁴ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). Chapter 7: Planning the Oncology Pharmacy. *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. pp. 7-3. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

Preparation of the interior surfaces of the BSC or CACI through surface decontamination followed by disinfection is a critical step in the aseptic preparation process. This step is to be performed by compounding personnel according to the frequencies set out in Table 9. If decontamination and disinfection are performed at a different frequency, it should be established and justified on the basis of environmental control results.

The material safety data sheets for many hazardous products indicate that they are deactivated by 2.4% sodium hypochlorite followed by 1% sodium thiosulfate (for rinsing). The deactivation frequency recommended for BSCs is indicated in Table 9.

Table 9

Minimum frequency of surface decontamination, deactivation and disinfection of the inside of a biological safety cabinet (BSC) or compounding aseptic containment isolator (CACI)				
Surface	Frequency ^{125,126,127,128,129}	Surface decontamination*	Deactivation†	Disinfection‡
Work surface in BSC or CACI	- Before start of compounding			✓
Work surface in BSC or CACI	- On each preparation change, upon removal from BSC or CACI - At the start or end of each shift - Where surface contamination is suspected - If there has been non-compliance with aseptic techniques	✓		✓
All surfaces inside BSC or CACI	- At start of workday - At start of workday if BSC or CACI has not been used for one or more days - When there has been a spill	✓		✓
All surfaces inside BSC or CACI and subfloor of BSC or CACI	- Weekly, at the end of a workday or as recommended by manufacturer	✓		✓
All surfaces inside BSC or CACI and subfloor of BSC or CACI	- At least once a month at the end of the workday ¹³⁰ - When a more significant spill is suspected	Cleaning with water only	✓	✓
*Surface decontamination = cleaning with mixture of water and germicidal disinfectant detergent, followed by rinsing with water. †Deactivation = application of sodium hypochlorite and sodium thiosulfate. ‡Disinfection = application of sterile 70% isopropyl alcohol.				

¹²⁵ BC Cancer Agency (BCCA). Module 1: Safe handling of hazardous drugs. In: *BC Cancer Agency pharmacy practice standards for hazardous drugs*. Vancouver, BC: BCCA; 2012. p. 11.

¹²⁶ American Society of Health-System Pharmacists. ASHP guidelines on handling hazardous drugs. *Am J Health Syst Pharm*. 2006;63(12):1172-93.

¹²⁷ McElhiney LF. Preparing nonsterile and sterile hazardous compounds in an institutional setting. *Int J Pharm Compound*. 2009;13(4):300-10.

¹²⁸ Occupational Safety and Health Administration (OSHA). *OSHA technical manual (OTM): controlling occupational exposure to hazardous drugs*. Section VI, Chapter 2. Washington, DC: US Department of Labor; 1999. p. 5. Available from: https://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html

¹²⁹ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. pp. 13–2 and 13–3. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

¹³⁰ Expert consensus based on (1) no known product for deactivating all hazardous products; (2) sodium hypochlorite is recommended in the material safety data sheets for multiple hazardous products; (3) sodium hypochlorite can damage work surfaces; (4) hypochlorite and thiosulfate wipes are available.

6.6.5 Aseptic techniques for compounding **hazardous** sterile products

6.6.5.1 General

Compounding personnel should prepare one batch of drugs or one type of preparation at a time.

In the event of non-compliance with aseptic technique, the preparation must be discarded. In this situation, new supplies must be used.

Gloved hands must be disinfected with sterile 70% isopropyl alcohol before re-introduction into the BSC or CACI or after gloves have come into contact with a microbiologically contaminated surface¹³¹. If gloves are torn, hands must be washed before new gloves are donned. Gloves must be changed regularly (**i.e., every 30 minutes or according to the manufacturer's recommendations**). **Outer gloves must be removed before hands are removed from the BSC**. The frequency and circumstances of glove changes must be defined in a procedure (**see also section 5.3.3.3**).

The external packaging of products and supplies must be intact, dry and unsoiled. Otherwise, the products and supplies must be discarded. Containers (e.g., bags of solution, vials and ampoules) must be examined before use. **Products exhibiting turbidity, cloudiness or particulates must not be used.**

All equipment with surfaces that can be disinfected must be disinfected with sterile 70% isopropyl alcohol before being introduced into the **BSC or CACI**. Non-shedding wipes or sterile swabs must be changed regularly while equipment is being disinfected.

Ophthalmic solutions prepared from sterile powder products that require dilution must always be filtered with a 5-µm filter. Filtration is not necessary when the products used are available as sterile solutions in vials¹³².

Vials must not be allowed to accumulate in the BSC or CACI, to reduce the risk of errors and air turbulence.

6.6.5.2 Aspects of compounding hazardous drugs

Sterile chemotherapy prep mat

All manipulations inside the BSC or CACI must be performed over a sterile chemotherapy prep mat.

To prevent cross-contamination, the mat must be changed¹³³ in the following situations:

¹³¹ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 380.

¹³² Buchanan EC, Schneider PJ. *Compounding sterile preparations*. 3rd ed. Bethesda, MD: American Society of Health-System Pharmacists; 2009. p. 29.

- when it becomes soiled
- when a spill occurs
- at each shift change¹³⁴ (at least twice a day)

Interior of BSC or CACI

Compounding personnel must adhere to the following requirements when working inside the BSC or CACI:

- install and prime the patient delivery system (tubing) before adding the hazardous product;
- use a ventilated system equipped with a 0.22-µm hydrophobic filter when diluting powder or sampling liquids;
- when use of a ventilated system is not possible, follow the technique for sampling under negative pressure;
- when sampling a hazardous product solution, comply with the maximum fill limit of the syringe, i.e., 75% (3/4) of total syringe capacity;
- when distributing a hazardous product in a syringe, use a protective Luer-Lok safety tip system;
- if possible, use a closed-transfer system (since the steps described above do not completely eliminate risk of exposure to the hazardous product);
- discard all materials used during compounding into a marked waste bin specifically designated for hazardous products;
- before removing a container holding a final hazardous compounded sterile preparation from the BSC, follow the surface decontamination procedure (sterile water with detergent or other agent)¹³⁵ on all surfaces of the container, including tubing.

Interior of clean room

While the final container is still inside the BSC or CACI¹³⁶, compounding personnel must label it and place it in a sealable plastic bag, along with the inner

¹³³ Occupational Safety and Health Administration (OSHA). *OSHA technical manual (OTM): controlling occupational exposure to hazardous drugs*. Section VI, Chapter 2. Washington, DC: US Department of Labor; 1999. Available from: https://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html

¹³⁴ Occupational Safety and Health Administration (OSHA). *OSHA technical manual (OTM): controlling occupational exposure to hazardous drugs*. Section VI, Chapter 2. Washington, DC: US Department of Labor; 1999. p. 5. Available from: https://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html

¹³⁵ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 8-7. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

¹³⁶ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 8-7. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

pair of gloves¹³⁷. All final hazardous compounded sterile preparations must be marked “cytotoxic.”

6.6.6 Verification of final hazardous compounded sterile preparations

6.6.6.1 Role of personnel in verification

The sterile compounding supervisor (or compounding pharmacist or pharmacy technician) must perform the following activities:

- ensure that all hazardous compounded sterile preparations comply with compounding protocols;
- verify the identity of the ingredients (drug and diluent);
- verify the volume of the ingredients (drug and diluent);
- regularly verify the quality of the manipulations.

When compounding, compounding personnel must undertake the following activities:

- perform a visual inspection of each unit for evidence of particulates, to verify the clarity, colour and volume of the solution, to check the container for possible leaks and to verify the integrity of the container;
- validate the information on the label;
- place final hazardous compounded sterile preparations that require storage at 2°C to 8°C in the refrigerator pending verification and delivery to patients or the patient care unit (ice packs are suitable for maintaining the temperature of a cooled item but cannot be used for the cooling process; therefore, final hazardous compounded sterile preparations must be cooled in the refrigerator before being placed in a cooler).

6.6.6.2 Process for verification

Verifications may be performed in one of three ways:

- direct observation during compounding;
- viewing of the identity and quantity of ingredients through an observation window located close to the BSC;
- remote observation using a digital camera connected to a monitor (see section 6.6.6.3 for additional detail).

6.6.6.3 Verification by image capture or live camera

Verification may be conducted by capturing images of the critical site (in the BSC) with a camera connected to a monitor. Such verification must be performed before the hazardous compounded sterile preparation is delivered to the patient.

¹³⁷ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 8-7. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

However, in this situation, if the verifying pharmacist notices that one or more procedures have not been followed correctly, all hazardous compounded sterile preparations compounded during this period must be destroyed, and the destruction of preparations (because of non-compliance identified during verification) must be entered in the preparations log.

Appendix 9 gives examples of compounded sterile preparations that must be verified at each step of the compounding process.

6.6.6.4 Verification not required

Some preparations need not be verified during compounding because of the packaging or compounding preparation system used. As with all preparations, however, the products and equipment used must be verified before and after compounding. An additional verification method, by counting vials, ampoules and remaining material, should be implemented.

Appendix 10 gives examples of compounded sterile preparations for which verification is not required during the compounding process.

6.6.6.5 Delegation of verification

The pharmacist may delegate verification during compounding to pharmacy technicians or TSP. Such personnel must be experienced and must have received appropriate training.

The delegation of container-content verification requires strict supervision, including

- implementation of policies and procedures;
- implementation of a quality assurance program, including regular evaluations of the TSP involved;
- verification of a percentage of preparations by the supervisor.

Some provincial/territorial jurisdictions have standards for delegating duties to TSP in a pharmacy.

Each preparation must be inspected by a person other than the individual who performed the aseptic technique. This person must inspect each unit against a black and white background for evidence of particulates, verify the clarity, colour and volume of the solution, check the container for possible leaks and verify its integrity.¹³⁸

Like the compounder, the verifier must sign the preparations log.

6.6.7 Labelling final **hazardous compounded sterile preparations**

6.6.7.1 General

¹³⁸ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 381.

The sterile compounding supervisor must establish a policy for the labelling of **hazardous** compounded sterile preparations and ensure that it is followed.

The information on labels must follow federal/provincial/territorial legislation and regulations for drugs prepared or sold with or without a prescription. More specifically, the labels for **hazardous** compounded sterile preparations must meet the requirements of the applicable legislation and regulation.

All active ingredients must be identified on the label. The label must also include the concentration of each ingredient.

Each container for a **hazardous** compounded sterile preparation must be labelled.

A label must be affixed to each prepared unit, accompanied, if necessary, by a supplementary document (see section 6.6.7.2) to complete the required information.

Compounding personnel must label the following items:

- final **hazardous** compounded sterile preparations;
- each unit of a **hazardous** compounded sterile preparation for an individual patient, along with required auxiliary labels;
- each unit of **hazardous** sterile preparations compounded in batches (with, at a minimum, drug name, concentration, route of administration, batch number and BUD);
- each package containing final preparation units, along with auxiliary labels indicating required storage conditions and special precautions.

The compounding pharmacist or pharmacy technician must similarly label **hazardous** sterile preparations that have been compounded for a patient care (dispensing) pharmacist, where compounding is undertaken by another pharmacy, as permitted by provincial/territorial legislation.

The patient care (dispensing) pharmacist must add a label containing all information required by the respective federal/provincial/territorial regulatory authority before administering the **hazardous** compounded sterile preparation received from the compounding pharmacist to the patient; a supplementary document must be prepared, if required. The label affixed by the compounding pharmacist or pharmacy technician must be retained.

6.6.7.2 Label and insert

The computer-generated self-adhesive label printed by the prescription and file management software may be too small to carry all relevant information to ensure safe, appropriate use of the **hazardous** compounded sterile preparation by the patient. In that situation, an insert must be prepared. The insert is considered to be an integral part of the label.

Together, the label and insert must provide all information required for proper use of the drug by the patient or for safe administration by a third party.

The label must contain the following information, at a minimum:

- pharmacy identification (name, address and telephone number of the compounder's or dispenser's pharmacy);
- drug identification (active ingredients, concentration, form, route of administration, volume, solute, amount prepared);
- special precautions (e.g., if product is cytotoxic);
- storage method;
- date when the **hazardous** sterile preparation was compounded;
- BUD;
- preparation batch number.

The package insert must include the following information:

- all information required by federal/provincial/territorial legislation and regulations regarding the labelling of medications **and poisons** that could not be included on the main label;
- details concerning mode of administration;
- special precautions related to drug storage (e.g., "Caution: contents must be refrigerated upon receipt — store between 2°C and 8°C. Do not freeze," "Do not store medication in the refrigerator door," "Keep out of reach of children");
- special precautions for disposal or destruction of the preparation;
- emergency contact information of the compounding pharmacy (where compounding is undertaken by another pharmacy, as permitted by provincial/territorial legislation), provided there is mutual agreement between the compounding pharmacist and the dispensing pharmacist.

6.7 Packaging

Appropriate packaging must be used for all preparations to be delivered to patients or other health care providers.

Preparations to be delivered must be packaged and labelled to ensure the safety of both the patient and the shipper.

The package must maintain the preparation's stability and integrity as well as storage conditions for stability.

6.7.1 Packaging process

During packaging, compounding personnel must

- **put all final hazardous compounded sterile preparations in a clear plastic bag (or an amber bag, if the preparation must be protected from light);**

- indicate storage requirements on the final package (e.g. temperature, protection from light);
- indicate additional precautions on the final packaging (e.g., pictogram indicating cytotoxicity);
- indicate transportation precautions (e.g., temperature, fragility, safety) and instructions (name and address of the patient) on the outside packaging of each item.

6.7.2 Packaging procedure

To maintain the integrity of hazardous compounded sterile preparations and the safety of patients and delivery personnel, the sterile compounding supervisor must develop and implement a packaging procedure for final hazardous compounded sterile preparations. Appendix 5 presents a model for writing such procedures. The packaging procedure must specify the following details:

- equipment to be used to prevent breakage, contamination, spills or degradation of the hazardous compounded sterile preparation during transport and to protect the carrier;
- equipment to be used to ensure that packaging protects hazardous compounded sterile preparations against freezing and excessive heat (packaging must maintain a temperature between 2°C and 8°C for hazardous compounded sterile preparations requiring refrigeration and a temperature between 19°C and 25°C for hazardous compounded sterile preparations to be kept at room temperature);
- method to be used to confirm whether the temperature of hazardous compounded sterile preparations has been maintained during transport (use of temperature maintenance indicator, min/max thermometer, certified cooler, etc.);
- packaging to be used to protect against extreme temperatures (i.e. excessive heat or freezing) during transport of hazardous compounded sterile preparations, unless information is available demonstrating stability at these temperatures.

6.8 Receipt and storage of hazardous products¹³⁹

A sample procedure for receiving, unpacking and storing hazardous products is provided in Appendix 11.

6.8.1 Receipt of hazardous products

¹³⁹ United States Pharmacopeial Convention (USP). General chapter <1079>: good storage and shipping practices. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008–2009. p. 880.

Products used for preparations must be unpacked outside of controlled areas (clean room and anteroom) to limit the introduction of dust and particles into the controlled areas.

If a hazardous product container is visibly damaged upon receipt, the following precautions apply:

- The situation is to be treated as a spill.
- The container must not be opened.
- The hazardous product must not be returned to the manufacturer.
- The manufacturer must be advised, in writing, of the incident (*see also* section 6.11.2).

6.8.1.1 Containers and packaging of goods received

A container, box or outside bag containing an order may be considered not chemically contaminated and may be returned to the supplier if so arranged.

Packaging within delivery containers (e.g., cartons, bubble wrap, foam, filling materials) that has not come into direct contact with product vials may also be considered not chemically contaminated and may be discarded in regular waste containers. These materials should not be used for other purposes.

If a spill has occurred inside the container, box or outside bag, then all packaging materials are to be considered chemically contaminated and must be discarded in a hazardous (cytotoxic) waste container.

Manufacturer's boxes or individual packaging that has been in direct contact with vials containing hazardous products is to be considered chemically contaminated and must be discarded in a hazardous waste container.

6.8.1.2 Garbing of personnel for unpacking

For unpacking intact hazardous products, the following garb is required¹⁴⁰:

- two pairs of ASTM International–approved gloves

For unpacking damaged hazardous products, the following garb is required¹⁴¹:

- two pairs of ASTM International–approved gloves
- gown approved for the compounding of hazardous sterile preparations
- hair, face, beard and shoe covers
- eye protection (goggles)
- face protection (e.g., shield)
- N95 or N100 mask

Damaged hazardous drugs must be unpacked in a Class I BSC.

¹⁴⁰ United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings [draft]. Rockville, MD: USP; 2014 Mar.

¹⁴¹ United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings [draft]. Rockville, MD: USP; 2014 Mar.

6.8.1.3 Decontamination

Containers or vials holding hazardous products must be decontaminated (i.e., surface decontamination) before they are stored. If a manufacturer has guaranteed that its containers are free of contaminants, it is not necessary to perform decontamination upon receipt of containers from that manufacturer. For products from other manufacturers, surface decontamination must be performed upon receipt.

If surface decontamination is not performed at the time of arrival (e.g., because of manufacturer's contamination-free guarantee), it must be performed when products are unpacked, by wiping down the exterior of the hazardous product containers with either a cloth moistened in a water–detergent solution or a pre-moistened wipe (e.g., Wet Ones® antibacterial hand wipes or a similar product)¹⁴² that is changed frequently. To prevent dispersal of any hazardous product particles into the work environment, chemical decontaminants must not be applied as a spray. Vials that have undergone surface decontamination with a wipe must be disinfected with sterile 70% isopropyl alcohol at the time of use, before they are introduced into the clean room, the BSC or the CACI.

When receipt and unpacking are complete, personnel must decontaminate the work surface that was used for receiving and unpacking the hazardous products.

6.8.2 Storage of hazardous products

6.8.2.1 Storage criteria

The sterile compounding supervisor must develop a storage procedure (see Appendix 5), and it must be followed at all times. In particular, hazardous products must be stored separately from all other products. In addition, product storage conditions specified by the manufacturer must be strictly observed, regardless of where the products are stored (warehouse, pharmacy, delivery vehicle, delivery loading dock, etc.).

After decontamination, hazardous products must be stored in a well-ventilated room (about 12 ACPH)¹⁴³ or in a refrigerator or dedicated biomedical freezer (see section 5.3.2.5, subsection “Area for storing hazardous products”).

Small quantities of hazardous products or final hazardous compounded sterile preparations may be stored in the same refrigerator or freezer as non-hazardous products, but hazardous materials must first be individually double-bagged in sealable plastic bags and then placed in a sealed rigid container.

6.8.2.2 Temperature control

¹⁴² Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 6-3. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

¹⁴³ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

For final hazardous compounded sterile preparations or hazardous products used for preparations, the storage temperature must be controlled and must remain within the limits specified in Appendix 12, Information on temperature in the storage area for hazardous drugs and the refrigerator or freezer, must be kept in the maintenance log¹⁴⁴.

During storage, the temperature must be maintained with the range specified by the BUDs of final preparations and products, regardless of the season. Alternative storage must be provided if the storage temperature exceeds acceptable variations and during cleaning of refrigerators and freezers.

6.8.2.3 Verification of stored products

Products that have been stored must be inspected before use, for evidence of deterioration.

The BUDs of final preparations and hazardous products in storage must be verified regularly. Preparations and products that have exceeded their BUDs must be discarded promptly.

6.9 Transport and delivery of final hazardous compounded sterile preparations

Policies and procedures must be developed and implemented for the transport of hazardous compounded sterile preparations and their delivery to patient care units, patients and dispensing pharmacists (see Appendix 5). A policy for return of expired or unused hazardous compounded sterile preparations from the patient's home or the patient care unit in a health care facility must also be developed.

The transport and delivery procedures must identify the delivery person and the times when the min/max thermometer must be checked during transport. The steps to be followed in the event of non-maintenance of target storage temperature during transport must be indicated in the procedure.

The transport and delivery procedures must include any precautions to be taken by the delivery person, especially during delivery (e.g., personal delivery of the hazardous compounded sterile preparation, rather than delegation to another person) and during return of medications, waste, and sharp or pointed items.

For community pharmacies and health care facility pharmacies making deliveries outside the facility, the delivery container should be lockable or sealed.

The sterile compounding supervisor must ensure that personnel involved in preparation and delivery of products (pharmacy technician, TSP and driver) receive training on the transport and delivery procedures, including the procedure for dealing with accidental exposure or spills.

The pharmacist must dispose of any unused hazardous compounded sterile preparations returned from a patient's home.

¹⁴⁴ United States Pharmacopeial Convention (USP). General chapter <1079>: good storage and shipping practices. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008–2009. p. 879.

In health care facilities, unused preparations returned from the patient care unit to the pharmacy may be reused if it can be shown they have been properly stored (at the correct temperature, with protection from light, etc.) and there is no evidence of tampering¹⁴⁵.

Hazardous compounded sterile preparations must be transported in rigid containers marked "Cytotoxic" and designed to minimize the risk of cracking or failure of the preparation containers. They should not be transported via pneumatic tube systems.

When a private carrier is used, the pharmacist must verify the steps taken to ensure maintenance of the cold chain throughout transport and storage of **hazardous** compounded sterile preparations. **The pharmacist must also ensure that the private carrier knows the procedures to be followed in the event of a spill, that a spill kit is available and that transport personnel have received appropriate training.**

Where compounding is undertaken by another pharmacy, as permitted by provincial/territorial legislation, the compounding personnel must ensure that the preparation is transported to the patient care (dispensing) pharmacist under conditions that maintain stability of the preparation.

The dispensing pharmacist must ensure that transport conditions are maintained until delivery to the patient.

All personnel involved in transporting hazardous compounded sterile preparations must be trained on the procedures for such transport and for spills or accidental exposure.

6.10 Recall of **hazardous sterile products or final **hazardous** compounded sterile preparations**

In community or hospital pharmacies, when information obtained as a result of an internal control, a complaint or a product recall shows that the grade or quality of a **hazardous** product or preparation does not meet expectations, the pharmacist must be able to

- identify patients who received the **hazardous** compounded sterile preparations;
- notify patients or their caregivers that there is a problem with the preparations;
- perform the necessary follow-up if the preparation has been administered.

The information on individual units or batches of **hazardous** compounded sterile preparations recorded in the patient's file and the preparation log must be sufficient to allow users to track recipients of **hazardous** compounded sterile preparations.

The sterile compounding supervisor must ensure that a procedure for recall of **hazardous** compounded sterile preparations has been developed and approved.

¹⁴⁵ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 384-5.

In health care facilities, the pharmacist must follow the established recall procedure, remove products already in circulation and follow-up appropriately with patients likely to have used them.

The causes of the problem that led to the recall must be reviewed, and corrective and preventive measures must be identified and implemented, regardless of the location of the pharmacist's practice.

6.11 Incident and accident management

6.11.1 Accidental exposure¹⁴⁶

Policies and procedures to be followed in case of accidental exposure of personnel to hazardous products must be established (see Appendix 2). For products that have material safety data sheets, those documents must be accessible in the workplace.

If a hazardous product comes into contact with skin or clothing, the person must immediately remove all PPE and contaminated personal clothing and wash the affected area with plenty of water and soap.

If a hazardous product comes into contact with the eyes, the eyes should be rinsed with water or physiological serum for at least 15 minutes. An appropriate eyewash station must be available for this purpose.

Persons wearing contact lenses must remove them promptly after exposure to flying particles or splashes.

In the event of a needlestick injury involving a hazardous product, bleeding should be induced by massaging toward the wound (without pinching). The area should then be rinsed abundantly with clear water for 5 minutes and then washed with plenty of water and soap¹⁴⁷. A physician should be consulted.

The exposure must be documented in the appropriate logs.

6.11.2 Spills

Policies and procedures

Policies and procedures for managing spills must be established (see Appendix 2).

Training and garb

¹⁴⁶ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 12-5. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

¹⁴⁷ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 12-5. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

Employees who clean up spills must have received adequate training, must wear appropriate garb while cleaning up a spill and must use a chemical-cartridge respirator for organic vapours equipped with a pre-filter. The respirator must be properly fitted to provide maximum protection in the presence of aerosolized or powdered products.

Spill kits

Spill kits must be available in locations where hazardous products are handled and must be present on carts used for transporting hazardous products. The contents of spill kits should be verified regularly and their expiration dates checked. For additional information, please see the *Prevention Guide — Safe Handling of Hazardous Drugs*, published by the ASSTSAS, which describes the content and use of spill kits.

Significant (major) spills

Additional safety procedures for significant (major) spills should be established in collaboration with the emergency measures team.

The ASSTSAS guide prescribes, among other things, the use of a chemical-cartridge respirator with a full facepiece for use during clean-up of significant spills.

6.11.3 Incidents and accidents

When an incident or accident involving a hazardous compounded sterile preparation occurs, the compounding personnel must complete an event report and explanation form (see Appendix 13). In health care facilities, a form developed or selected by the facility may be used.

Complaints, accidents, incidents and reported side effects must be evaluated to determine their cause, and the necessary steps must be taken to prevent recurrence.

6.12 Hazardous waste management

In the performance of assigned duties, the pharmacist must¹⁴⁸

- ensure that medications and sharp or pointed instruments are disposed of safely in compliance with the environmental protection laws in force in the jurisdiction;
- ensure that medications to be destroyed are safely stored in a location separate from other medications in inventory;
- develop and implement a procedure for destruction of pharmaceutical waste.

¹⁴⁸ National Association of Pharmacy Regulatory Authorities (NAPRA). *Model standards of practice for Canadian pharmacists*. Ottawa, ON: NAPRA; 2009. Available from: http://napra.ca/Content_Files/Files/Model_Standards_of_Prac_for_Cdn_Pharm_March09_Final_b.pdf

Pharmaceutical products that are expired or otherwise no longer usable are considered pharmaceutical waste.

Hazardous products must be destroyed in accordance with regulations governing such products.¹⁴⁹ A list of hazardous products in use must be available in the pharmacy. The list produced by NIOSH, which is part of the US Centers for Disease Control and Prevention¹⁵⁰ can be used to determine if a particular product is hazardous.

Policies and procedures for the management of hazardous waste¹⁵¹ must be developed and followed. These policies and procedures must comply with local, provincial and federal requirements.

The policies and procedures must include the following provisions:

- **All personnel involved in the management of hazardous product waste must receive appropriate training on destruction procedures to ensure their own protection and to prevent contamination of the premises or the environment¹⁵².**
- **All equipment, products and vials used in the compounding of hazardous sterile products must be discarded in a container reserved for hazardous waste.**
- **Bins reserved for hazardous waste must be identified with a self-adhesive label marked "Hazardous waste – cytotoxic"¹⁵³. Such bins should be filled to only three-quarters of their capacity¹⁵⁴. Once a bin is three-quarters full, it should be sealed. Personnel should never attempt to compress the contents of a hazardous waste bin.**
- **Sharps waste used in aseptic techniques for the compounding of hazardous sterile products must be placed in rigid containers designated for sharps, placed inside the BSC or CACI, decontaminated and then discarded into a hazardous waste container or sent for destruction.**
- **Non-sharps waste used in the compounding of hazardous sterile products must be placed in a sealable plastic bag inside the BSC or CACI or in a rigid container and then discarded in a hazardous waste container.**

¹⁴⁹ American Society of Health-System Pharmacists. ASHP guidelines on handling hazardous drugs. *Am J Health Syst Pharm.* 2006;63(12):1172-93.

¹⁵⁰ National Institute for Occupational Safety and Health (NIOSH). NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2012. Publ. No. 2012-150. Atlanta, GA: Department of Health and Human Services, Centers for Disease Control and Prevention, NIOSH; 2012 June. Available from: <http://www.cdc.gov/niosh/docs/2012-150/pdfs/2012-150.pdf>

¹⁵¹ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 12-2. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

¹⁵² United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 369.

¹⁵³ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 12-2. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

¹⁵⁴ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 12-3. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

- Outer gloves must be removed inside the BSC or CACI and placed either in a sealable plastic bag (which is also placed inside the BSC or CACI) or in the cytotoxic waste container in the BSC or CACI. If a sealable plastic bag is used, the bag must be discarded into the hazardous waste container.
- All PPE must be discarded into the hazardous waste container.
- Bins used for hazardous product waste must comply with local, provincial and federal requirements. These bins must be incinerated and may not be sent for decontamination by autoclave and subsequent burial.

6.13 Special situation: preparation of BCG solution

BCG solution is a hazardous product for which the manufacturer provides a closed-transfer system. It must not be prepared for patient administration inside a BSC or a CACI or in any room used for the compounding of other sterile products or associated in any way with the compounding of sterile products¹⁵⁵.

A BCG solution should ideally be prepared in a BSC or CACI dedicated to BCG preparation, located in a negative-pressure clean room where all air is vented to the exterior.

If the aforementioned conditions are not available, then a closed-circuit system may be used for preparing the BCG solution. The system should be in a closed room under neutral or slightly negative pressure, with low circulation, where no other activities are performed concurrently. Access to this room must be limited to authorized personnel.

In situations involving the preparation of BCG/interferon, the interferon must be prepared in a BSC and then added to the BCG under the preparation conditions set out in the preceding paragraph, using an appropriate closed-circuit system.

The garbing procedure for the compounding of hazardous sterile products is to be followed (see section 6.6.2.2). Personnel preparing the BCG must be trained in the use of the closed-circuit system¹⁵⁶. Compounding waste must be handled in the same manner as product waste from the compounding of hazardous products.

7. QUALITY ASSURANCE PROGRAM

Pharmacists who prepare hazardous compounded sterile preparations must establish a quality assurance program to ensure the clear definition, application and verification of all activities that will affect the quality of the hazardous compounded sterile preparations and the protection of personnel.

¹⁵⁵ Merck Canada. Oncotice® (organon) [product monograph]. 145040, Kirkland, QC: Merck Canada; 2011 Mar 11.

¹⁵⁶ Association des pharmaciens des établissements de santé du Québec (APÉS), Regroupement des pharmaciens en oncologie. *Recueil d'information pharmaceutique en oncologie*. Montréal, QC: APÉS; 2001 [revised 2003 Oct].

The quality assurance program is established to give personnel and other responsible individuals information showing that the personnel, facilities and equipment (BSC, CACI, etc.) attain and maintain the conditions required for contamination-free compounding of hazardous sterile preparations and also that the hazardous sterile preparations are being compounded in compliance with established procedures.

The verifications required by the quality assurance program help to acquire data and identify trends, which in turn allow corrective and preventive actions to be taken, if necessary.

7.1 Program content

The sterile compounding supervisor must establish a quality assurance program that has four components:

1. verification of equipment, including the BSC or CACI;
2. verification of controlled areas (clean room and anteroom);
3. verification of aseptic compounding processes;
4. verification of final preparations.

Each component of the quality assurance program and its activities must be documented (see Appendix 14).

7.2 Results and action levels

For each of the specified components, the sterile compounding supervisor must establish a verification process, the results of which are assigned one of three levels:

- compliance (no action required): mandatory specifications have been attained
- alert (tendency toward non-compliance): increased vigilance is required to prevent non-compliance
- action required (non-compliant): more in-depth investigation, immediate corrective action and/or preventive action are needed to avoid return to non-compliance

7.3 Verification of equipment and facilities

7.3.1 Verification of equipment supporting compounding activities

7.3.1.1 Certification

Equipment that supports compounding activities, especially refrigerators, freezers, incubators and air sampling devices, must be certified with respect to its installation and operation and must be calibrated before being put into service.

A maintenance plan must be established, taking into account the manufacturer's recommendations for each device. If no manufacturer's recommendations are available, maintenance activities must be performed at least once a year by a qualified technician. The maintenance report must be saved in the general maintenance log.

7.3.1.2 Temperature readings

At least once a day, compounding personnel must check the temperature log of equipment with an integrated recording device (e.g., refrigerator, freezer, incubator), to review temperatures over the previous 24 hours and must take corrective actions in case of substantial variance with respect to specified parameters.

When a thermometer is used as a verification instrument, the temperature must be read twice a day (at specified but different times of day; e.g., morning and night). The pharmacist must record and retain proof of calibration of the thermometer.

7.3.2. Verification of controlled rooms and **BSC or CACI**

7.3.2.1. Certification

The controlled areas of facilities and the **BSC or CACI** must be certified by a recognized organization

- at least every 6 months¹⁵⁷;
- during installation of new equipment or a new controlled area;
- during maintenance or repair of equipment (repair of **BSC**, ventilation system, etc.) or a controlled area (repair of hole in a wall, etc.) that might alter environmental or operational parameters;
- when investigation of a contamination problem or a problem involving non-compliance in the aseptic compounding process requires exclusion of malfunctioning facilities.

The program for monitoring facilities and the **BSC or CACI** must include a plan for sampling viable and non-viable particles.

7.3.2.2 Certificate provided by manufacturer (in factory)

¹⁵⁷ Occupational Safety and Health Administration (OSHA). *OSHA technical manual (OTM): controlling occupational exposure to hazardous drugs*. Section VI, Chapter 2. Washington, DC: US Department of Labor; 1999. Available from: https://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html

The sterile compounding supervisor should retain, for all HEPA filters and for the **BSC or CACI**, the manufacturers' certificates issued in the factory before delivery.

7.3.2.3 Environmental verification

An environmental monitoring program must be established to ensure that facilities maintain established specifications and uphold the quality and safety standards set by the industry.

The program must include monitoring for chemical contamination by hazardous materials on surfaces used for reception, storage, preparation and verification of products and preparations, in addition to monitoring the microbiological contamination of controlled areas twice per year.

Compliance with specifications for environmental parameters of facilities and proper operation of devices

The sterile compounding supervisor must ensure that personnel on site

- have full knowledge of the measuring instruments used for monitoring;
- know the specifications for each parameter being monitored;
- know the procedure to be followed in case of non-compliance with respect to air pressure and temperature.

The temperature of ISO Class 7 and ISO Class 8 areas must be monitored and documented at least once a day.

The pressure differential between controlled areas must be kept constant according to the specifications described in section 5.3.2.5 (see Tables 2 and 4; Figure 1). Pressure must be measured continuously, and a security system must be in place to immediately advise personnel of non-compliance with specifications and to direct that action be taken, should it be necessary. A procedure must be developed to outline and explain the actions to be taken should the pressure differential be non-compliant.

The indicators for proper operation of any device (**BSC, CACI**, ACD, etc.) should be monitored every day, and data should be recorded in the general maintenance log.

Sampling of non-viable, viable and surface particles in controlled areas and the **BSC or CACI**^{158 159}

A sampling plan for controlled areas and the **BSC or CACI** must be established.

Sampling plan

¹⁵⁸ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. In: *USP pharmacists' pharmacopeia*. 2nd ed., Suppl. 2. Rockville, MD: USP; 2008. Section "Sampling plan," p. 12.

¹⁵⁹ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 373-5.

The plan for sampling air (for viable and non-viable particles) and surfaces must be established according to the specifications of a recognized standard, such as ISO 14644-1.

The air and surface sampling plan must include, for each controlled area (clean room and anteroom),

- sampling site diagram
- type of sampling to be done
- sampling methods to be used
- number of samples to be obtained at each site
- frequency of sampling
- number of CFUs triggering action

The sampling plan must allow for three types of samples:

- non-viable particles per cubic metre of air
- viable particles per cubic metre of air
- viable surface particles

Sampling specifications

Samples must be obtained at least every 6 months from the air in controlled areas and in the BSC¹⁶⁰ or CACI *and* every time that the following conditions are present:

- during installation of new equipment or a new controlled area;
- during maintenance or repair of equipment (repair of BSC, ventilation system, etc.) or a controlled area (repair of hole in the wall);
- during investigation of a contamination problem or a problem involving non-compliance of personnel with aseptic processes.

Samples for determining the number of non-viable particles per cubic metre of air, viable particles per cubic metre of air and viable surface particles must always be obtained under dynamic operating conditions during each facility and **BSC or CACI** certification.

Sampling of non-viable particles in air

Non-viable particles in the air in controlled areas and the BSC must be sampled at least every 6 months¹⁶¹, as follows:

- by the qualified certifier, during certification of facilities;
- by employees of the community or health care facility pharmacy, provided the employees have been trained within the framework of an internal verification program (including training in use of a calibrated particle meter), to ensure proper operation of facilities and equipment.

The sterile compounding supervisor must ensure the competency of the certifier and the personnel chosen to conduct the sampling. Appendix 6 describes the certification activities.

¹⁶⁰ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 374.

¹⁶¹ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 374.

The values obtained must comply with the specifications established for each controlled area (ISO 14644-1 classification for air quality). See Table 1 for the classifications of air cleanliness by concentration of particles in controlled rooms and areas according to the ISO standard, and section 5.3.2 on the installation of areas reserved for activities related to the compounding of **hazardous** sterile products.

Calibration certificates for the equipment used to conduct the certification must accompany the report prepared after each certification.

The sterile compounding supervisor must ensure that the certification is performed in accordance with the most recent certification standards in force for the facilities and equipment used to compound sterile products.

Appendices 6 and 7 describe the certification activities and the standards used by the certifiers.

Sampling of viable particles in air and on surfaces

Sampling for viable particles must include

- sampling of viable particles per cubic metre of air for each established sampling site, using an air sampler;
- surface sampling of each established sampling site, using a direct contact or swabbing method.

The sampling of viable air and surface particles must be performed by a qualified certifier or by employees of the community or health care facility pharmacy, provided that an established sampling procedure is followed and personnel have received and successfully completed the proper training.

The sterile compounding supervisor must

- obtain from the manufacturer a calibration certificate for the viable air sampler, to ensure that it is regularly calibrated according to the manufacturer's recommendations and to properly train personnel in its use;
- use the appropriate nutrient medium for plating of samples:
 - tryptic soy agar (low sulphur content) or soybean–casein digest medium for air samples
 - tryptic soy agar with lecithin and polysorbate for surface samples
- assure the microbial proliferation capacity of each batch of nutrient medium used (the certificate for this test, provided by the manufacturer, must be retained¹⁶²).

The samples obtained must be either

- sent to a certified external laboratory; or
- incubated in the community or health care facility pharmacy, provided that
 - the incubator used is certified periodically;

¹⁶² United States Pharmacopeial Convention (USP). General chapter <51>: antimicrobial effectiveness. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008–2009. p. 706-8.

- procedures are in place for use and maintenance of the incubator and for surveillance of temperatures;
- personnel are properly trained and are competent to read and interpret the results and to take appropriate preventive or corrective actions.

Samples must be incubated, in an inverted position¹⁶³, between 30°C and 35°C, to be read in 48 to 72 hours; alternatively, another equivalent method must be used.

The contamination level at which corrective action is required will vary depending on the desired ISO air classification¹⁶⁴. The following examples indicate contamination levels that would trigger corrective action with different types of sampling.

Volumetric sampling of facility air:

- Areas requiring ISO Class 5 air quality, threshold contamination > 1 CFU/m³ of air
- Areas requiring ISO Class 7 air quality, threshold contamination > 10 CFU/m³ of air
- Areas requiring ISO Class 8 air quality, threshold contamination > 100 CFU/m³ of air

Surface sampling of LAFW (direct contact or swabbing method, 55-mm agar plate):

- Areas requiring ISO Class 5 air quality, threshold contamination > 3 CFU/plate
- Areas requiring ISO Class 7 air quality, threshold contamination > 5 CFU/plate
- Areas requiring ISO Class 8 air quality, threshold contamination > 100 CFU/plate

GFTS (total for two hands):

- Areas requiring ISO Class 5 air quality, threshold contamination > 3 CFU total

During the first months of sampling, the sterile compounding supervisor should ensure that samples are obtained more frequently than the minimum 6-month interval, to create a baseline for comparison.

The sterile compounding supervisor must analyze the data obtained and the trends observed with respect to the microbial load in controlled areas, as well as the types of microorganisms found, to establish corrective and preventive actions; if necessary, the sterile compounding supervisor should consult a microbiologist or infectious diseases specialist.

¹⁶³ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 375.

¹⁶⁴ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 375, 379.

Chemical contamination

With regard to chemical contamination of the workplace setting, laboratories such as the toxicology laboratory of the Institut national de santé publique Québec offer testing for surface contamination with certain hazardous drugs.

The level of chemical contamination should be measured at least once a year, more frequently if a major change is made in placement of furniture, aseptic processes, or cleaning and disinfecting practices.

The sterile compounding supervisor or a delegate should sample the various sites, especially those most likely to be contaminated (e.g., outside the BSC or CACI, floor surrounding the BSC or CACI). The sites sampled and the frequency of monitoring should be established on the basis of results obtained on previous monitoring.

A baseline assessment should precede any preventive measure put in place (as described in the ASSTSAS guide¹⁶⁵), and monitoring should be repeated after implementation of such measures to determine their effectiveness.

Surface contamination by hazardous antineoplastic drugs, as determined by environmental monitoring, must be recorded in the maintenance log.

7.4. Quality assurance of personnel involved in aseptic compounding

The quality assurance program for the aseptic compounding process for personnel must include GFTS and a media fill test, which are the two final steps of initial and periodic qualification of personnel, as mentioned in section 5.1.2.2.

7.4.1 Gloved Fingertip Sampling¹⁶⁶

GFTS must include

- a sample obtained after sterile gloves are put on (after aseptic washing of hands and forearms) but before application of sterile 70% isopropyl alcohol (disinfecting gloves with sterile 70% isopropyl alcohol immediately before sampling would lead to “false negatives”);
- a sample obtained after the media fill test, making sure that the employee has not applied sterile 70% isopropyl alcohol to his or her gloves in the minutes before sampling.

¹⁶⁵ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

¹⁶⁶ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 378.

Using tryptic soy agar contact plates with lecithin and polysorbate¹⁶⁷, the assessor takes thumbprints and prints of each gloved fingertip from both hands of the assessed employee, asking the employee to gently press each thumb and fingertip on the agar in the contact plate.

When the sampling is complete, the gloves must be taken off and thrown away, and hands must be re-sterilized according to established procedure.

The samples must be incubated between 30°C and 35°C, to be read in 48 to 72 hours.

The results obtained for each hand must be recorded. The number of CFUs determining the action level for gloved fingertips, as set out in section 7.3.2.3 (subsection “Sampling of viable particles in air and on surfaces”), refers to the total for both hands.

7.4.2 Media fill test

The media fill test is a compounding simulation test conducted with nutrient media that promote bacterial growth to verify maintenance of the aseptic process for a given employee. For more information on this test, consult General Chapter <797> in the USP–NF¹⁶⁸.

For the media fill test, the simulation chosen for assessment of personnel must be representative of activities performed under real compounding conditions in the particular environment and must represent the most complex preparations according to the microbiological risk level of preparations made there¹⁶⁹.

A tryptic soy agar (low sulphur content) or soybean–casein digest nutrient medium must be used. For hazardous compounded sterile preparations with low or medium risk of microbial contamination, the nutrient medium must be sterile. For hazardous compounded sterile preparations with a high risk of microbial contamination, the nutrient medium must be non-sterile and must include simulation of sterilization by filtration.

The proliferation capacity of every batch of the nutrient medium used must have been tested by the manufacturer, and the certificate for this test result must be retained by the compounding pharmacy¹⁷⁰.

The containers used for media fill tests should be sent to a certified external laboratory or may be incubated in the pharmacy provided that the incubator is certified periodically and that procedures are in place for its use and maintenance and for the surveillance of required temperatures. Personnel must be properly trained to read the results.

¹⁶⁷ United States Pharmacopeial Convention (USP). General chapter <1116>: microbial evaluation of clean rooms and other controlled environments. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008–2009. p. 900-8.

¹⁶⁸ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 365-8.

¹⁶⁹ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 365-8.

¹⁷⁰ United States Pharmacopeial Convention (USP). General chapter <51>: antimicrobial effectiveness. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008–2009. p. 706-8.

The containers filled with the nutrient medium to be used for the media fill test must be incubated between 20°C and 25°C or between 30°C and 35°C for 14 consecutive days¹⁷¹. If two temperatures are used, the containers should be incubated for 7 consecutive days at each of the temperatures, starting with the lower temperature.

7.5 Quality assurance of **hazardous** compounded sterile preparations

The sterile compounding supervisor must establish a quality assurance program to ensure that **hazardous sterile** preparations are compounded in compliance with established procedures.

The program must monitor, among other things,

- the presence of a compounding protocol for each compounded sterile preparation;
- compliance of the preparation with the prescription issued;
- compliance (with legislation and regulations) of labels affixed to containers;
- compliance with required documentation in a patient's **hazardous** compounded sterile preparations log and the batch **hazardous** compounded sterile preparations log, ensuring the performance of all verification steps required during and after compounding.

7.6 Documentation of quality control activities

Written documentation related to the quality assurance program must be verified, analyzed and signed by the sterile compounding supervisor and retained for a period designated in federal/provincial/territorial regulations.

The sterile compounding supervisor must

- investigate missing documentation, situations of non-compliance (where action is required) and deviations from protocols;
- identify trends concerning microbial load in controlled areas and types of microorganisms found;
- consult a microbiology specialist, if necessary;
- take corrective and preventive actions.

For the sampling of viable air and surface particles, the nutrient medium readings should be documented on a separate form for each type of sampling.

¹⁷¹ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 365-9.

All completed documentation concerning components of the environmental verification of controlled areas, the **BSC or CACI** and support equipment must be filed and retained with other compounding records in an easily accessible location inside the pharmacy.

Documents concerning purchase, organization and certification must be accessible throughout the entire service life of the facility and the **BSC**.

All completed documentation concerning the quality assurance program for the aseptic compounding process for personnel (by GFTS and media fill test), including nutrient medium readings, should be retained and made accessible.

8. GLOSSARY

Term	Definition
Accident	Action or situation in which the risk event occurs and has or could have an impact on the health status or well-being of the user (patient), personnel, professional concerned or third party. An accident differs from an incident, which has no effect on the patient.
Anteroom	A room equipped with two doors, with an interlocking system that allows only one door to open at a time, which allows passage or movement of someone or something from one environment to another, while keeping these environments isolated from each other.
Aseptic techniques	Steps in the aseptic process that include all manipulations performed inside the primary engineering control by compounding personnel.
Assessment	Action of assessing and defining an employee's performance and competency. It is also the action of determining something's value or importance.
Beyond-use date (BUD)	For the purposes of these Model Standards, the date after which the final compounded sterile preparation can no longer be used or administered. It is determined from the date or time that the preparation is compounded ¹⁷² .
Biological safety cabinet (BSC)	<p>Laminar airflow workbench that is ventilated to protect personnel, hazardous sterile compounded products and the immediate environment. The open front of a BSC has the following features:</p> <ul style="list-style-type: none"> • air intake, to protect compounding personnel from hazardous sterile preparations; • descending air curtain filtered with a high-efficiency particulate air filter to protect the hazardous sterile product; • air evacuation system equipped with high-efficiency particulate air filters for environmental protection¹⁷³.
Cleaning and disinfecting (housekeeping)	Cleaning activities involving the removal of dirt, dust and other substances that may host microorganisms, guaranteeing access to a clean and healthy environment ¹⁷⁴ .
Clean room	A room in which atmospheric properties (temperature, humidity, particle and microorganism content, pressure, airflow, etc.) are controlled. The room's functional parameters are kept at a specific level. The room is designed to minimize introduction, generation and retention of particles.
Commercial container	Container holding a commercially manufactured drug or sterile nutrient, the consumption and sale of which are authorized in Canada; if the drug or sterile nutrient is authorized by Health Canada's Special Access Programme, such consumption and sale may be limited.

¹⁷² United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

¹⁷³ Commission de la santé et de la sécurité du travail (CSST). *Material safety data sheet user's guide*. CSST; 2010. Available from: <http://www.csst.qc.ca/en/prevention/reptox/whmis/material-safety-data-sheet-users-guide/pages/table-contents.aspx>

¹⁷⁴ United States Pharmacopeial Convention (USP). General chapter <1072>: disinfectants and antisepsis. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008–2009.

Competencies	Significant job-related knowledge, skills, abilities, attitudes and judgments required for competent performance of duties by members of a profession,
Compounding	Act of preparing something, through preliminary work, to put it into a usable state. Also refers to the material that has been compounded (e.g., a chemical or pharmaceutical preparation).
Compounding aseptic containment isolator (CACI)	<p>Isolator specifically used for compounding hazardous sterile products. Designed to protect personnel from any undesirable exposure to airborne medicinal products during compounding and transfer of hazardous material and drugs and to provide an aseptic environment for sterile preparations.</p> <p>The device must not allow any exchange of air between the inside of the clean room and the isolator, unless the air is filtered by a high-efficiency particulate air filter capable of filtering out airborne particles of the drugs being prepared. For the compounding of hazardous drugs, the air exiting the isolator should be evacuated to the building's exterior by an appropriate ventilation system.</p>
Compounding personnel	Pharmacists, pharmacy technicians or technical support personnel assigned to the compounding of sterile products.
Compounding pharmacist or pharmacy technician	Pharmacist or pharmacy technician who compounds or supervises the compounding of sterile products according to prescriptions issued to the pharmacy where the pharmacist or pharmacy technician works or for a dispensing pharmacist who has requested this service (where compounding is undertaken by another pharmacy, as permitted by provincial/territorial legislation).
Compounding procedure	Procedure that describes all the steps to be followed in the compounding of sterile products and performed according to a particular packaging method (e.g., syringe filled for intravenous use, elastomeric preparation).
Compounding protocol	Protocol that describes all steps to be followed in the compounding of a specific sterile preparation and with which the compounder must comply. The protocol must include all of the information to be recorded in the preparation log.
Containment system	Arrangement or equipment to contain the particles of hazardous products in the chosen space.
Contiguous	<p>A term describing a location or space that adjoins another.</p> <p>Example: The clean room is contiguous with the anteroom and the surrounding pharmacy areas.</p> <p>Synonyms: adjacent, adjoining, bordering, abutting, surrounding, neighbouring</p>
Controlled area or room	An area or space where the only activities taking place are those related to the compounding of sterile products. In such locations, to obtain the specified ISO class parameters, the concentration of viable and non-viable particles suspended in the air is verified according to a sampling plan. Corrective measures are taken when necessary so that the area remains at the expected ISO class level. ¹⁷⁵ The clean room and anteroom are examples of controlled areas. May also be known as a classified area or room.

¹⁷⁵ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

Critical area	Work area inside a laminar airflow workbench ensuring ISO Class 5 air quality, where personnel compound sterile products and where critical sites are exposed to unidirectional airflow from a high-efficiency particulate air filter.
Critical site	Any surface likely to come into contact with a sterile drug or liquid (e.g., vial septa, injection sites) or any exposed opening (open vials, needle hubs) and likely to be in direct contact with the ambient air or air filtered by means of a high-efficiency particulate air filter or humidity (oral secretions or mucous membranes) or likely to be contaminated by touch ¹⁷⁶ .
Deactivation	Rendering of a chemical compound (such as a hazardous drug) less dangerous by treating it with another chemical compound, heat or another agent ¹⁷⁷ .
Decontamination	Inactivation, neutralization or removal of a toxic product, typically by using chemical compounds ¹⁷⁸ .
Detergent	Product that eliminates accumulated dirt from a solid medium by resuspension or dissolution.
Disinfectant	A disinfecting agent, typically of a chemical nature, that can destroy microorganisms or other pathogens, but not necessarily bacterial spores or fungal spores. Refers to substances applied to inanimate objects ¹⁷⁹ .
Disinfection	Treatment that eliminates most of the pathogens present on an object or surface ¹⁸⁰ .
Facilities	All devices, rooms and spaces that are organized, arranged and modified to better adapt them to the activities to be conducted therein. Facilities include the clean room and the anteroom.
Filling a prescription	All activities relating to the validation (including therapeutic appropriateness), preparation and packaging of a patient's medication prepared pursuant to a prescription.
Final sterile preparation	A sterile preparation ready to be stored and then administered to a patient, which has been prepared according to a preparation-specific compounding protocol which respects the prescribing physician's prescription.
Gloved fingertip sampling (GFTS)	A process that involves microbiological examination based on imprints from the person being assessed, obtained by having the person press gloved

¹⁷⁶ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

¹⁷⁷ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

¹⁷⁸ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

¹⁷⁹ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

¹⁸⁰ United States Pharmacopeial Convention (USP). General chapter <1072>: disinfectants and antiseptics. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008–2009.

	thumbtips and fingertips into the contact plate agar. Both hands are tested in this manner ¹⁸¹ .
Hand hygiene	All methods related to handwashing that is performed using soap and water, followed by a waterless, alcohol-based hand rub containing, for example, chlorhexidine and alcohol.
Hazardous drug	A drug for which research on humans or animals has shown that any exposure to the substance has the potential to cause cancer, lead to a developmental or reproductive toxicity or damage organs ¹⁸² . Drugs are considered hazardous because they involve risks for the worker, because of their effects ¹⁸³ .
Hazardous material	A material that, because of its properties, constitutes a danger to an employee's health, safety or physical integrity ¹⁸⁴ . Hazardous materials are dangerous products regulated by a workplace hazardous material information system; as such, they are considered "controlled" products under the <i>Controlled Products Regulations</i> ¹⁸⁵ .
Hazardous products	Substances that entail risks for the worker because of their effects. For the purposes of these Model Standards, the term "hazardous product" refers to both hazardous drugs and hazardous materials, depending on the situation.
Housekeeping	See "Cleaning and disinfecting"
Incident	An action or situation that has no impact on the health status or well-being of the user (patient), personnel, professional concerned or third party, but which as an unusual result that could, on other occasions, lead to consequences. An incident differs from an accident, which has or could have an impact on the patient ¹⁸⁶ .
Incubator	Microbial culture sterilizer, a device used in microbiology to keep cultures at a constant temperature
Insert	Document or leaflet containing information about a drug additional to that written on the computer-generated label produced by the prescription management software; provides the patient with information as required by regulations.

¹⁸¹ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

¹⁸² National Institute for Occupational Safety and Health (NIOSH). NIOSH alert: preventing occupational exposures to antineoplastic and other hazardous drugs in health care settings. Publ. No. 2004-165. Atlanta, GA: Department of Health and Human Services, Centers for Disease Control and Prevention, NIOSH; 2004 Sep. Available from: <http://www.cdc.gov/niosh/docs/2004-165/pdfs/2004-165.pdf>

¹⁸³ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

¹⁸⁴ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

¹⁸⁵ *Controlled Products Regulations*, SOR/88-66, 1987. Available from: <http://laws-lois.justice.gc.ca/eng/regulations/SOR-88-66/>

¹⁸⁶ Commission de la santé et de la sécurité du travail (CSST). *Material safety data sheet user's guide*. CSST; 2010. Available from: <http://www.csst.qc.ca/en/prevention/reptox/whmis/material-safety-data-sheet-users-guide/pages/table-contents.aspx>

Label (for identifying a sterile preparation)	Label that identifies the drugs prepared or sold with or without a prescription. It is usually computer-generated and adhesive. It must bear the information required by federal/provincial/territorial regulations.
Laminar airflow workbench (LAFW)	A device that provides an ISO class 5 environment for the exposure of critical sites when sterile preparations are being compounded. The airflow is unidirectional (laminar flow), and the first air (air exiting the HEPA filter ¹⁸⁷) is free from airborne particulates.
Laminar flow hood	See "Laminar airflow workbench"
Log	Book or notebook in which data are recorded or compiled to demonstrate that the quality of the pharmacy aseptic compounding process has been maintained. A log may be in computerized format.
Maintenance of competency	Continued ability to integrate and apply knowledge, know-how, judgment and personal qualities necessary to practise in a safe and ethical fashion in a designated role and framework ¹⁸⁸ .
Maintenance (of facilities and equipment)	Operations for maintaining the proper functioning of facilities or equipment according to established specifications or for re-establishing the satisfactory operational condition of facilities, including the heating, ventilation and air conditioning system and related equipment.
Material safety data sheet (MSDS)	A "document that provides information on a controlled product, namely its toxic effects, the protective measures for avoiding overexposure or chemical hazards, and the procedures to follow in an emergency. The supplier sends the MSDS to the employer when the product is sold. It must be ... kept on the premises by the employer in a location known by the workers, and be easily and rapidly accessible to those who are likely to come in contact with the product. The employer should have it before a product is used for the first time" ¹⁸⁹ .
Media fill test	Test used to qualify aseptic techniques of compounding personnel and the environment's ability to produce preparations that are "sterile." For this test, a nutrient medium replaces the actual product when the aseptic technique is performed ^{190,191} .

¹⁸⁷ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

¹⁸⁸ Canadian Nurses Association (CNA). *Joint position statement: Promoting continuing competence for registered nurses*. Ottawa, ON: CNA; 2004. Available from: http://www.cna-aic.ca/~media/cna/page-content/pdf-en/ps77_promoting_competence_e.pdf

¹⁸⁹ Commission de la santé et de la sécurité du travail (CSST). *Material safety data sheet user's guide*. CSST; 2010. Available from: <http://www.csst.qc.ca/en/prevention/reptox/whmis/material-safety-data-sheet-users-guide/pages/table-contents.aspx>

¹⁹⁰ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

¹⁹¹ Health Canada, Health Products and Food Branch Inspectorate. *Good manufacturing practices (GMP) guidelines – 2009 edition, Version 2 (GUI-0001)*. Ottawa, ON: Health Canada; 2009, revised 2011 Mar 4. p. 85. Available from: <http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/docs/gui-0001-eng.php>

Multiple-dose vial	Commercial drug container in multiple-dose format for parenteral administration only. The product usually contains an antimicrobial preservative ¹⁹² .
Patient care (dispensing) pharmacist	Pharmacist providing care to patients, who delivers or administers a product after verification of its therapeutic appropriateness; the product may be prepared by the patient care (dispensing) pharmacist or by compounding personnel in another pharmacy, where compounding is undertaken by another pharmacy, as permitted by provincial/territorial legislation.
Personal protective equipment (PPE)	All garb and accessories, such as mask, gloves, smock and safety goggles, that protect the sterile preparation and the worker. It enables compliance with the expected specifications of a controlled environment and protects the worker from exposure to physical or chemical risks ^{193 194} .
Pharmacist	Registrant in good standing of one of the pharmacy regulatory authorities in Canada.
Pharmacy bulk vial	Commercial container for parenteral sterile preparations, intended for packaging containing several individual doses. Such packaging is used only by pharmacies with an intravenous admixture program. During the final packaging, in several doses, the pharmacy bulk vial must be perforated with a transfer device only once, by introducing a needle or transfer “spike”.
Pharmacy technician	An adult who has earned a college degree or diploma from an accredited pharmacy technician program and has passed the national examination. Such persons are licensed or authorized by a provincial/territorial health professional regulatory authority to practise as a pharmacy technician.
Policy	All the general principles adopted by a private or public organization for conducting its activities. By extension, the term “policy” also refers to the text or document that presents the policy.
Prescription validation	The pharmacist’s decision to declare a prescription valid after verifying its legality, contents and relevance with respect to the patient and the patient’s condition.
Primary engineering control	Equipment ensuring ISO Class 5 level for the quality of filtered air (i.e., with high-efficiency particulate air filter) at the critical sites exposed during the aseptic technique. Primary engineering controls for non-hazardous products include laminar

¹⁹² United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

¹⁹³ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

¹⁹⁴ National Institute for Occupational Safety and Health (NIOSH). NIOSH alert: preventing occupational exposures to antineoplastic and other hazardous drugs in health care settings. Publ. No. 2004-165. Atlanta, GA: Department of Health and Human Services, Centers for Disease Control and Prevention, NIOSH; 2004 Sep. Available from: <http://www.cdc.gov/niosh/docs/2004-165/pdfs/2004-165.pdf>

	<p>airflow workbenches and compounding aseptic isolators.</p> <p>Primary engineering controls for compounding hazardous preparations are called biological safety cabinets and compounding aseptic containment isolators¹⁹⁵.</p>
Procedure	All steps to be taken, the means to be used and the methods to be followed in performing a task.
Process for aseptic compounding	All activities leading to completion of a final compounded sterile preparation, especially hand hygiene and garbing, introduction of products and materials into the clean room, the disinfection of the primary engineering control, use of aseptic techniques for compounding products in the primary engineering control, and verification and labelling of compounded sterile preparations. Its purpose is to maintain the sterility of a product or drug compounded from sterile components.
Protocol	Document describing in detail all steps to be followed or behaviours to adopt in precise clinical circumstances.
Repack/repacking	The process of packing again or the action of repacking (“reprocessing”). Examples include making 12-tablet packages from a pack (bottle) of 100 tablets and filling 1-mL syringes from a 10-mL pack (vial).
Single-dose vial	Single-dose commercial container corresponding to a fixed dose of a drug intended for parenteral administration only. ¹⁹⁶
Stability (period of)	Length of time during which a properly compounded sterile preparation maintains, within specified limits and throughout the storage and usage period, the properties and characteristics that it had when it was compounded.
Sterile compounding supervisor	A person assigned by the department head of the health care facility or by the pharmacist owner of a community pharmacy to supervise and organize all activities related to the compounding of sterile products.
Sterilization by filtration	For situations or products with high risk of microbial contamination, any sterilization procedure using a sterilizing-grade membrane to produce a sterile final solution (where a sterilizing-grade membrane is a membrane approved for filtering 100% of a <i>Brevundimonas [Pseudomonas] diminuta</i> culture to a concentration of 10 ⁷ colony-forming units/cm ² of filtering surface and to a minimum pressure of 50 psi; depending on the manufacturer, the nominal size of the membrane pores is 0.22 µm or 0.2 µm ¹⁹⁷).
Technical support personnel (TSP)	An adult who has earned a vocational school diploma for completing a pharmacy technician assistant course or any adult person who has received proper training that is deemed equivalent.
Training	Acquisition of a totality of theoretical, technical and practical knowledge concerning pharmacy preparation.
Unidirectional airflow	Airflow moving in a single direction in a robust and uniform manner and at sufficient speed to reproducibly sweep particles away from the critical site.

¹⁹⁵ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 263.

¹⁹⁶ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

¹⁹⁷ United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

9. LIST OF TABLES

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Table 2	Functional parameters of the clean room and anteroom for the compounding of hazardous sterile products
Table 3	Required conditions for a hazardous products storage area
Table 4	Functional parameters of a shared anteroom for the compounding of hazardous and non-hazardous sterile products
Table 5	Masks and chemical-cartridge respirators
Table 6	Beyond-use dates (BUDs) for hazardous compounded sterile preparations when a preservative-free vial is used
Table 7	Contamination risk levels
Table 8	Beyond-use dates (BUDs) for hazardous compounded sterile preparations, according to risk of microbial contamination
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10. APPENDICES

APPENDIX 1 - EXCERPTS FROM AN ACT RESPECTING OCCUPATIONAL HEALTH AND SAFETY (PROVINCE OF QUEBEC)

All workers and employers have legal responsibilities related to health and safety. Chapter III of the Quebec *Act Respecting Occupational Health and Safety* sets out the rights and obligations of both workers and employers, as follows.

General rights of the worker

Section 9: Every worker has a right to working conditions that have proper regard for his health, safety and physical well-being.

Obligations of the worker

Section 49: A worker must:

- (1) become familiar with the prevention program applicable to him;
- (2) take the necessary measures to ensure his health, safety or physical well-being;

...

General rights of the employer

Section 50: Every employer is entitled, in particular, in accordance with this Act and the regulations, to training, information and counselling services in matters of occupational health and safety.

General obligations of the employer

Section 51: Every employer must take the necessary measures to protect the health and ensure the safety and physical well-being of his worker. He must, in particular:

- (1) see that the establishments under his authority are so equipped and laid out as to ensure the protection of the worker;

...

- (5) use methods and techniques intended for the identification, control and elimination of risks to the safety or health of the worker;

...

- (7) supply safety equipment and see that it is kept in good condition;

- (8) see that no contaminant emitted or dangerous substance used adversely affects the health or safety of any person at a workplace;

- (9) give the worker adequate information as to the risks connected with his work and provide him with the appropriate training, assistance or supervision to ensure that he possesses the skill and knowledge required to safely perform the work assigned to him;

...

Source: *An Act Respecting Occupational Health and Safety*, C.Q.L.R., c. S-2.1. Available from:
http://www2.publicationsduquebec.gouv.qc.ca/dynamicSearch/telecharge.php?type=2&file=/S_2_1/S2_1_A.html

APPENDIX 2 - POLICIES AND PROCEDURES FOR THE COMPOUNDING OF NON-HAZARDOUS AND HAZARDOUS STERILE PRODUCTS

Part I		NON-HAZARDOUS STERILE PRODUCTS	
Policy #	Topic		✓
A	PERSONNEL AND FACILITIES		
	1.	Obligations of personnel	
	1.1	Attire and dress code (e.g., personal clothing, jewelry, makeup, hairstyles)	
	1.2	Health condition (reasons for temporary withdrawal from compounding activities)	
	1.3	Expected behaviour in controlled areas (e.g., no drinking, eating, or other activities not related to compounding; expectation that procedures will be followed; avoidance of unnecessary conversations)	
	2.	Training and assessment of personnel	
	2.1	Initial training and assessment program	
	2.2	Program to assess maintenance of competency	
	2.3	Training and assessment of cleaning and disinfecting personnel	
	3.	Delegation of activities	
	3.1	Delegation of pharmaceutical activities to persons other than pharmacists	
	4.	Facilities and equipment	
	4.1	Access to controlled areas	
	4.2	Necessary facilities and equipment	
	4.3	Maintenance of facilities and equipment (e.g., certification of rooms and devices, calibration, maintenance of pre-filters and HEPA filters, verification of pressure)	
	4.4	Cleaning and disinfecting activities for facilities and equipment	
B	COMPOUNDED STERILE PREPARATIONS		
	1.	Bringing equipment and products into the clean room and laminar airflow workbench	
	2.	Determining beyond-use date of products used in a preparation	
	3.	Determining beyond-use date of final preparations	
	4.	Hand and forearm hygiene	
	5.	Garbing in compounding areas and for compounding	
	6.	Cleaning and disinfecting the Laminar Airflow Workbench	
	7.	Aseptic techniques (with details for each of the techniques used)	

	8.	Verification of the compounding process (including validation of calculations by a pharmacist) and of final preparations	
	9.	Labelling of final preparations	
	10.	Packaging of final preparations	
	11.	Preparation of injectable products outside regular operating hours of the compounding department of a health care facility	
	12.	Storage of products used and final preparations	
	13.	Transport and delivery of final preparations (to the patient, to patient care units or to the dispensing pharmacist)	
	14.	Recording of preparations in the patient's file	
	15.	Biomedical waste management (e.g., at the pharmacy, returns from patients or patient care units, instructions to patients)	
	16.	Recall of sterile products or compounded sterile preparations	
C	QUALITY ASSURANCE PROGRAM		
	1.	Verification and maintenance of equipment	
	2.	Environmental control of facilities and laminar airflow workbench (e.g., pressure verification, air and surface sampling plan)	
	3.	Quality assurance of aseptic process for personnel (e.g., gloved fingertip sampling, media fill tests)	
	4.	Quality assurance of compounded sterile preparations (e.g., existence of a protocol, compliance with prescription, documentation in logs)	

Part II		<u>HAZARDOUS STERILE PRODUCTS</u>	
Policy #	Topic		✓
A	PERSONNEL AND FACILITIES		
	1.	Obligations of personnel	
	1.1	Attire and dress code (e.g., personal clothing, jewelry, makeup, hairstyles)	
	1.2	Health condition (reasons for temporary withdrawal from compounding activities)	
	1.3	Expected behaviour in controlled areas (e.g., no drinking, eating, or other activities not related to compounding; expectation that procedures will be followed; avoidance of unnecessary conversations)	

	2.	Training and assessment of personnel	
	2.1	Initial personnel training and competency assessment program, including the details of compounding hazardous drugs	
	2.2	Program to assess maintenance of competency, including the characteristics of compounding hazardous sterile products	
	2.3	Training and assessment of cleaning and disinfecting personnel, including the characteristics of compounding hazardous sterile products	
	3.	Delegation of activities	
	3.1	Delegation of pharmaceutical activities to persons other than pharmacists	
	4.	Facilities and equipment	
	4.1	Access to controlled areas	
	4.2	Facilities and equipment for the compounding of hazardous sterile products	
	4.3	Reservation of facilities and equipment for the compounding of hazardous sterile products	
	4.4	Maintenance of facilities and equipment, including the characteristics of compounding hazardous sterile products (e.g., certification of rooms and devices, calibration, maintenance of pre-filters and HEPA filters, pressure verification)	
	4.5	Cleaning and disinfecting activities for facilities and equipment	
B		COMPOUNDED STERILE PREPARATIONS	
	1.	Receiving and unpacking of hazardous sterile products	
	2.	Storage of hazardous sterile products	
	3.	Determining beyond-use date of products used in a preparation	
	4.	Determining beyond-use date of final preparations	
	5.	Hand and forearm hygiene	
	6.	Garbing in compounding areas and for compounding	
	7.	Bringing equipment and products into the clean room and biological safety cabinet	
	8.	Verification of the compounding process (including validation of calculations by a pharmacist) and of final preparations	
	9.	Cleaning, decontamination, deactivation and disinfection of the biological safety cabinet	
	10.	Aseptic techniques for compounding hazardous sterile products	
	11.	Packaging of hazardous compounded sterile preparations	
	12.	Labelling of hazardous compounded sterile preparations	

	13.	Storage of final hazardous compounded sterile preparations	
	14.	Recording of preparations in the patient's file	
	15.	Transport and delivery of final hazardous compounded sterile preparations (to the patient, patient care units or dispensing pharmacist)	
	16.	Hazardous waste management (e.g., at the pharmacy, returns from patients or patient care units, instructions to patients)	
	17.	Accidental exposure of personnel to hazardous drugs (e.g., eyewash station, log)	
	18.	Spills (e.g., spill management, chemical-cartridge respirator, kit)	
	19.	Recall of hazardous products or final hazardous compounded sterile preparations	
C		QUALITY ASSURANCE PROGRAM	
	1	Verification and maintenance of equipment	
	2	Environmental control of facilities and biological safety cabinet (e.g., pressure verification, air and surface sampling plan)	
	3	Quality assurance of aseptic process for personnel (e.g., gloved fingertip sampling, media fill tests)	
	4	Quality assurance of compounded sterile preparations (e.g., existence of a protocol, compliance with prescription, documentation in logs)	
D		ENVIRONMENTAL MONITORING PROGRAM	
	1	Environmental monitoring of chemical contamination	

APPENDIX 3 MANDATORY AND SUPPLEMENTAL DOCUMENTATION

Compounding personnel must be able to consult a wide variety of up-to-date references in the pharmacy at any time.

A. Mandatory documentation

At a minimum, the sterile compounding supervisor must make a recent edition of the following publications available:

- Standards, guidelines and policies of the relevant pharmacy regulatory authority
- Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>
- National Institute for Occupational Safety and Health (NIOSH). NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2012. Publ. No. 2012-150. Atlanta (GA): Department of Health and Human Services, Centers for Disease Control and Prevention, NIOSH; June 2012. Available from: <http://www.cdc.gov/niosh/docs/2012-150/pdfs/2012-150.pdf>
- Trissel LA. *Handbook on injectable drugs*. Bethesda, MD: American Society of Health-System Pharmacists.
- United States Pharmacopeial Convention (USP). *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008-2009 (contains all USP chapters useful to pharmacists, including General Chapter <797>: Pharmaceutical Compounding — Sterile Preparations).

B. Supplemental documentation

1. GENERAL TEXTS ON STERILE PREPARATIONS

Volumes

- Buchanan EC, Schneider PJ. *Compounding sterile preparations*. 3rd ed. Bethesda, MD: American Society of Health-System Pharmacists; 2009. 481 pages.

Periodicals

- *American Journal of Health System Pharmacists*. Available at: www.ajhp.org
- *Canadian Journal of Hospital Pharmacy*. Available from: <http://www.cjhp-online.ca/index.php/cjhp>
- *International Journal of Pharmaceutical Compounding*. Available at: www.ijpc.com

Websites: associations and agencies

- ASHP Sterile Compounding Resource Center: www.ashp.org/compounding
- Pharmacy Compounding Accreditation Board: www.pcab.info

2. REFERENCE TEXTS: PHYSICAL-CHEMICAL STABILITY, COMPATIBILITY AND STABILITY

- *Compendium of pharmaceuticals and specialties*. Ottawa, ON: Canadian Pharmacists Association. Updated yearly.
- King JC. *King guide to parenteral admixtures* [electronic version]. Napa, CA: King Guide Publications Inc. Updated quarterly.
- Trissel LA. *Trissel's 2 clinical pharmaceuticals database* [electronic database]. Cashiers, NC: TriPharma Communications. Updated regularly.

3. REFERENCE TEXT: PHARMACOKINETICS

DiPiro JT, Spruill WJ, Wade WE, Blouin RA, Pruemmer JM. *Concepts in clinical pharmacokinetics*. Bethesda, MD: American Society of Health-System Pharmacists. About 250 pages.

APPENDIX 4 TRAINING OF COMPOUNDING PERSONNEL AND CLEANING AND DISINFECTING PERSONNEL

A. Training of compounding personnel

#	COMPETENCIES, KNOWLEDGE OR SKILLS COVERED IN TRAINING			
1.	FOR THE COMPOUNDING OF NON-HAZARDOUS AND HAZARDOUS STERILE PREPARATIONS	PH	PT	TSP
1.1	Know the relevant federal/provincial/territorial legislation and regulations related to pharmacy compounding, as well as other governing standards, guides or guidelines.	X	X	
1.2	Know and apply all policies and procedures related to the pharmacy compounding of sterile products, especially those related to hand hygiene, garbing, aseptic techniques, airflow principle, facilities (ISO Classes 5, 7 and 8), material, equipment, behaviour of personnel in compounding rooms, forms and logs to be completed, labelling, storage, distribution to patients, quality controls (sampling) and maintenance and cleaning of sterile-product compounding areas.	X	X	X
1.3	Know physical and chemical properties such as stability, physical-chemical compatibility and incompatibility, osmolality and osmolarity.	X		
1.4	Know pharmaceutical and medical abbreviations.	X	X	X
1.5	Know and understand the importance of particulate and microbial contamination.	X	X	X
1.6	Perform pharmacy sterile-product compounding tasks meticulously, precisely and competently.	X	X	X
1.7	Know and apply appropriate aseptic techniques in the workplace.	X	X	X
1.8	Know the operation and correct use of equipment, materials and automated devices available for the sterile preparations to be compounded. Know how to calibrate the devices used.	X	X	X
1.9	Be able to recognize errors in the compounding technique of compounding personnel.	X		
1.10	Have a good command of the pharmaceutical calculations required to compound sterile products.	X	X	X
1.11	Understand the importance of and apply accurate measurements.	X	X	X
1.12	Apply disinfection measures for sterile-product compounding rooms, facilities and materials.	X	X	X
1.13	Know the data to be monitored in controlled areas (temperature, pressure, humidity) and document in the appropriate logs. Know and apply the corrective measures to be applied when irregularities are found.	X	X	X

1.14	Know how the laminar airflow workbench and secondary ventilation system (heating, ventilation and air conditioning system) operate. Know, apply or enforce appropriate corrective measures when an irregularity is identified.	X	X	X
1.15	Know and apply quality assurance measures for the various compounded sterile preparations.	X	X	X
1.16	Know and follow the pharmacist's verification process.	X	X	X
1.17	Know and use the incident and accident documentation logs.	X	X	X
1.18	Know drug delivery systems.	X	X	X
1.19	Know and establish levels of risk and beyond-use dates.	X		
1.20	Know and, if applicable, perform additional sterility testing.	X	X	X
2.	FOR THE COMPOUNDING OF HAZARDOUS STERILE PREPARATIONS	PH	PT	TSP
2.1	Have the competency required to compound sterile preparations.	X	X	X
2.2	Identify hazardous drugs in the composition of sterile preparations.	X	X	X
2.3	Know and apply deactivation measures.	X	X	X
2.4	Know and use the protection measures necessary to avoid exposure to hazardous substances.	X	X	X
2.5	Know and use personal protective equipment specifically for handling hazardous products.	X	X	X
2.6	Safely handle hazardous drugs (i.e., receive, unpack, store and deliver hazardous drugs).	X	X	X
2.7	Know and apply the appropriate aseptic technique for hazardous drugs in the workplace.	X	X	X
2.8	Know and use the emergency measures to be applied in the case of accidental exposure, accidents or spills.	X	X	X
2.9	Know how to safely destroy hazardous drugs and the materials used in their preparation.	X	X	X
3.	FOR THE COMPOUNDING OF HIGH-RISK NON-HAZARDOUS AND HAZARDOUS STERILE PREPARATIONS (MADE WITH NON-STERILE PRODUCTS)			
3.1	Have the competency required to compound sterile preparations.	X	X	X
3.2	Know and correctly perform the filter integrity verification.	X	X	X
3.3	Know and correctly perform sterilization by filtration.	X	X	X
3.4	Know and correctly perform the analytical method to test for pyrogens.	X		

B. Training of cleaning and disinfecting personnel

#	COMPETENCIES, KNOWLEDGE OR SKILLS COVERED IN TRAINING	PH/PT	TSP	C & D
1.	FOR CLEANING AND DISINFECTING THE GENERAL AREA FOR COMPOUNDING OF NON-HAZARDOUS STERILE PREPARATIONS			
1.1	Know all policies and procedures related to cleaning and disinfecting the equipment, furniture and facilities, notably those related to hygiene and asepsis, personal protective equipment, and cleaning and disinfecting tasks.	X	X	X
1.2	Know and don the correct garb.	X	X	X
1.3	Know and correctly apply hand hygiene.	X	X	X
1.4	Know, correctly perform and document cleaning and disinfecting tasks for the general area for compounding of sterile preparations.	X	X	X
2.	FOR CLEANING AND DISINFECTING THE AREA USED FOR COMPOUNDING HAZARDOUS STERILE PREPARATIONS			
2.1	Know, correctly perform and document cleaning and disinfecting tasks for the general area for compounding of hazardous sterile preparations.	X	X	X
2.2	Know and use personal protective equipment specifically for handling hazardous products.	X	X	X
2.3	Know and use the emergency measures to be applied in case of accidental exposure, accidents or spills.	X	X	X
PH = pharmacist; PT = pharmacy technician; TSP = technical support personnel; C&D = cleaning and disinfecting personnel.				

APPENDIX 5 PROCEDURE TEMPLATE

Pharmacy name Or Hospital XYZ pharmacy department	Procedure # _____ Revised: Yes <input type="checkbox"/> No <input type="checkbox"/> Approved by _____ Date _____ Effective date: _____
Procedure title: 	
Aim and objective: ➤ Describe the objective of the procedure.	
Target personnel: Use this section to describe the expected responsibilities for each group that will be affected by this procedure. <input type="checkbox"/> Head pharmacist <input type="checkbox"/> Compounding personnel <input type="checkbox"/> Pharmacy technician <input type="checkbox"/> Technical support personnel <input type="checkbox"/> Cleaning and disinfecting personnel <input type="checkbox"/> Other:	
Required facilities, equipment and material: Include the following types of information here: <input checked="" type="checkbox"/> Facilities and equipment required to apply the procedure. <input checked="" type="checkbox"/> Materials (e.g., devices, instruments) required to apply the procedure.	

- ✓ Products to be used.
- ✓ Containers to be used.
- ✓ Logs to be used or completed.

Procedures

Describe in detail what must be done by each person affected by the procedure, for each step or part of the procedure. Include examples of labels, symbols, logs, etc., that are to be used. Attach relevant documents, such as contracts, copies of legislation or regulations, manufacturers' instruction manuals, copies of administrative decision, other related procedures.

List of logs and assessment of competencies required for this procedure:

- 1.
- 2.

References

Indicate here the references used to draft the procedure, with relevant publication dates and edition numbers, to facilitate successive updates.

Procedure history: **Procedure #** _____

Drafted by: _____, pharmacist **Date:** _____ (dd/mm/yyyy)

Revised by: _____, pharmacist **Date:** _____ (dd/mm/yyyy)

Revision: Full Partial **Amended version:** Yes No

Change made:

Revised by: _____, pharmacist Date: _____ (dd/mm/yyyy)
Revision: Full <input type="checkbox"/> Partial <input type="checkbox"/> Amended version: Yes <input type="checkbox"/> No <input type="checkbox"/>
Change made:

APPENDIX 6 - BEST PRACTICE INDICATORS FOR CERTIFICATION OF CONTROLLED ROOMS, LAMINAR AIRFLOW WORKBENCHES AND BIOLOGICAL SAFETY CABINETS

Note: The following appendix lists the responsibilities of the certifier, a person engaged to certify sterile-product compounding rooms, laminar airflow workbenches (LAFWs) and biological safety cabinets (BSCs). This information is provided for the benefit of sterile compounding supervisor pharmacists, to allow them to assess the services provided during the certification of areas and equipment in their respective pharmacies.

<p>I. Before certification</p>	
<ul style="list-style-type: none"> ▪ Ideally meets the client (sterile compounding supervisor) to discuss the certification process; during the meeting, the certifier <ul style="list-style-type: none"> ✓ asks whether problems have occurred since the last certification; ✓ asks whether there are any concerns about the operation of rooms or devices (LAFW, BSC, CAI, CACI). ▪ Knows the PPE required to enter a controlled room and the garbing sequence. ▪ Knows the required procedure for washing and disinfecting hands before putting on gloves and entering a controlled room. 	
<p>II. General precertification requirements</p>	
<ul style="list-style-type: none"> ▪ Cleans and disinfects all equipment brought into the controlled rooms; ▪ Performs certification of the controlled rooms, LAFWs or BSCs following the steps and methods recommended by the applicable standards; ▪ Uses the applicable standards for certification (see Appendix 6); ▪ Uses the devices required by the standards (see Appendix 6); ▪ Uses calibrated devices that are in good condition; ▪ Knows the standards to be used for certification and knows how to apply them; ▪ Wears the appropriate PPE to enter and work in the compounding rooms for hazardous and non-hazardous sterile products; ▪ Is familiar with the products used, especially if they are hazardous; ▪ Does not touch hazardous products; if touching a hazardous product is required, asks qualified personnel to do so; ▪ If applicable, sets up a protective wall (plastic or other) before opening the device, to limit contamination of the controlled room by hazardous drugs; ▪ Performs the work meticulously and professionally. 	

III. Certification steps	
1. Certification of controlled areas	
<ul style="list-style-type: none"> ▪ Begins the certification of a clean room by measuring non-viable particles according to ISO 14644-1 specifications; ▪ Uses the criteria of standard IEST-RP-CC-006.3 for the certification of the clean room; ▪ Measures the volume of air supply or the velocity for each HEPA filter in the room; ▪ Measures the air velocity profile for each terminal or line HEPA filter (as applicable) in the controlled room, if the air volume for the HEPA filter cannot be measured; ▪ Calculates the air volume for the HEPA filter, if the velocity profile was measured; ▪ Verifies the integrity of the HEPA filter with a photometer; ▪ Verifies temperature; ▪ Verifies humidity; ▪ Verifies sound (noise) level;* ▪ Verifies light level;* ▪ Verifies the behaviour of the room and its equipment using smoke tests; ▪ Ensures that the doors to each room are fully closed when measuring pressure differentials between rooms; ▪ Obtains the dimensions of the room and its total volume of air supply, to allow calculation of number of air changes per hour. <p>* Note: The frequency of certain verifications, such as sound and light levels, may vary depending on needs and agreements.</p>	
2. Certification of BSC	
<ul style="list-style-type: none"> ▪ Certifies the BSC according to NSF Standard 49-2012 (Appendix F – Field Tests) and the manufacturer's specifications, which can be found on the BSC information plate or in the report included with the BSC at the time of purchase (when there is no information plate); ▪ Takes readings to measure the velocity of the air supply of a BSC according to NSF Standard 49-2012 or the manufacturer's specifications; ▪ In accordance with ISO 14644-1, <ul style="list-style-type: none"> ✓ Proceeds with the count of non-viable particles; ✓ Verifies the count of non-viable particles 0.5 µm in diameter; ✓ Verifies the count of non-viable particles in at-rest (optional) and in-operation (dynamic) states, measured at five reading points, with a minimum of two 1-minute and 1 m³ samples per reading point (the acceptable limit is 3520 particles). 	

<p>3. Certification of LAFW</p>	
<ul style="list-style-type: none"> ▪ Certifies the LAFW in accordance with IEST-RP-CC-002.3; ▪ Measures the velocity of the LAFW's air supply by taking a minimum of eight readings in the centre of every 12 square inches, at a distance 12 inches from the surface of the HEPA filter or protective screen; ▪ In accordance with ISO 14644-1, <ul style="list-style-type: none"> ✓ Proceeds with the count of non-viable particles; ✓ Verifies the count of non-viable particles 0.5 µm in diameter; ✓ Verifies the count of non-viable particles in at-rest (optional) and in-operation (dynamic) states, measured at five reading points, with a minimum of two 1-minute and 1 m³ samples per reading point (the acceptable limit is 3520 particles); ▪ Recommends that LAFW pre-filters be changed, if required. 	
<p>4. Certification of CAI and CACI</p>	
<ul style="list-style-type: none"> ▪ Certifies devices according to the manufacturer's recommendations, referring to CETA CAG-002-2006 (Compounding Isolator Testing Guide); ▪ Certifies, using the following tests, at minimum (other tests are indicated in CETA CAG-002-006): <ul style="list-style-type: none"> ✓ Airflow test ✓ Verification of internal pressure ✓ Verification of installation site ✓ Verification of HEPA filter ✓ Containment integrity and enclosure leak test ✓ Recovery time test ✓ Smoke test ✓ Test of preparation entry and output ✓ Count of non-viable particles 	
<p>IV. After certification</p>	
<ul style="list-style-type: none"> ▪ Answers questions and requests from the sterile compounding supervisor related to the certification and its procedure; ▪ Does the required quick cleaning of rooms and devices; ▪ Groups all waste contaminated by hazardous products and disposes of it as hazardous waste in the appropriate containers; ▪ Verifies that all certification labels are correctly printed and affixed; ▪ Provides the sterile compounding supervisor with a preliminary report (recommended but not mandatory) in writing or, at a minimum, verbally; ▪ Submits a final certification report that includes all information required by pharmacy regulatory authorities to confirm certification; ▪ Submits recent calibration certificates for the devices used in the certification, attached to the final certification report. 	

CAI = compounding aseptic isolator; CACI = compounding aseptic containment isolator; CETA = Controlled Environment Testing Association; HEPA = high-efficiency particulate air; NSF = NSF International (public health and safety organization); PPE = personal protective equipment.

APPENDIX 7 - CERTIFICATION OF CONTROLLED ROOMS, LAMINAR AIRFLOW WORKBENCHES AND BIOLOGICAL SAFETY CABINETS

TARGET	CERTIFICATION STANDARDS	CERTIFICATIONS
<p>Laminar airflow workbench (vertical or horizontal laminar flow hoods)</p>	<ul style="list-style-type: none"> • IEST-RP-CC-002.3: Unidirectional-Flow, Clean-Air Devices • ISO 14644-1 	<p><u>LAFW certification includes steps carried out:</u></p> <p>1- <u>In accordance with IEST-RP-CC-002.3:</u></p> <ul style="list-style-type: none"> • Measurement of air supply profile • HEPA filter integrity test <p>2- <u>In accordance with ISO 14644-1:</u></p> <ul style="list-style-type: none"> • Count of non-viable particles (0.5 µm diameter) in operational (dynamic) state; at-rest state is optional • Measurement of air intake velocity • Smoke test <p><u>Equipment used:</u></p> <ul style="list-style-type: none"> • Particle counter • Thermal anemometer • Smoke machine • Photometer
<p>Biological safety cabinet, Class II, type B2 (For certification of other types of BSC, please refer to the standards.)</p>	<ul style="list-style-type: none"> • NSF Standard 49-2012: Biological Safety Cabinetry: Design, Construction, Performance and Field Certification • ISO 14644-1 	<p><u>Class II, type B2 BSC certification includes steps carried out:</u></p> <p>1. <u>In accordance with NSF Standard 49-2012:</u></p> <ul style="list-style-type: none"> • Measurement of air supply profile • Measurement of air intake velocity • Smoke test • HEPA filter integrity test • Verification that interlock system (between discharge probe and air supply motor) is working properly (for Class II, type B2 BSC) • Verification of device calibration (less than 20% air loss in 15 seconds) (for Class II, Type B2 BSC) <p>2. <u>In accordance with ISO 14644-1:</u></p> <ul style="list-style-type: none"> • Count of non-viable particles (0.5 µm) in operational (dynamic) state; at-rest state is optional

		<ul style="list-style-type: none"> • Measurement of air intake velocity <p><u>Equipment used:</u></p> <ul style="list-style-type: none"> • Particle counter • Thermal anemometer • Smoke machine and aerosol generator • Photometer • Direct volume measurement device
Compounding aseptic isolator	<ul style="list-style-type: none"> • Primarily manufacturer's recommendations • CETA CAG-002-2006: Compounding Isolator Testing Guide 	<p><u>Isolator certification includes steps carried out according to manufacturer's recommendations, with reference to CETA/CAG-002-2006.</u></p> <p><u>Specific tests used:</u></p> <ul style="list-style-type: none"> • Airflow test • Verification of internal pressure • Verification of installation site • Verification of HEPA filter • Containment integrity and enclosure leak test • Recovery time test • Smoke test • Test of preparation entry and output • Count of non-viable particles
Compounding aseptic containment isolator	<ul style="list-style-type: none"> • Primarily manufacturer's recommendations • CETA CAG-002-2006: Compounding Isolator Testing Guide 	<p><u>Equipment used:</u></p> <ul style="list-style-type: none"> • Thermal anemometer • Pressure measurement device (in inches of water or pascals) • Tools for adjusting alarms • Smoke machine • Photometer • Particle counter (small) • Aerosol generator • Chronometer
Clean room for the compounding of sterile products and controlled areas	<ul style="list-style-type: none"> • NEBB Procedural Standards for Certified Testing of Clean rooms • IEST-RP-CC-006.3: Testing Clean Rooms 	<p><u>Certification of controlled areas and rooms includes the following steps:</u></p> <ul style="list-style-type: none"> • Count of non-viable particles in operational (dynamic) state (ISO 14644-1)

	<ul style="list-style-type: none"> • CETA CAG-003: Certification Guide for Sterile Compounding Facilities • ISO 14644-1 (section on number of particles, particle counters, and sampling plan and methods). 	<ul style="list-style-type: none"> • Certification of HEPA filter (IEST-RP-CC-006.3) • Verification of terminal or line HEPA filter • Measurement of pressure differential between controlled rooms • Verification of air changes per hour (by measuring volumes of air or room velocity) • Verification of behaviour of rooms and equipment using smoke tests • Temperature verification • Relative humidity verification • Measurement of luminosity • Measurement of noise level (sound) <p><u>Equipment used:</u></p> <ul style="list-style-type: none"> • Particle counter • Tripod for the room • Tripod for the LAFW or BSC • 0.3-µm filter (for cleaning) • "Tent" to capture air volume • Thermal anemometer • Smoke machine • Photometer • Pressure measurement device (in inches of water or pascals) • Thermometer • Hygrometer • Light meter • Sound level meter
<p>ANSI = American National Standard Institute; CETA = Controlled Environment Testing Association; IEST = Institute of Environmental Sciences and Technology; NEBB = National Environmental Balancing Bureau</p> <p>Note: Some certifying technicians have credentials from certain US agencies (e.g., NSF International, NEBB, CETA). These credentials, obtained from the agencies in question after appropriate training, indicate that the holder has sound knowledge of the standard and how it must be applied and verified.</p> <p>Information on certifiers can be found on the following websites: http://www.nsf.org (select the following options: regulatory resources / NSF certification / search certified products and systems / Class II Biosafety Cabinet Field Certifiers / search by country) and http://www.nebb.org (Certified firms/Directory of firms/NEBB certified firm/Search by country/Canada).</p>		

APPENDIX 8 TEMPLATE FOR THE DRAFTING OF COMPOUNDING PROTOCOLS TO BE COMPLETED FOR EACH DRUG

<p>Name of compounded product:</p> <p>Concentration:</p> <p>Pharmaceutical form:</p> <p>Route of administration:</p>	<p>Protocol number and version (e.g., 001-01)</p> <p>Effective date: (dd/mm/yyyy)</p> <p>Authorized by: _____, pharmacist</p>
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FORMULA			
Ingredients	Quantities	Physical description	Other information

Additional information about the ingredients:

Include any additional pertinent information about the ingredients required for compounding.

Indicate any specific precautions to be taken when handling the ingredients.

Notes on calculations and measurements:

Indicate any characteristics of the calculations, measurements or ingredient preparation that must be done before the specific procedure is carried out.

Indicate any requirement for verification by the pharmacist.

Examples:

- Quality control of devices to be carried out and documented before measurements are taken.
- Accuracy of measurement devices.
- Verification and documentation of ingredients, batch numbers and beyond-use dates.
- Type of report required on the compounding form.

Required devices, instruments and materials

Indicate all materials and equipment that will be required to compound the sterile products.

Compounding method

Describe all steps of the sterile-product compounding process.

<p>Quality controls</p> <p>Specify the procedure for determining the lot number of the final compounded sterile preparation.</p> <p>Specify all quality control procedures that are to be carried out during compounding and documented by the pharmacy technician and/or pharmacist.</p> <p>Specify all quality controls are to be carried out by the pharmacist on the final compounded sterile preparation. Indicate the expected specifications.</p>	
Example Quality control	Expected specification
Appearance of the preparation	Clear, colourless solution with no visible particles
<p>Packaging</p> <p>Describe the type of packaging in which the final compounded sterile preparation shall be presented to the patient.</p>	
<p>Stability and storage</p> <p>Specify the preservation requirements of the compounded sterile preparation.</p> <p>Specify the shelf life of the compounded sterile preparation (beyond-use date).</p> <p>Indicate the references used to determine shelf life.</p>	
Labelling	Sample label
Indicate mandatory information that must be on the label of the compounded sterile preparation.	

<p>A) When kept at the pharmacy or sent to another pharmacy</p>	<p>Name of preparation:</p> <p>Date when preparation was made:</p> <p>Lot:</p> <p>Quantity prepared:</p> <p>Beyond-use date:</p> <p>Shelf life:</p> <p>Verified by:</p>
<p>B) When dispensed to a patient</p>	<p>Customer label</p> <p>In addition to the legally mandated information, add:</p> <ul style="list-style-type: none"> - lot number of compounded sterile preparation - beyond-use date - precautions and pharmacovigilance
<p>Training</p> <p>Indicate the training that personnel must undergo before the specific sterile compounding procedure is implemented.</p>	
<p>References consulted:</p> <p>Indicate the source of the specific sterile compounding procedure.</p> <p>Indicate any documentation supporting the stability of the final compounded sterile preparation.</p>	

Preparation data sheet history No.:	
Date drafted: (dd/mm/yyyy)	Drafted by:
Revised: (dd/mm/yyyy)	Revised by:
Change made:	Version number changed: <input type="checkbox"/> YES <input type="checkbox"/> NO
Revised: (dd/mm/yyyy)	Revised by:
Change made:	Version number changed: <input type="checkbox"/> YES <input type="checkbox"/> NO

APPENDIX 9 EXAMPLES OF STERILE PREPARATIONS THAT MUST BE VERIFIED AT EACH STAGE OF COMPOUNDING

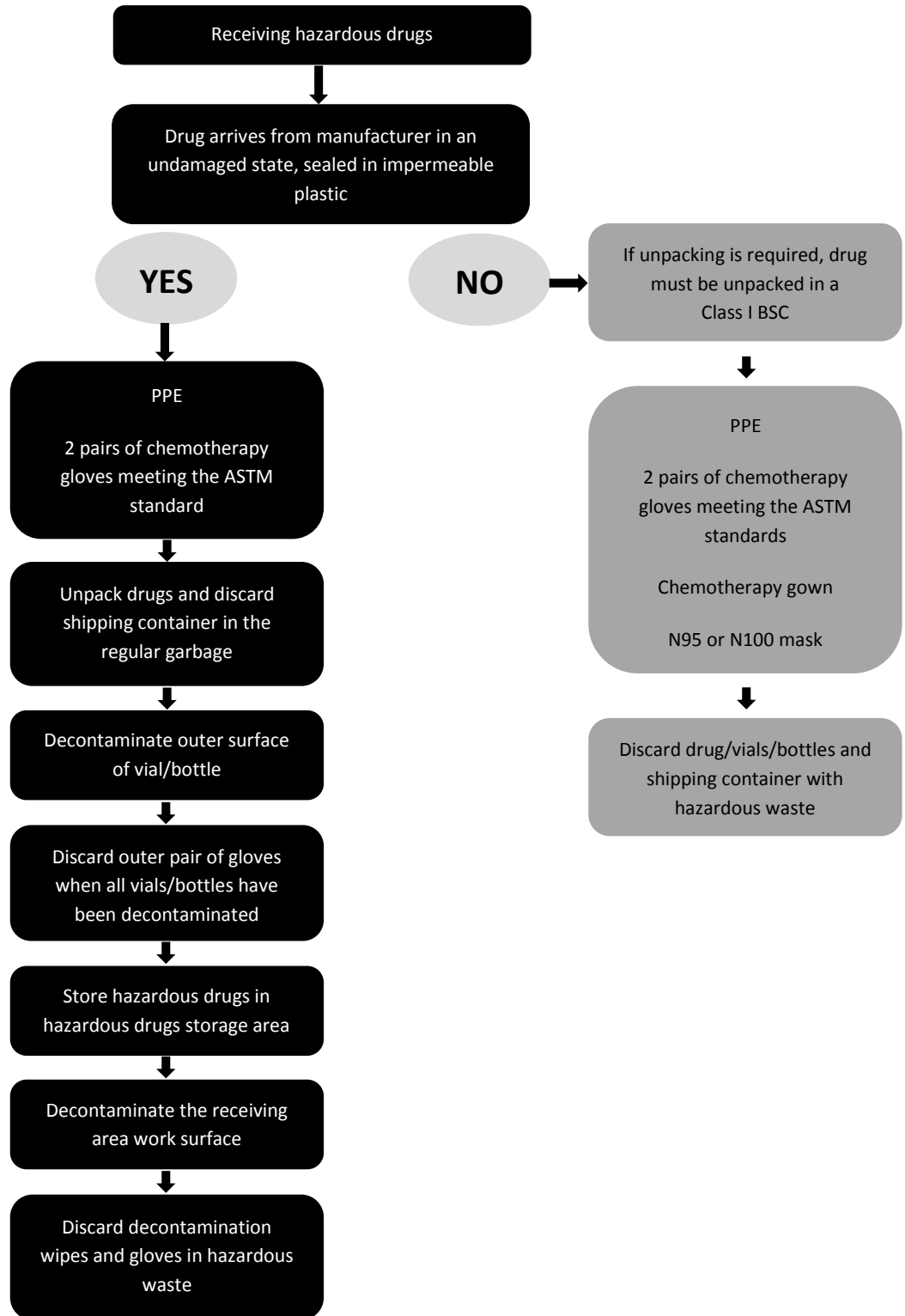
Packaging or system used	Examples
<p>Contents of vial or ampoule to be injected into a bag, minibag, Intermate or other container, when the entire contents of the vial (powder) will not be used or when a liquid product is packaged in a vial or ampoule</p>	<p>1 g cefazolin IV every 8 hours Dose prepared using a 10-g vial of powder diluted in 50 mL of 0.9% NaCl. The diluent and product taken from the vial must be checked for each dose before injection into the bags.</p>
<p>Ophthalmic drops</p>	<p>50 mg/mL vancomycin ophthalmic solution prepared from a 500-mg vial. The vehicle used and product taken from the vial must be checked before insertion into the dispenser bottle.</p>
<p>Diluted cassette</p>	<p>50 mg/mL Morphine-HP® in a 10-mL vial diluted to a final concentration of 10 mg/mL for subcutaneous infusion. The volume of morphine and the volume of diluent must be checked before they are put into the cassette.</p>
<p>Preparation made using a volumetric pump (e.g., Baxa-Repeater®, PharmAssist)</p>	<p>Verification of the pump setting each time the volume is changed, and more frequently if necessary (e.g., if a large number of units is prepared).</p>

APPENDIX 10 EXAMPLES OF STERILE PREPARATIONS THAT DO NOT REQUIRE VERIFICATION DURING THE COMPOUNDING PROCESS

Packaging or system used	Examples
Syringe filled with a single product	Syringe of 300 µg filgrastim for subcutaneous administration three times per week, prepared from a 300 µg/mL vial of filgrastim
ADD-Vantage™ or Mini-Bag Plus type system	500 mg Primaxin® IV every 6 hours, prepared using the ADD-Vantage™ system (http://www.hospira.com/Products/addvantagesystem.aspx) or vial compatible with a Mini-Bag Plus
Contents of vial (powder) to be injected into a bag, minibag, Intermate or other container, when the entire contents of the vial will be used	1 g cefazolin IV every 8 hours Dose prepared using a 1-g vial of powder diluted in 50 mL of 0.9% NaCl
Morphine or hydromorphone cassette, when starting with the product at the same concentration (at this point, it is the concentration per millilitre that is important, so the number of empty vials must be counted)	Cassette of morphine at a concentration of 5 mg/mL for subcutaneous administration, prepared from 30-mL vials of 5 mg/mL morphine (undiluted)

APPENDIX 11 PROCEDURE EXAMPLE

Receiving, unpacking and storing hazardous products



APPENDIX 12 TEMPERATURES FOR DIFFERENT TYPES OF STORAGE

	Temperature range
Freezing	-25°C to -10°C*
Refrigeration (cold)	2°C to 8°C*
Temperature (cool)	8°C to 15°C*
Controlled room temperature	15°C to 20°C†
Drug conservation temperature	15°C to 30°C

*United States Pharmacopeial Convention (USP). General notices and requirements. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008. p. 29.

†United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

APPENDIX 13 INCIDENT/ACCIDENT REPORTING AND FOLLOW-UP FORM

Note: This form is intended for pharmacists who do not use a health care facility's suggested form.

Incident/accident* reporting and follow-up		
Reporting an incident <input type="checkbox"/> accident <input type="checkbox"/>		
General information		
Date and time of incident/accident:	Reported by:	
Name of patient affected, if applicable:	Full address:	Phone number:
Pharmacy personnel involved:		
Information about incident/accident		
(Summary of the situation and consequences)		
Disclosed to the patient concerned: <input type="checkbox"/>		
Name of pharmacist responsible for follow-up:		
Analysis of causes		
Causes: (Identify causes of the problem)	Options for corrections or changes: (Assess potential corrections or changes to be made)	Corrections or changes chosen: (Indicate the corrections or changes to be made)
Action plan		

Actions (Describe the actions to be taken and the steps required to correct the situation, with a specific timeline. Determine who will be responsible for implementation.)	Responsible	Deadline	✓
Monitoring			
Verifications (Verifications to ensure that the corrections and changes are effective and fully implemented.)	Responsible		✓
Closing of the file			
Pharmacist responsible for follow-up: (signature)		Date file closed:	

*An accident is an action or situation in which the risk event occurs and has or could have an impact on the health status or well-being of the user (patient), personnel, professional concerned or third party. An incident is an action or situation that has no impact on the health status or well-being of the user (patient), personnel, professional concerned or third party, but which has an unusual result that could, on other occasions, lead to consequences.

APPENDIX 14 COMPONENTS OF A QUALITY ASSURANCE PROGRAM

COMPONENT	CONTROLS	FREQUENCY
FACILITIES	Certification of clean rooms and anteroom	<ul style="list-style-type: none"> • Every 6 months • When the controlled area is installed • When new equipment is installed • When rooms or equipment are maintained or repaired • When a contamination problem is identified • When investigation of a contamination problem or non-compliance in the aseptic preparation process requires exclusion of malfunctioning facilities
	Sampling of controlled areas under operational (dynamic) conditions: <ul style="list-style-type: none"> - Viable and non-viable particles, air and surfaces - According to a sampling plan 	<ul style="list-style-type: none"> • Every 6 months (more frequently at the start of the quality assurance program) • When the controlled area is installed • When new equipment is installed • When the controlled area or equipment is repaired or maintained (e.g., high-efficiency particulate-air filter changed) • When a contamination problem is identified • When investigation of a contamination problem or non-compliance in the aseptic preparation process requires exclusion of malfunctioning facilities • According to an internal verification program

	Verification of temperature and humidity in controlled areas	<ul style="list-style-type: none"> • Once a day
	Pressure differential between controlled areas	<ul style="list-style-type: none"> • Continuous reading and notification system to prevent non-compliance • Periodic verification (once a week) by the sterile compounding supervisor • Notification system (if reading is not continuous, assign personnel to verify and record the differential twice a day)
EQUIPMENT		
	Certification of LAFWs and equipment	<ul style="list-style-type: none"> • Before first use • Every 6 months • When new equipment is installed • When equipment is repaired or maintained • When a contamination problem is identified • When investigation of a contamination problem or non-compliance in the aseptic preparation process requires exclusion of malfunctioning facilities
	Temperature verification (e.g., refrigerator, freezer, incubator)	<ul style="list-style-type: none"> • Once a day (if unit has a built-in reading device) • Twice a day (if unit has no built-in reading device)
	Operational indicators of LAFWs and other devices used (e.g., automated compounding device)	<ul style="list-style-type: none"> • Verified daily before use • Verified continuously by personnel
	<p>Sampling of LAFWs under operational (dynamic) conditions:</p> <ul style="list-style-type: none"> - Viable and non-viable particles, air and surfaces - According to a sampling plan 	<ul style="list-style-type: none"> • Every 6 months (more frequently at the start of the quality assurance program) • When a new LAFW is installed • When the LAFW is maintained or repaired • When a contamination problem is identified • When investigation of a contamination problem or non-compliance in the aseptic preparation process requires exclusion of malfunctioning facilities • According to an internal verification program

PERSONNEL	Competency assessment	<ul style="list-style-type: none"> • At initial qualification: theoretical and practical aspects • At periodic qualifications: theoretical and practical aspects • When assessing incidents and accidents • When a contamination problem is identified
	Gloved fingertip sampling	<ul style="list-style-type: none"> • At initial qualification: theoretical and practical aspects • At periodic qualifications: theoretical and practical aspects • When assessing incidents and accidents • When a contamination problem is identified
	Media fill tests	<ul style="list-style-type: none"> • At initial qualification: theoretical and practical aspects • At periodic qualifications: theoretical and practical aspects • When assessing incidents and accidents • When a contamination problem is identified
FINAL COMPOUNDED STERILE PREPARATION	Verification of compounding protocols (usage and maintenance)	<ul style="list-style-type: none"> • In accordance with the quality assurance program
	Verification that preparation matches prescription	<ul style="list-style-type: none"> • In accordance with the quality assurance program
	Verification of label compliance	<ul style="list-style-type: none"> • In accordance with the quality assurance program
	Entry in logs	<ul style="list-style-type: none"> • In accordance with the quality assurance program
LAFW = laminar airflow workbench.		

11. BIBLIOGRAPHY

Note to readers: The references cited in these Model Standards reflect the references appearing in the source document, “Préparation de produits stériles dangereux en pharmacie – Norme 2014.02,” published by the Ordre des pharmaciens du Québec, 2014. Where possible, certain details have been verified against the source documents. URLs for online documents are current as of July 2014.

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