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Guidance Document for Pharmacy Compounding of Non-Sterile Preparations

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GUIDANCE DOCUMENT

FOR PHARMACY COMPOUNDING OF NON-STERILE PREPARATIONS

COMPANION TO THE MODEL STANDARDS FOR PHARMACY COMPOUNDING OF NON-STERILE PREPARATIONS



National Association of Pharmacy Regulatory Authorities[®]
Association nationale des organismes de réglementation de la pharmacie

Guidance Document for Pharmacy Compounding of Non-sterile Preparations — Companion to the Model Standards for Pharmacy Compounding of Non-sterile Preparations

Approved by the National Association of Pharmacy Regulatory Authorities' (NAPRA) Board of Directors November 2017, published March 2018. Revision June 2018.

Adapted with permission from “Préparations magistrales non stériles en pharmacie — Norme 2012.01”, Ordre des pharmaciens du Québec, 2012

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1. INTRODUCTION

The “Guidelines to Pharmacy Compounding” published by the National Association of Pharmacy Regulatory Authorities (NAPRA) in October 2006 have recently been reviewed, a process that has resulted in a new set of documents: the Model Standards for Pharmacy Compounding of Non-hazardous Sterile Preparations¹, the Model Standards for Pharmacy Compounding of Hazardous Sterile Preparations², and the Model Standards for Pharmacy Compounding of Non-sterile Preparations with its accompanying document, the Guidance Document for Pharmacy Compounding of Non-sterile Preparations (referred to hereafter as the Guidance Document).

The NAPRA Model Standards for Pharmacy Compounding of Non-sterile Preparations and this accompanying Guidance Document have been adapted from standards originally developed by the Ordre des pharmaciens du Québec, which are in turn based on *General chapter <795>* of the United States Pharmacopeia – National Formulary (USP–NF) in effect in the United States since 2004. Their preparation was led by the NAPRA National Advisory Committee on Pharmacy Practice and involved extensive consultation with experts and stakeholders. The Model Standards and this Guidance Document are intended to ensure the safety of both patients and the personnel involved in compounding non-sterile drugs.

This Guidance Document has been developed to provide direction on and assistance with implementation of the new Model Standards. Individual pharmacies should review their own compounding practices to determine which standards apply. This Guidance Document can then be consulted for more details on how the standards can be achieved. The requirements of the applicable pharmacy regulatory authorities must also be consulted.

1 National Association of Pharmacy Regulatory Authorities (NAPRA). *Model standards for pharmacy compounding of non-hazardous sterile preparations*. Ottawa, ON: NAPRA; 2015. Available from: <http://napra.ca/general-practice-resources/model-standards-pharmacy-compounding-non-hazardous-sterile-preparations>

2 National Association of Pharmacy Regulatory Authorities (NAPRA). *Model standards for pharmacy compounding of hazardous sterile preparations*. Ottawa, ON: NAPRA; 2016. Available from: <http://napra.ca/general-practice-resources/model-standards-pharmacy-compounding-hazardous-sterile-preparations>



2. OBJECTIVES

The aim of this Guidance Document is to support implementation of the corresponding Model Standards and to provide pharmacists and pharmacy technicians who compound non-sterile preparations with the details 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 non-sterile preparations. The use of other technologies, techniques, materials and procedures may be acceptable, if they have been proven to be equivalent or superior to those described in this Guidance Document.

This Guidance Document should be used in conjunction with the Model Standards for Pharmacy Compounding of Non-sterile Preparations, as well as NAPRA's Model Standards of Practice for Canadian Pharmacists and Pharmacy Technicians^{3,4} and other policies and guidelines that may be in place in provincial/territorial jurisdictions.

As for all prescriptions, it is expected that a pharmacist will review the prescription for each non-sterile preparation and use personal expertise to determine whether the compounded prescription is appropriate for the particular patient.

In addition, the pharmacist and/or pharmacy technician who is designated as the compounding supervisor must determine whether the appropriate knowledge and resources to develop the formulation and/or the appropriate equipment and competency to compound the preparation are available. Section 2.1, below, lists questions that may be helpful in making this determination. Once a determination has been made that it is appropriate to compound the preparation, the Model Standards must be applied.

2.1 General guidance on whether to compound a preparation

- Are the active ingredients already available in a manufactured product?
- Do you have a referenced formulation?
- Do you have the beyond-use date (BUD) and relevant stability data?
- Do you have a dedicated space for compounding that is clean and uncluttered?
- Do you have the appropriate equipment and ingredients to make the compounded preparation?
- Are your pharmacy personnel competent to perform compounding of the preparation?
- Can your pharmacy personnel compound the preparation without interruption?
- Should you refer this compounded preparation to another pharmacy with appropriate facilities, equipment and expertise?

3 National Association of Pharmacy Regulatory Authorities (NAPRA). *Model standards of practice for Canadian pharmacists*. Ottawa, ON: NAPRA; 2009. Available from: <http://napra.ca/pharmacists/model-standards-practice-canadian-pharmacists>

4 National Association of Pharmacy Regulatory Authorities (NAPRA). *Model standards of practice for Canadian pharmacy technicians*. Ottawa, ON: NAPRA; 2011. Available from: <http://napra.ca/pharmacy-technicians/model-standards-practice-canadian-pharmacy-technicians>



3. REGULATORY FRAMEWORK

Although compounded non-sterile preparations are sometimes prepared by other healthcare professionals, including nurses, physicians and veterinarians, the majority of non-sterile compounding is performed by pharmacy personnel under the supervision or direction of pharmacists. Although the Model Standards and this Guidance Document could serve as best practices for other healthcare practitioners, they pertain specifically to compounding by pharmacy personnel for human or animal use⁵ in all pharmacy settings where non-sterile preparations are compounded.

In January 2009, Health Canada developed its “Policy on Manufacturing and Compounding Drug Products in Canada”⁶. It is expected that this Health Canada policy will be followed, along with the Model Standards. Compounding must always be carried out within a patient–healthcare professional relationship or, in the case of a compounded veterinary product, within a veterinarian–client–patient relationship. In the absence of a patient-specific prescription, and with a prescriber’s order for office use, compounders may prepare a compounded product at an appropriate scale, time or frequency to ensure it is being used within a patient–healthcare professional relationship. Compounders may also prepare batches of compounded product in limited quantities in anticipation of future prescriptions. Requests to compound preparations in bulk quantities for distribution or sale outside a patient–healthcare professional relationship generally fall into the realm of manufacturing and are thus outside the jurisdiction of pharmacies. The chart below provides general guidelines on differentiating between compounding and manufacturing activities.

3.1 General guideline on compounding and manufacturing activities⁷

- 1) Is there a demonstrated patient–healthcare professional relationship?
 - Compounding - Yes
 - Manufacturing - No
- 2) Is there third-party reselling of the product outside of a patient–healthcare professional relationship?
 - Compounding - No
 - Manufacturing - Yes
- 3) Is the activity regulated, and the facility possibly inspected, by the province/territory?
 - Compounding - Yes
 - Manufacturing - No
- 4) If the product is being compounded in anticipation of a prescription, is the amount consistent with the history of prescriptions received?
 - Compounding - Yes
 - Manufacturing - No
- 5) Is a large quantity of the product produced on a regular basis?
 - Compounding - No
 - Manufacturing - Yes

5 Canadian Veterinary Medical Association (CVMA). *Guidelines for the legitimate use of compounded drugs in veterinary practice*. Ottawa, ON: CVMA; 2006. The CVMA guidelines state that the veterinarian is responsible for the safety and efficacy of the prescribed drug and for establishing adequate withdrawal times to avoid residues when the drug is used in animals intended for consumption.

6 Health Canada, Health Products and Food Branch Inspectorate. *Policy on manufacturing and compounding drug products in Canada (POL-0051)*. Ottawa, ON: Health Canada; 2009. Available from: http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpfi/docs/pol_0051-eng.php

7 Health Canada, Health Products and Food Branch Inspectorate. *Policy on manufacturing and compounding drug products in Canada (POL-0051)*. Ottawa, ON: Health Canada; 2009. Available from: http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpfi/docs/pol_0051-eng.php. Modified from Appendix 1.

- 6) Is an identical product (e.g., dosage form, strength, formulation) commercially available?
 - Compounding - No
 - Manufacturing - Yes

- 7) Does the drug product require only minor modification before direct administration when such modification amounts to mere directions for use?
 - Compounding - No
 - Manufacturing - Yes

- 8) Is the compound a non-prescription product produced and offered for sale to the general public in the pharmacy?
 - Compounding - No
 - Manufacturing - Yes



4. ASSESSING RISK FOR COMPOUNDING NON-STERILE PRODUCTS

A risk assessment must be undertaken to identify the appropriate level of requirements to minimize contamination of each compounded product and to provide adequate protection for personnel. In addition to assessing the risk associated with compounding of individual products, the compounding supervisor must also consider the cumulative risk associated with all preparations compounded in the pharmacy. For example, if small quantities of one preparation are compounded occasionally, and the preparation has a low risk, it may be possible to mitigate the risk by taking certain steps. However, if small quantities of several different preparations, each of which individually has low risk, are compounded within the same timeframe, then the total cumulative risk must be considered.

If it is necessary to compound a preparation requiring procedures or processes that are not currently in place within the pharmacy, the documentation should specify the potential risks of compounding the product, the extra steps that must be taken to mitigate the risks and references confirming that these steps actually will minimize risks to the quality of the product and safety of personnel. The following examples illustrate these concepts:

- For a complex compound, the documentation should specify extra measures required, such as measures to ensure uninterrupted workflow, extra verification steps, extra equipment and supporting references.
- If a small quantity of a hazardous product is used in compounding, there must be documentation of alternative containment strategies and/or work practices being employed for specific dosage forms to minimize occupational exposure.

Safety data sheets and other applicable references must be consulted, and appropriate procedures for safe compounding must be documented on the [Master Formulation Record](#) (see section 6.2) for each compound. Additional laws and regulations governing the compounding of hazardous preparations and the handling of hazardous products, whether at the federal, provincial, or territorial level, must also be consulted.

Each pharmacy should customize its list of drugs and materials being used, including hazardous drugs and hazardous materials. The requirements for safe compounding of all materials should be researched and documented. Some useful references are listed in section 4.3.

4.1 Some factors to consider in risk assessment

- Complexity of compounding the preparation
- Need for verification and uninterrupted workflow
- Frequency of compounding high-risk or low-risk preparations
- Risk of cross-contamination with other products (e.g., allergens)
- Concentration of ingredients in the product
- Quantity of ingredients being handled
- Physical characteristics of ingredients, such as liquid vs. solid vs. powders, or water-soluble vs. lipid-soluble
- Education and competency of compounding personnel
- Availability of appropriate facilities and equipment
- Classification of ingredients if identified by WHMIS⁸ as presenting a health hazard or a drug classified by NIOSH as hazardous (see reference to NIOSH in [section 4.3](#))
- Type of hazardous drug (i.e., anti-neoplastic, non-antineoplastic, reproductive risk only)

8 Canadian Centre for Occupational Health and Safety (CCOHS). *WHMIS 2015 - Hazard classes and categories*. Hamilton, ON: CCOHS; 2015. [Last modified June 17, 2016.] Available from: http://www.ccohs.ca/oshanswers/chemicals/whmis_ghs/hazard_classes.html

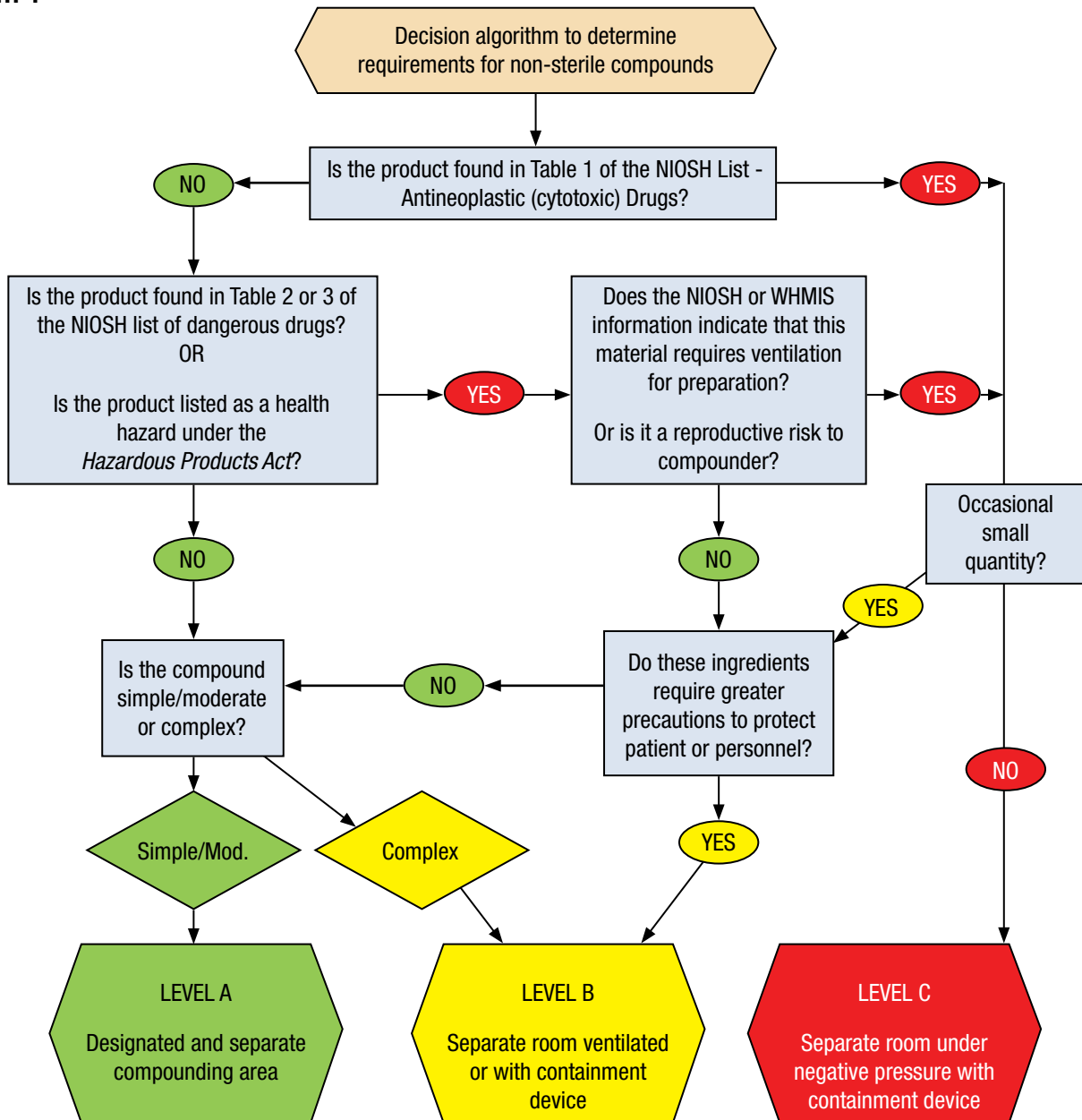
- Exposure to compounding personnel for each preparation and accumulation of exposure over time
- Risk of microbial contamination (liquids, creams and ointments may be particularly susceptible to microbial and other contamination)

The risk assessment must be reviewed at least every 12 months to ensure that it is still valid. A decision algorithm to assist in determining requirements for non-sterile compounding can be found in section 4.2.

Note: Occasional small quantities of materials must not be considered in isolation. If several different high-risk or low-risk preparations are being compounded, the cumulative risk must be considered, even if they are compounded on different days. This must be documented in the risk assessment.

4.2 Decision algorithm for risk assessment

Diagram 1



4.3 References for assessing risk

General
<p>United States Pharmacopeial Convention (USP). In: <i>USP compounding compendium</i>. Rockville, MD: USP; 2016. Available from: https://www.usp.org/compounding [Contains all USP chapters useful to pharmacists, including <i>General chapter <795>: pharmaceutical compounding — nonsterile preparations</i>]</p>
<p>Canadian Society of Hospital Pharmacists (CSHP). <i>Compounding: guidelines for pharmacies</i>. Ottawa, ON: CSHP; 2014. Available from: https://www.cshp.ca/compounding-guidelines-pharmacies</p>
<p><i>PIC/S guide to good practices for the preparation of medicinal products in healthcare establishments</i>. Geneva, Switzerland: Pharmaceutical Inspection Convention, Pharmaceutical Inspection Co-operation Scheme; March 1, 2014. Available from: https://www.picscheme.org/layout/document.php?id=156</p>
Hazardous drugs and hazardous materials
<p>Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). <i>Prevention guide — safe handling of hazardous drugs</i>. Montreal, QC: ASSTSAS; 2008. Available from: https://www.irsst.qc.ca/media/documents/PubIRSST/CG-002.pdf</p> <p>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 healthcare facility at the various stages of the preparation, distribution and administration of hazardous drugs.</p> <p>The guide explains that the principles of precaution “unequivocally apply to all antineoplastic drugs, regardless of whether they are used in oncology or to treat other conditions (e.g. methotrexate for arthritis). However, some precautions could be adapted for other categories (e.g., hormones) based on the specific risks for each category.”</p>
<p><i>Hazardous Products Act and Hazardous Products Regulations</i> available from: http://laws-lois.justice.gc.ca/eng/acts/H-3/ and http://laws-lois.justice.gc.ca/eng/regulations/SOR-2015-17/index.html</p> <p>Schedule 2 of the <i>Hazardous Products Act</i> divides hazardous products into two categories: physical hazards (flammable, gas under pressure, explosive) and health hazards. The health hazard class includes agents causing acute toxicity, skin corrosion/irritation, serious eye damage/eye irritation, respiratory or skin sensitization, germ cell mutagenicity, carcinogenicity, reproductive toxicity, specific target organ toxicity through repeated exposure, aspiration hazard, biohazardous infectious materials and health hazards not otherwise classified.</p>
<p>National Institute for Occupational Safety and Health (NIOSH). <i>NIOSH list of antineoplastic and other hazardous drugs in healthcare settings; 2016</i>. Cincinnati, OH: Department of Health and Human Services, Centers for Disease Control and Prevention, NIOSH; 2016. Available from: https://www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf</p> <p>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 regularly updates a list of hazardous drugs. Recognizing that no single approach can cover the diverse potential of occupational exposures to hazardous drugs, the NIOSH approach involves three groups of drugs, each having its own list within the document.</p> <p>The lists contain the criteria and sources of information for determining whether a drug is hazardous, given its genotoxicity, carcinogenicity, reproductive and developmental effects, and organ toxicity. These NIOSH lists can be used by individual pharmacies to develop their own lists of hazardous drugs that require special handling precautions, given that a list of hazardous drugs used must be available at every pharmacy. Each of these products must be handled and disposed of properly. The NIOSH lists are updated regularly, but all new drugs in the antineoplastic, immunosuppressant and sexual hormone classes belong on the hazardous drugs list unless the manufacturer provides evidence to the contrary. New powder forms of these products also belong on the hazardous drugs list.</p> <p>In addition, NIOSH published an alert on preventing occupational exposure to antineoplastic and other hazardous drugs in 2004.</p>



United States Pharmacopeial Convention (USP). In: *USP compounding compendium*. Rockville, MD: USP; 2016. Available from: <https://www.usp.org/compounding> [Contains many USP chapters useful to pharmacists, including *General chapter <800>: hazardous drugs – handling in healthcare settings*]

In February 2016, the USP published *General chapter <800>*, which describes practice and quality standards for handling hazardous drugs, including the receipt, storage, compounding, dispensing, administration and disposal of sterile and non-sterile products and preparations. The chapter is scheduled to become official December 1, 2019.

Workplace Hazardous Materials Information System (WHMIS)

Canadian Centre for Occupational Health and Safety (CCOHS). *WHMIS 2015 - hazard classes and categories*. Hamilton, ON: CCOHS; 2015. [Last modified June 17, 2016.] Available from: http://www.ccohs.ca/oshanswers/chemicals/whmis_ghs/hazard_classes.html

The WHMIS is “a comprehensive system for providing health and safety information on hazardous products intended for use, handling, or storage in Canadian workplaces”⁹. It has been aligned with the Globally Harmonized System of Classification and Labelling of Chemicals for a more uniform worldwide system of hazardous product recognition and information.

In Canada, legislation requires that products used in the workplace that meet the criteria for classification as hazardous products must be labelled. Labels are the first alert to the user about major hazards associated with a product, and outline the basic precautions or safety steps that should be taken. There are two main groups of hazardous: the physical hazards group, based on the physical or chemical properties of the product, such as flammability, reactivity or corrosivity to metals; and the health hazards group, based on the product’s ability to cause a health effect, such as eye irritation, respiratory sensitization (e.g., causing allergy or asthma symptoms or breathing difficulties if inhaled) or carcinogenicity.

Compounders can refer to WHMIS safety data sheets for these materials. These documents are required by the regulations, are essential sources of information about the risks of using hazardous materials and must be available to all employees.

Worksafe BC. *Best practices for the safe handling of hazardous drugs*. Richmond, BC: Workers’ Compensation Board of British Columbia; 2015. Available from: <https://www.worksafebc.com/en/resources/health-safety/books-guides/best-practices-safe-handling-hazardous-drugs?lang=en>

This guide is intended primarily for healthcare workers to minimize exposure to hazardous drugs in the workplace. Part 1 presents an overview of current knowledge on hazardous drugs. Part 2 describes how to perform a risk assessment. Part 3 gives examples of best practices for each stage of handling hazardous drugs.

⁹ Canadian Centre for Occupational Health and Safety (CCOHS). *WHMIS 2015 – hazard classes and categories*. Hamilton, ON: CCOHS; 2015. [Last modified June 17, 2016.] Available from: http://www.ccohs.ca/oshanswers/chemicals/whmis_ghs/hazard_classes.html



5. REQUIREMENTS FOR ALL LEVELS¹⁰ OF NON-STERILE COMPOUNDING ACTIVITIES

5.1 Compounding personnel

If the pharmacy is small, one pharmacist may be responsible for fulfilling all roles and tasks; however, it is best practice to have another person verify calculations and measurements.

5.1.1 Pharmacy manager¹¹ or pharmacy department head¹²

The pharmacy manager or pharmacy department head is responsible for the development, organization and supervision of all activities related to compounding of non-sterile preparations in the pharmacy. These responsibilities may be assigned to a pharmacist or pharmacy technician, who will be designated as the non-sterile compounding supervisor.

5.1.2 Non-sterile compounding supervisor

The non-sterile compounding supervisor is a pharmacist or pharmacy technician who develops, organizes and oversees all activities related to compounding of non-sterile preparations in the pharmacy, as assigned by the pharmacy manager or pharmacy department head.

The non-sterile compounding supervisor may assign technical tasks related to compounding non-sterile preparations to non-regulated pharmacy personnel with the appropriate training and competencies. This assignment of tasks must be carried out using a formal delegation process or under supervision in accordance with the requirements of the provincial/territorial regulatory authority.

Responsibilities

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

- Measures are in place (i.e., personnel training and assessment program) to ensure that personnel are competent to perform compounding, which includes training for any specific populations (e.g., pediatric, geriatric, veterinary).
- Personnel know and fully comply with policies and procedures.
- The existing compounding process yields high-quality non-sterile preparations.
- A risk assessment is performed to determine appropriate requirements for each compounded preparation.
- Appropriate measures are taken to ensure the safety of personnel during each preparation.
- Procedures for incident/accident reporting and follow-up, as well as recall procedures, are in place.
- Policies and procedures covering all activities are developed, regularly reviewed and updated.
- The facilities and equipment used to compound non-sterile preparations meet requirements and are maintained, calibrated or certified according to manufacturers' specifications or standards, whichever are more stringent.
- The available, recognized scientific literature is used to determine stability and to establish the BUD for each non-sterile preparation.
- Master Formulation Records are developed, reviewed and updated.

¹⁰ Additional information on the compounding of hazardous preparations can be found in section 9 of this document.

¹¹ In the context of this document, a pharmacy manager in the province of Quebec is the pharmacist who owns the pharmacy; in other Canadian jurisdictions, a pharmacy manager is the pharmacist designated as the manager by the pharmacy owner and/or recognized as the manager by the provincial/territorial regulatory authority.

¹² In the context of this document, the pharmacy department head must be a pharmacist licensed to practice pharmacy by the relevant pharmacy regulatory authority.



- An ongoing 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, followed, evaluated and updated as required.
- Current editions of mandatory and supplementary references, which should be in compliance with provincial/territorial requirements, are available. Safety data sheets are available and updated regularly, or are readily accessible in an electronic format.
- All records of decisions, activities or specifications required by the Model Standards are completed, and any changes are documented and traceable. The records are retained and readily available for audit and inspection purposes, as required by the provincial/territorial pharmacy regulatory authority.

5.1.3 Regulated pharmacy personnel

When more than one pharmacist or pharmacy technician is involved in compounding a non-sterile preparation, whether working in the same or different facilities/pharmacies, responsibilities toward the patient are shared between them. In such instances, all parties must comply with provincial/territorial requirements and standards regarding inter- and intra-professional collaboration.

Pharmacy students and interns may also compound non-sterile preparations, in accordance with their level of training and the scope of practice set out by the pharmacy regulatory authority.

Responsibilities

The responsibilities of the compounding pharmacist or pharmacy technician may include:

- perform and/or supervise compounding activities;
- ensure compliance with policies and procedures related to the compounding of non-sterile preparations, including handling of hazardous drugs and materials where applicable;
- enforce compliance with required rules relating to hygiene, cleanliness and safety;
- ensure that all records related to ongoing activities are completed and that documentation clearly indicates who completed and who verified each activity;
- 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 record for each compounded preparation, including any deviations from the Master Formulation Record;
- ensure the accuracy of calculations and measurements;
- ensure that appropriate equipment and instruments are used for each compounded preparation;
- follow the compounding process defined in the Master Formulation Record;
- perform verification during the various stages of compounding and verify the final preparation;
- ensure that all required verification and quality control measures are performed to ensure the quality 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;
- when a non-sterile preparation is prepared on behalf of another facility/pharmacy (where permitted by provincial/territorial legislation), provide any information required for storing and transporting such preparations (storage method, precautions, BUD, etc.) to the pharmacist or pharmacy technician at the facility/pharmacy where the preparation will be dispensed;



- ensure that the final preparation is properly stored until delivery to the patient or to the pharmacist who ordered it (where compounding has been undertaken by another pharmacy, as permitted by provincial/territorial legislation);
- when a preparation must be recalled, notify the patient and any pharmacist or pharmacy technician at any pharmacy/facility where the product was dispensed;
- before dispensing or releasing a preparation to the patient, ensure that all standards of practice associated with dispensing the preparation have been met, including an assessment of therapeutic appropriateness, patient consultation and education, documentation and other patient care activities;
- when a non-sterile preparation has been prepared on behalf of another facility/pharmacy (where permitted by provincial/territorial legislation), ensure that effective communication and collaboration occurs between the healthcare professionals at both facilities to clarify who is responsible for which aspects of patient care and to ensure continuity of care¹³.

5.1.4 Non-regulated pharmacy personnel

Non-regulated pharmacy personnel with appropriate training¹⁴ may compound non-sterile preparations or perform other technical tasks related to compounding non-sterile preparations only when assigned to do so by the non-sterile compounding supervisor and only after completion of a formal delegation of duties from a pharmacist or under appropriate supervision, in compliance with the requirements of the provincial/territorial pharmacy regulatory authority.

Responsibilities

The responsibilities of non-regulated pharmacy personnel assigned to compound non-sterile preparations or perform other technical tasks related to non-sterile compounding are determined at the discretion of the non-sterile compounding supervisor. The non-sterile compounding supervisor should assign only those tasks permitted by provincial/territorial legislation and for which the non-regulated pharmacy personnel has the appropriate training¹⁵. Non-regulated pharmacy personnel must be supervised by a pharmacist or pharmacy technician according to established supervision protocols and appropriate quality measures.

5.2 Training and skills assessment

5.2.1 Training of compounding personnel

All personnel involved in compounding must possess expertise commensurate with their responsibilities. Therefore, before they undertake non-sterile compounding, they must have received the proper orientation, training and a skills assessment concerning their work and the type of compounding to be done.

A skills assessment program, which considers the type and complexity of operations performed, must be established for all personnel involved in non-sterile compounding. Compliance with operating procedures and application of non-sterile compounding techniques must be evaluated regularly and must be included in the skills assessment program for compounding personnel. The results of these evaluations and any corrective action taken should be noted in the employee's file.

The following table of knowledge, skills and abilities is intended to assist in ensuring that personnel have the required competencies. This table should be used as appropriate, in accordance with regulations and policies in the particular pharmacy and jurisdiction.

¹³ National Association of Pharmacy Regulatory Authorities (NAPRA). *Model standards of practice for Canadian pharmacists*. Ottawa, ON: NAPRA; 2009. Available from: <http://napra.ca/pharmacists/model-standards-practice-canadian-pharmacists>

¹⁴ The relevant provincial/territorial pharmacy regulatory authority should be consulted for the training or supervision requirements defined in each jurisdiction.

¹⁵ The relevant provincial/territorial pharmacy regulatory authority should be consulted for regulatory and/or supervision requirements defined in each jurisdiction.



Table 1

#	ELEMENTS TO COVER IN TRAINING OF COMPOUNDING PERSONNEL	PH	PT	NR
1.	FOR THE COMPOUNDING OF NON-STERILE PREPARATIONS	PH	PT	NR
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 non-sterile preparations, especially those related to hand hygiene, personal protective equipment, airflow principle, facilities, 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 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 non-sterile compounding tasks meticulously, precisely and competently.	X	X	X
1.7	Know the operation and correct use of equipment, materials and automated instruments available for the non-sterile preparations to be compounded. Know how to calibrate the equipment and instruments used.	X	X	X
1.8	Be able to recognize errors in the compounding technique of compounding personnel.	X	X	
1.9	Have a good command of the pharmaceutical calculations required to compound non-sterile preparations.	X	X	X
1.10	Understand the importance of and apply accurate measurements.	X	X	X
1.11	Apply cleaning measures for non-sterile preparation compounding rooms, facilities and materials.	X	X	X
1.12	Know the data to be monitored in controlled rooms (temperature, pressure) and document the data in the appropriate logs. Know and apply the corrective measures to be applied when irregularities are identified.	X	X	X
1.13	Know how the secondary ventilation system (heating, ventilation and air conditioning system) operates. Know, apply or enforce appropriate corrective measures when an irregularity is identified.	X	X	X
1.14	Know and apply quality assurance measures for the various compounded non-sterile preparations.	X	X	
1.15	Know and follow the verification process.	X	X	X
1.16	Know and use the incident/accident documentation logs.	X	X	X
1.17	Know drug delivery systems.	X	X	X
1.18	Perform a risk assessment to determine level of risk.	X	X	
1.19	Determine beyond-use date.	X	X	
1.20	Develop Master Formula.	X	X	
2.	FOR THE COMPOUNDING OF HAZARDOUS NON-STERILE PREPARATIONS	PH	PT	NR
2.1	Have the competency required to compound non-sterile preparations.	X	X	X
2.2	Identify hazardous products in the composition of non-sterile preparations.	X	X	X
2.3	Know and apply deactivation and decontamination measures.	X	X	X
2.4	Know and use the protection measures necessary to avoid exposure to hazardous products.	X	X	X



2.5	Know and use personal protective equipment specifically for handling hazardous products and preparations.	X	X	X
2.6	Safely handle (i.e., receive, unpack, store and deliver) hazardous products.	X	X	
2.7	Know and use the emergency measures to be applied in the case of accidental exposure, accidents or spills.	X	X	X
2.8	Know how to safely destroy hazardous products and the materials used in their preparation.	X	X	
PH = pharmacist; PT = pharmacy technician, NR = non-regulated personnel.				

5.2.1.1 Skills assessment checklist for compounding process

Below is an example of a checklist that personnel could use individually or with each other to assess their compounding skills.

To avoid errors and maximize the therapeutic effect for the patient, compounding personnel should follow each compounding step and sign off at appropriate intervals.

Checklist 1

Compounding steps		Compliant (✓)	Non-compliant (✓)
1.	Consider whether the compounded preparation prescribed is appropriate and safe for the patient, based on the therapeutic intention (pharmacist).		
2.	Determine whether a valid formula exists; if not, develop a Master Formula, in consultation with experts and/or reliable resources. Ensure that the Master Formula includes instructions for special handling considerations.		
3.	Calculate and verify the quantities of each ingredient required on the compounding record (pharmacist/pharmacist or pharmacist/pharmacy technician).		
4.	Ensure that personnel responsible for compounding are wearing the appropriate personal protective equipment (cap, mask, gloves) and a clean laboratory coat or disposable gown.		
5.	For preparations that contain hazardous products, ensure that personnel wear the appropriate personal protective equipment: cap, safety goggles, two pairs of gloves, an N95 mask and face protection, a gown and shoe covers, depending on the substance used.		
6.	Ensure that only one preparation is being compounded at a time.		
7.	Gather the ingredients and necessary equipment. Ensure that the equipment is ready for use (clean and in good repair).		
8.	Measure each ingredient using appropriate equipment in accordance with the compounding record.		
9.	Use an independent check to confirm each ingredient and its quantity with the compounding record, before the preparation is compounded ¹⁶ .		
10.	Ensure that compounding of the preparation is in line with the Master Formulation Record and the prescription, as well as with good practice and pharmacy science (compounding pharmacist/pharmacy technician).		
11.	Verify that the labelling complies with requirements of the provincial/territorial pharmacy regulatory authority:		
	a. All active ingredients and the concentration of each ingredient are identified on the label.		

¹⁶ Institute for Safe Medication Practices Canada (ISMP Canada). Death due to pharmacy compounding error reinforces need for safety focus. *ISMP Canada Safety Bulletin*. 2017; 17(5): 1-5. Available from: <https://www.ismp-canada.org/download/safetyBulletins/2017/ISMPCSB2017-05-Tryptophan.pdf>



	b. The beyond-use date is marked on the label.		
	c. The storage information has been added.		
12.	Approve, through an independent check, the appearance of the final preparation (clarity, odour, colour, consistency, pH, etc.) and sign the compounding record.		
13.	Ensure that the area and equipment are cleaned immediately after use, according to manufacturer's directions or standards, and dried.		
14.	Ensure that the products, ingredients and equipment are put away immediately after use for proper storage.		

5.2.2 Knowledge required for cleaning personnel

Table 2

#	ELEMENTS TO COVER IN TRAINING OF CLEANING PERSONNEL	PH/PT	NR	CP
1.	FOR CLEANING AND DISINFECTING THE GENERAL AREA FOR COMPOUNDING OF NON-STERILE PREPARATIONS			
1.1	Know all policies and procedures related to cleaning and decontaminating the equipment, furniture and facilities, notably those related to hygiene, personal protective equipment, and cleaning and disinfecting tasks.	X	X	X
1.2	Know and use personal protective equipment specifically for handling hazardous products.	X	X	X
1.3	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; NR = non-regulated pharmacy personnel; CP = cleaning personnel.				

5.3 Policies and procedures^{17, 18}

- Established policies and procedures provide detailed descriptions of all activities, including cleaning; regarding the pharmacy's compounding of non-sterile preparations (*see* section 5.3.1 for a list of potential policies and procedures). The procedure template presented in section 5.3.2 can be used as a model for developing various procedures. The non-sterile supervisor must ensure application of and compliance with these policies and procedures.
- Established policies and procedures are promptly updated whenever there is a change in practice or in standards. At a minimum, policies and procedures are reviewed every 3 years to ensure currency. The review should be documented.
- For handling or compounding hazardous drugs or materials, additional policies and procedures must be developed; including the safe receipt, storage, handling, compounding, labelling, transport and disposal of hazardous drugs and materials (*see* Section 9).
- When compounding is undertaken by another pharmacy, where permitted by provincial/territorial legislation, the dispensing facility should include in its general procedures manual information about policies and procedures for acquiring compounded non-sterile preparations for patients (originating pharmacy, entry in the file, delivery, etc.).

¹⁷ United States Pharmacopeial Convention (USP). General chapter <795>: pharmaceutical compounding — nonsterile preparations. In: *USP compounding compendium*. Rockville, MD: USP; 2016. pp. 31, 37.

¹⁸ Pharmacy Compounding Accreditation Board (PCAB). Standard 1.40: standard operating procedures compliance indicators. In: *PCAB accreditation manual*. Washington, DC: PCAB; 2011. p. 7.



5.3.1 Examples of policies and procedures

Table 3

		NON-STERILE PREPARATIONS	
Policy #	Topic		✓
A		PERSONNEL AND FACILITIES	
1	Obligations of personnel		
1.1	Attire and dress code (e.g., personal clothing, jewelry, hairstyles)		
1.2	Health conditions (reasons for temporary withdrawal from compounding activities)		
1.3	Expected behaviour in compounding 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		
2.4	Additional training in all aspects of handling and compounding complex or hazardous products		
3	Delegation and appropriate supervision of activities		
3.1	Delegation of technical activities to persons other than pharmacists or pharmacy technicians		
4	Facilities and equipment		
4.1	Access to controlled area or room		
4.2	Necessary facilities and equipment		
4.3	Maintenance of facilities and equipment (e.g., certification of rooms and instruments, calibration, maintenance of pre-filters and high-efficiency particulate air filters, verification of pressure)		
4.4	Cleaning activities for facilities and equipment		
B		COMPOUNDED NON-STERILE PREPARATIONS	
1	Determining beyond-use dates of products used in a preparation		
2	Determining beyond-use dates of final preparations		
3	Hand hygiene		
4	Personal protective equipment in compounding areas and for compounding		
5	Bringing equipment and products into the room		
6	Deactivation, decontamination and cleaning of the C-PEC		
7	Receipt, unpacking and storage of hazardous products		
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	Storage of products used and final preparations		
12	Transport and delivery of final preparations (to the patient, to patient care units or to the dispensing pharmacist)		
13	Recording of preparations in the patient file		
14	Hazardous waste management (e.g., at the pharmacy, returns from patients or patient care units, instructions to patients)		



	15	Action to be taken in case of accidental exposure of personnel to hazardous products (eyewash station, log)	
	16	Spills and spill management	
	17	Recall of products, ingredients or compounded non-sterile preparations	
C		QUALITY ASSURANCE PROGRAM	
	1	Verification and maintenance of equipment, verification of appropriate storage of ingredients	
	2	Environmental control of facilities and primary engineering control (e.g., pressure verification, air and surface sampling plan)	
	3	Environmental monitoring of chemical contamination for hazardous products	
	4	Quality assurance of compounded sterile preparations (e.g., existence of a protocol, compliance with prescription, documentation in logs)	
C-PEC = containment primary engineering control.			

5.3.2 Template for developing a procedure

The following template can be used to develop procedures for activities such as hand hygiene, cleaning compounding areas and storing products, as listed in section 5.3.1, above.

Template 1

Pharmacy name: Or Hospital XYZ pharmacy department:	Procedure # _____ Revised: <input type="checkbox"/> Yes <input type="checkbox"/> No Approved by _____ Date _____ (dd/mm/yyyy) Effective date: _____ (dd/mm/yyyy)
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"/> Non-sterile compounding supervisor <input type="checkbox"/> Pharmacist <input type="checkbox"/> Pharmacy technician <input type="checkbox"/> Non-regulated personnel <input type="checkbox"/> Cleaning and disinfecting personnel <input type="checkbox"/> Other: _____	



Required facilities, equipment and material:

Include the following types of information here:

- Facilities and equipment required to apply the procedure, including personal protective equipment for compounding personnel.
- Materials (e.g., accessories, instruments) required to apply the procedure.
- Active pharmaceutical ingredients and other 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 decisions and 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 Partial **Amended version:** Yes No

Change made:



5.4 Facilities and equipment

Areas reserved for non-sterile compounding should be used only by personnel who are authorized to compound non-sterile preparations. This space should be designated for compounding, but may also be used for preparing or reconstituting marketed products. If a pharmacy or healthcare facility compounds any sterile preparations, the area of the pharmacy reserved for this purpose must be separate and distinct from the area of the pharmacy set aside for non-sterile compounding¹⁹.

5.4.1 Facilities for non-sterile compounding

5.4.1.1 General

All compounding must be performed in a separate space specifically designated for compounding of prescriptions. This space would provide for the orderly placement of equipment and materials to prevent errors²⁰. It should be designed and arranged to prevent cross-contamination between products, and should be located away from parts of the pharmacy where there is a considerable amount of traffic (aisles, entrance and exit doors, etc.), to avoid contamination of the compounded product with dust and dirt, as well as to avoid interrupting or distracting compounding personnel^{21,22}. L'Ordre des pharmaciens du Québec has produced a video about non-sterile compounding (<https://www.youtube.com/watch?v=TTtguuj83f8> – French only), which demonstrates, among other things, examples of designated compounding spaces.

Compounding areas must be large enough for compounding personnel to work comfortably and safely, with room to store equipment and products in an orderly manner, in clean and secure surroundings. All components, equipment, and containers must be stored off the floor, in a manner that prevents contamination and allows for inspection and cleaning of the compounding and storage area. To limit the accumulation of dust and particles, packaging and cardboard boxes from products used should not be allowed in the non-sterile compounding area.

The compounding area must be conducive to necessary cleaning, containing no areas that are difficult to clean. Special attention should be given to fixtures liable to collect dust (e.g., ceiling lamps, plumbing, window frames, wire) and horizontal surfaces serving no purpose; such fixtures and surfaces should be covered, sealed up, modified or removed from the area reserved for non-sterile compounding.

The areas used for non-sterile compounding shall be maintained in clean, orderly and sanitary conditions with appropriate and sanitary waste disposal, and shall be maintained in a good state of repair.

5.4.1.2 Lighting

The lighting fixtures should be located so as to provide a well-lit area facilitating the compounding process and allowing verification at all stages of compounding.

19 United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations [Environmental quality and control]. USP 39. Rockville, MD: USP; 2016.

20 United States Pharmacopeial Convention (USP). General chapter <795>: pharmaceutical compounding — nonsterile preparations. USP 39. Rockville, MD: USP; 2016. p. 33.

21 Ordre des pharmaciens du Québec (OPQ). Norme 2012.01 : préparations magistrales non stériles en pharmacie. Montréal, QC: OPQ; 2012. p. 35. Available from: www.opq.org

22 PIC/S guide to good practices for the preparation of medicinal products in healthcare establishments. Geneva, Switzerland: Pharmaceutical Inspection Convention, Pharmaceutical Inspection Co-operation Scheme; March 1, 2014. p. 13. Available from: www.picscheme.org



5.4.1.3 Heating, ventilation and air conditioning system

The heating, ventilation and air conditioning system must be controlled in such a way as to avoid decomposition and contamination of chemicals, to maintain the quality and efficacy of stored products and to ensure the safety and comfort of compounding personnel. Appropriate temperature and humidity monitoring should be performed, as required for certain ingredients and compounded dosage forms. Air vents should not be located directly over work areas, to avoid contamination of the products.

5.4.1.4 Water supply²³

A clean water supply, with hot and cold running water, must be available in or close to the compounding area or, for Level B and Level C requirements, in the compounding room.

There should be a sink with hot and cold running water, preferably made of stainless steel and having touchless controls, to supply potable water for washing hands and equipment. The plumbing system should be free of defects that could contribute to contamination of any compounded preparation. Purified water should be used for compounding non-sterile drug preparations when the formulations indicate inclusion of water. Purified water may also be used for rinsing equipment, instruments and accessories.

5.4.1.5 Work surfaces, furniture, walls and flooring

Work surfaces and furniture should be constructed of smooth, impervious and non-porous materials, preferably stainless steel. Any material used for work surfaces should be able to withstand repeated cleaning and disinfecting and be resistant to damage from cleaning and disinfecting products. Any breakage should be repaired and sealed at the earliest opportunity.

All furniture, as well as the floor and wall surfaces, must be designed and placed to facilitate cleaning and disinfecting.

5.4.1.6 Cleaning

Cleaning in the areas reserved for non-sterile compounding should be performed in a manner that maintains the cleanliness and hygiene needed to ensure the quality and integrity of the final preparations. A cleaning schedule appropriate to the level and type of non-sterile compounding should be established.

The worktop surface used for non-sterile compounding should be cleaned before and after each compounding session. The sink should be thoroughly cleaned with detergent before and after compounding instruments and accessories are washed or at least once a day and whenever it appears soiled. The overall area used for non-sterile compounding, including storage areas, should be kept clean.

Easy-to-clean waste containers of suitable size and made of materials resistant to damage from cleaning products should be available. The waste should be collected in plastic bags and removed with minimal agitation. The waste containers should be emptied and cleaned at a time when no compounding is occurring.

Equipment and products required to clean both the premises and the instruments used for non-sterile compounding should be available (e.g., hot and cold water, soap or detergent, disinfectant, disposable towels in a dispenser, a bucket, a mop and cloths). Cleaning accessories should be disposable, or should be washed and disinfected between uses, and should be stored separately to avoid contamination from the cleaning process or equipment.

²³ United States Pharmacopeial Convention (USP). General chapter <795>: pharmaceutical compounding — nonsterile preparations. USP 39. Rockville, MD: USP; 2016. p. 33.



5.4.2 Equipment for non-sterile compounding

The equipment, instruments and accessories chosen must be appropriate for the type of preparations to be compounded, and should be reserved for compounding activities.

Any surfaces of instruments and accessories that come into contact with preparations should not negatively affect the purity or quality of the preparation being compounded. These surfaces should be completely clean and should not be reactive, additive or sorptive (glass or stainless steel preferred).

5.4.2.1 Routine maintenance

To ensure precision and reliability, all equipment, instruments and accessories should be routinely inspected, checked to ensure proper performance and if applicable, calibrated at appropriate intervals as recommended by the manufacturer, or at least once a year if there are no manufacturer recommendations.

Every note documented on a maintenance form should indicate the person doing the maintenance (pharmacist, pharmacy technician, cleaning personnel).

The requirements of provincial/territorial pharmacy regulatory authorities should be followed for equipment such as balances/weights or refrigerator/freezers.

5.4.2.2 Cleaning equipment, instruments and accessories

All specialized equipment and instruments used for compounding must be cleaned regularly, as recommended by the manufacturer. Cleaning work recommended by the manufacturer must be noted in the maintenance log.

Equipment, instruments and accessories used for several different preparations must be completely and thoroughly cleaned after each compounding session to remove all traces of the previous product and any remaining water and solvent, thus preventing any cross-contamination between preparations. It is not sufficient to use only isopropyl alcohol 70% as the cleaning agent. All equipment, instruments and accessories should be rinsed with purified water.

After each use and cleaning, the equipment, instruments and accessories used for compounding should be neatly stored to protect them from contamination. Immediately before initiation of compounding operations, the equipment, instruments and accessories should be inspected by the compounder to determine suitability for use.

5.4.2.3 General maintenance log

A maintenance log must be kept to record the dates of cleaning and/or calibration of specialized equipment and instruments; these entries should include the name of the person carrying out the cleaning or calibration. This information may also be documented in any log used to record information about general pharmacy maintenance (e.g., dates and times when the temperatures of refrigerators and freezers used to store drugs are checked, dates of cleaning of premises and equipment).



6. PRODUCT AND PREPARATION REQUIREMENTS

6.1 Beyond-use date and dating methods

The BUD is the date after which a non-sterile compounded preparation should no longer be used. Non-sterile preparations are compounded for immediate use or for short-term storage; therefore, their BUDs are assigned on the basis of criteria different from those applied in assigning an expiry date to manufactured drug products.

Extensive experience in non-sterile compounding and broad scientific knowledge are required to determine a BUD and to interpret stability data in relation to the actual compounded formulations. BUDs should be assigned conservatively. When assigning a BUD, compounders should consult the literature and documentation available on stability in general and on the specific stability of the active pharmaceutical ingredient (API). When a manufactured drug is used as the API, information provided by the manufacturer may be used as a reference. The manufacturer's expiry date for the drug should not be used as the BUD for the final preparation. As recommended in Table 1, below, the BUD for non-aqueous formulations is not later than the time remaining until the earliest expiry date of any ingredient or 6 months, whichever is earlier.

The nature of the ingredient to be used, the compounding method, degradation mechanisms, compatibility, dosage form, potential for microbial proliferation in the preparation, the container in which the preparation is packaged, the expected storage conditions, and the intended use and duration of therapy should all be considered, and the BUD assigned conservatively.

The product should be observed at all stages of compounding for signs of instability and/or degradation.

6.1.1 General guidelines for assigning beyond-use dates

In the absence of any stability data for a drug or a specific non-sterile compounded preparation, Table 4 presents maximum BUDs recommended for non-sterile compounded preparations that are packaged in air-tight, light-resistant containers and stored at controlled room temperature, unless otherwise indicated²⁴. Drugs and chemicals known to be labile to decomposition will require shorter BUDs.

Table 4

Beyond-use date (BUD) by type of formulation* ²⁵
Non-aqueous formulations – The BUD is not later than the time remaining until the earliest expiry date of any API or 6 months, whichever is earlier.
Water-containing oral formulations – The BUD is not later than 14 days with storage at controlled cold temperatures.
Water-containing topical/dermal, mucosal liquid and semi-solid formulations – The BUD is not later than 30 days.

* These maximum BUDs are recommended for non-sterile compounded drug preparations in the absence of stability information that is applicable to a specific drug or preparation. The BUD shall not be later than the expiration date on the container or any component.

Where possible, susceptible preparations should contain suitable antimicrobial agents to protect against bacteria, yeast and mould contamination that may be introduced during or after the compounding process. When antimicrobial agents are contraindicated, susceptible compounded products should be stored at a controlled cold temperature, and patients educated about proper storage. Antimicrobial preservatives should not be used in place of good compounding practices.

24 United States Pharmacopeial Convention (USP). General chapter <659>: packaging and storage requirements. In: *USP compounding compendium*. Rockville, MD: USP; 2016.

25 United States Pharmacopeial Convention (USP). General chapter <795>: pharmaceutical compounding — nonsterile preparations. In: *USP compounding compendium*. Rockville, MD: USP; 2016. p. 35.

6.2 Master Formulation Record

The Master Formulation Record for a non-sterile preparation includes all necessary information to compound the preparation.

To ensure preparation quality and safety, the Master Formulation Record should be current; changes made in the Master Formulation Record should include supporting rationale and references, and compounding personnel must be informed of the change. The development of a new Master Formulation Record is based on scientific data, and includes appropriate references.

Master Formulation Records should be kept together, in hard copy or electronic format, and be readily available.

The Master Formulation Record should include the following information as required to compound the preparation^{26,27}:

- official or assigned name, strength and dosage form of the preparation
- expected yield
- calculations needed to determine and verify quantities of ingredients and doses of APIs for quantity produced
- description of all ingredients, along with their quantities, sources and lot numbers (if applicable)
- compatibility and stability data, including references when available
- references used to develop the formula and the consultation date, as appropriate
- equipment needed to compound the preparation (and any special cleaning instructions)
- special precautions to be observed by compounding personnel, including personal protective equipment (PPE)
- source or origin of the formula
- mixing instructions, which may include:
 - order of mixing
 - mixing temperatures or other environmental controls
 - duration of mixing
 - other factors pertinent to replication of the preparation as compounded
- sample labelling information, which should contain, in addition to legally required information:
 - generic name and quantity or concentration of each active ingredient
 - assigned BUD
 - storage conditions
 - prescription or control number, whichever is applicable
- type of container used in dispensing
- packaging and storage requirements
- description of final preparation
- quality control procedures and expected results

26 United States Pharmacopeial Convention (USP). General chapter <795>: pharmaceutical compounding — nonsterile preparations. In: *USP compounding compendium*. Rockville, MD: USP; 2016. p. 35.

27 Ordre des pharmaciens du Québec (OPQ). Norme 2012.01 : préparations magistrales non stériles en pharmacie. Montréal, QC: OPQ; 2012. p. 35. Available from: www.opq.org



6.2.1 Template for a Master Formulation Record

Template 2

TO BE COMPLETED FOR EACH PREPARATION (AS APPLICABLE)

Name of compounded product: Concentration: Pharmaceutical form: Route of administration:	Protocol number and version (e.g., 001-01) Effective date: _____ (dd/mm/yyyy) Developed by: _____ Verified by: _____		
FORMULA			
Ingredients	Quantities	Physical description	Other information (e.g., DIN, lot number, manufacturer, expiry date, expected yield)
Additional information about the ingredients: Include any additional pertinent information about the ingredients required for compounding. Indicate any specific precautions that were taken when handling the ingredients.			
Notes on calculations and measurements: Indicate any characteristics of the calculations, measurements or ingredient preparation that were done before the specific procedure was carried out. Ensure that the unit of measure in this record is the same as the unit of measure on the measuring device. Indicate any requirement for verification by the pharmacist. Examples: <ul style="list-style-type: none"> - Quality control of instruments to be carried out and documented before measurements are taken - Accuracy of measurement instruments - Verification and documentation of ingredients, batch numbers and beyond-use dates - Type of report required on the compounding form 			
Required equipment, instruments and materials Indicate all materials and equipment that were required to compound the non-sterile preparations.			
Compounding method Describe all steps of the compounding process.			



Quality controls

Specify the procedure for determining the lot number of the final compounded preparation.

Specify all quality control procedures that were carried out during compounding and documented by the pharmacy technician and/or pharmacist.

Specify all quality controls that were carried out by the pharmacist on the final compounded non-sterile preparation. Indicate the expected specifications.

Example

Quality control	Expected specification
Appearance of the preparation	Clear, colourless solution with no visible particles

Packaging

Describe the type of packaging in which the final compounded non-sterile preparation shall be presented to the patient.

Stability and storage

Specify the preservation requirements of the compounded non-sterile preparation.

Specify the beyond-use date for the compounded non-sterile preparation

Indicate the references used to determine the beyond-use date.

Labelling

Indicate mandatory information that must be on the label

A) When kept at the pharmacy or sent to another pharmacy

Name of preparation:

Date when preparation was made:

Lot:

Quantity prepared:

Beyond-use date:

B) When dispensed to a patient

In addition to the legally mandated information, add:

- beyond-use date

- precautions and other patient information leaflet

Sample label

Patient label

Training

Indicate any specialized training that personnel must undergo before the specific compounding procedure is implemented.



References consulted:	
Indicate the source of the specific compounding procedure. Indicate any documentation supporting the stability of the final compounded non-sterile preparation.	
Preparation data sheet history no.:	
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

6.3 Ingredients used for non-sterile compounding – quality and storage

Reasonable measures should be taken to determine the purity and safety of the ingredients used for compounding, by means of analyzing the batch or verifying the manufacturer's reputation and the supplier's reliability.

All ingredients (powders, liquids, etc.) that require special precautions when used or stored should be identified. Ingredients and raw materials should be stored and kept safely under conditions that will preserve their quality and purity, as directed by the manufacturer or according to pharmacopeia monographs.

6.3.1 Selection of ingredients

In choosing active or inactive ingredients to be used for compounding, compounders should take the following information into account:

- physicochemical properties of the ingredients
- efficacy of the ingredients
- stability of the ingredients
- compatibility of the ingredients
- toxicity of the ingredients
- information about the patient and disease state
- prescriber's therapeutic objective
- possible interactions
- planned treatment duration
- route of administration
- frequency of administration

Purified water²⁸ (e.g., distilled water, deionized water) or water of equivalent or superior quality (e.g., sterile irrigation water) must be used for non-sterile compounding whenever the formula specifies water as an ingredient. A dispenser of bottled water, programmed or unprogrammed and independent of the pharmacy's plumbing, cannot currently be recommended for non-sterile compounding because no data are available on whether the quality of water supplied by these dispensers is maintained during use. Tap water does not meet this standard and must not be used for compounding or reconstituting products.

28 United States Pharmacopeial Convention (USP). General chapter <1231>: water for pharmaceutical purposes. In: *USP compounding compendium*. Rockville, MD: USP; 2016. pp. 456-462.



6.3.2 Sources of ingredients

Ingredients used for compounding must be obtained from recognized and reliable sources. Non-sterile preparations should be compounded using approved ingredients that have been assigned a Drug Identification Number (DIN), for products approved for use in Canada or APIs and other ingredients that meet the requirements of monographs in a current version of a recognized pharmacopoeia, that is, the United States Pharmacopoeia, European Pharmacopoeia, French Pharmacopoeia, International Pharmacopoeia, British Pharmacopoeia, Canadian Formulary, National Formulary of the United States or Schedule B of the *Food and Drugs Act*, in keeping with the recommendations of Health Canada's Policy 0051²⁹.

When ingredients of compendial quality cannot be obtained, high-quality ingredients, such as those mentioned in the Food Chemicals Codex, those that are chemically pure (analytical reagent grade) or those certified by the American Chemical Society (ACS), may be used³⁰. However, such components should be used with caution, because the standards for analytical reagents and ACS-grade materials do not consider whether any impurity that is present will raise concern about human or animal safety.

6.3.3 Quality of ingredients

High-quality ingredients (in terms of identity and purity) should be chosen for compounded non-sterile preparations, and supporting documents obtained, including certificates of analysis for the ingredients. The sources of all ingredients and associated information, including lot numbers, expiry dates, and date of receipt in the pharmacy, must be traceable.

If the product is not sourced from a recognized supplier, a qualified laboratory should analyze the product and confirm its identity, purity and quality, according to the requirements of a recognized pharmacopoeia. The analysis results and certificates should be kept in an ingredients log. Federal regulations currently prohibit compounding pharmacists in pharmacies from shipping controlled substances for such analysis.

Drugs approved by Health Canada (i.e., those with a DIN) may be used as active ingredients. When using one of these products, all ingredients (active and inactive) in the approved drug must be considered, with respect to chemical interactions or patient allergies and sensitivities. Ingredients that have been recalled or withdrawn from the market for safety reasons must not be used for compounding. Health Canada publishes on its website a list of drugs that have been recalled from the market (<http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/index-eng.php?cat=3>).

When ingredients are derived from ruminant animals (e.g., bovine, caprine, ovine), the supplier should provide written assurance that the ingredient is in compliance with all federal regulations governing processing, use and importation of these materials.

For components with an expiry date on the container received from the manufacturer or distributor, the material may be used for compounding before that date, provided the material is stored in its original container under conditions suitable to avoid decomposition of the chemicals; this means minimal exposure of the remaining material each time material is withdrawn from the container and any withdrawals from the container are performed by personnel trained in the proper handling of the material. If the component has been transferred to another container, that container should be identified with the component name, original supplier, lot or control number, transfer date and expiry date, and the container's integrity shall be at least equivalent to that of the original container. For ingredients without an expiry date assigned by the manufacturer, the container shall be labelled with the date of receipt and a conservative expiry date, not to exceed 3 years after receipt, depending on the nature of the ingredient, the container and storage conditions³¹.

All ingredients should be inspected before use to identify any signs of deterioration.

29 Health Canada, Health Products and Food Branch Inspectorate. *Policy on manufacturing and compounding drug products in Canada (POL-0051)*. Ottawa, ON: Health Canada; 2009. Available from: http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/docs/pol_0051-eng.php

30 United States Pharmacopoeial Convention (USP). General chapter <795>: pharmaceutical compounding — nonsterile preparations. USP 39. Rockville, MD: USP; 2016. p. 34.

31 United States Pharmacopoeial Convention (USP). General chapter <795>: pharmaceutical compounding — nonsterile preparations. USP 39. Rockville, MD: USP; 2016. p. 34.



6.3.4 Safety data sheets

The safety data sheets (formerly known as material safety data sheets) published by suppliers under provisions of the *Hazardous Products Act* are documents that provide information about the risks and preventive measures to be applied in the use of products and their storage conditions. Safety data sheets are available from the supplier or through the Canadian Centre for Occupational Health and Safety³². These sheets should be kept together and made available to all personnel involved in non-sterile compounding. All employees should know where they are kept, and this location must be readily accessible.

Safety data sheets are updated by suppliers every 3 years. It is therefore important that the dates of the available sheets be verified to ensure that the pharmacy is always using each supplier's latest version.

6.3.5 Storage

All ingredients (powder, liquids, etc.) that require special precautions when used or stored should be identified. Ingredients and raw materials should be stored and kept safely under conditions that will preserve their quality and purity as directed by the manufacturer or according to pharmacopeia monographs.

6.4 Compounding record

The pharmacy must keep a compounding record (paper-based or computerized) for each individual prescription, as well as for non-sterile preparations made in batches. These records should be filed and retained for future reference as required by the provincial/territorial pharmacy regulatory authority.

In cases where there is a marketed drug available, the rationale for compounding should be documented in the patient's file with the appropriate justification (e.g., allergy, drug temporarily in short supply, difficult to swallow).

In cases where the preparation was made by another pharmacy, (as permitted by provincial/territorial legislation), the origin of the compounded non-sterile preparation dispensed to the patient should be recorded in the patient file. Any pharmacy (in the healthcare facility or the community) should be able to track information related to preparations that it dispenses, even if those preparations were made by another pharmacy.

The compounding record for non-sterile compounded preparations should contain the following information³³:

- official or assigned name, strength and dosage of the preparation
- reference to Master Formulation Record for the preparation
- names and quantities of all ingredients
- sources, lot numbers and expiry dates of ingredients
- total quantity compounded
- name of the person who prepared the preparation, name of the person who performed the quality control procedures and name of the person who approved the preparation
- date of preparation
- assigned preparation batch number or prescription number
- assigned BUD
- results of quality control procedures as appropriate (e.g., weight range of filled capsules, pH of aqueous liquids)
- documentation of any quality control issues and any adverse reactions or preparation problems reported by the patient or caregiver

³² Safety data sheets are available in a database maintained by the Canadian Centre for Occupational Health and Safety, and are available from: <http://ccinfoweb.ccohs.ca/msds/search.html>

³³ United States Pharmacopeial Convention (USP). General chapter <795>: pharmaceutical compounding — nonsterile preparations. USP 39. Rockville, MD: USP; 2016. p. 36.



6.5 Conduct of personnel in compounding areas

Personnel must behave in a professional manner, following all pertinent policies and procedures.

For reasons of hygiene and safety and to avoid possible contamination during non-sterile compounding, personnel must follow the procedures on the Master Formulation Record. In addition, the following procedures should be followed:

- Perform appropriate hand hygiene, before and after compounding, with regular soap or antimicrobial soap³⁴ and low particle-release paper for drying. Slip on powder-free gloves after proper hand hygiene. Powder-free gloves should be appropriate for the type of compounding to be done. Given the possibility that patients or personnel may be allergic to latex, nitrile or neoprene gloves are preferred.
- Wear a clean laboratory coat that is reserved for compounding or a disposable gown; the latter option is highly recommended. If a clean laboratory coat is worn, it should be reserved for making these preparations and not worn outside the compounding area. When employees leave the compounding area, they should leave their laboratory coats behind. Used laboratory coats may be put on again when the employees return to the compounding area, provided the coats are **clean and unsoiled**. Laboratory coats should be changed as soon as they become soiled or according to established protocols. Disposable gowns should be changed every day or as soon as they become soiled.
- Avoid other sources that might contaminate the preparation, such as loose hair, long or false nails, jewellery on hands and wrists, chewing gum, consuming food or drink or using tobacco in the compounding area.
- Notify the compounding supervisor if the compounder has an active respiratory tract infection, an eye or skin infection, a hand lesion or other ailment, determine the person's fitness to carry out compounding activities or to identify specific protective measures that should be taken to avoid contamination of the product³⁵.
- If indicated on the Master Formulation Record, wear a cap and mask, eye protection and, a beard guard.
- Take any other reasonable measures to prevent cross-contamination and to ensure protection from chemical exposure.

6.6 Verification of final compounded non-sterile preparations

The following verifications should be performed for each compounding process:

- Ensure that all compounded non-sterile preparations comply with compounding protocols.
- Verify the formula and calculated amounts of each ingredient.
- Verify the identity of the ingredients selected before preparation.³⁶
- Verify the volume, quantity or weight of the ingredients prior to compounding, or through a retrievable format such as a photograph or video.³⁷
- Verify the ingredient information documented on the compounding record.
- Review the Master Formulation Record and compounding record to ensure that no errors have occurred in the compounding process and that the preparation is suitable for use.
- Verify all information on the final label, including the BUD, and ensure that this information is documented on the compounding record.

34 Public Health Agency of Canada (PHAC). *Infectious disease prevention and control: hand hygiene practices in healthcare settings*. Ottawa, ON: PHAC; 2012. p. 33 (part C, section 2.2). Available from: http://publications.gc.ca/collections/collection_2012/aspc-phac/HP40-74-2012-eng.pdf

35 *PIC/S guide to good practices for the preparation of medicinal products in healthcare establishments*. Geneva, Switzerland: Pharmaceutical Inspection Convention, Pharmaceutical Inspection Co-operation Scheme; March 1, 2014. p. 12. Available from: www.picscheme.org

36 Institute for Safe Medication Practices Canada (ISMP Canada). Death due to pharmacy compounding error reinforces need for safety focus. *ISMP Canada Safety Bulletin*. 2017; 17(5): 1-5. Available from: <https://www.ismp-canada.org/download/safetyBulletins/2017/ISMPCSB2017-05-Tryptophan.pdf>

37 Institute for Safe Medication Practices Canada (ISMP Canada). Death due to pharmacy compounding error reinforces need for safety focus. *ISMP Canada Safety Bulletin*. 2017; 17(5): 1-5. Available from: <https://www.ismp-canada.org/download/safetyBulletins/2017/ISMPCSB2017-05-Tryptophan.pdf>



- Regularly verify the quality of the compounding technique.
- Verify the integrity of the container and ensure that the container is appropriate for the physical and chemical properties of the compounded preparation (to avoid a container–drug interaction)³⁸.
- Approve the final prepared product using factors such as weight, adequacy of mixing, clarity, odour, colour, consistency, pH and analytical testing as appropriate, and sign the compounding record³⁹.
- Verify that products requiring refrigeration are stored appropriately pending delivery to the patient.

6.7 Labelling and packaging

6.7.1 Labelling policy

A policy for labelling and packaging of compounded non-sterile preparations must be established and followed. The labels for compounded non-sterile preparations should meet the requirements of the applicable provincial/territorial pharmacy regulatory authority.

All active ingredients and the concentration of each active ingredient should be identified on the label. The label should include the BUD, as well as storage and handling information.

Non-sterile preparations that have been compounded at the request of another pharmacy (where permitted by provincial/territorial legislation) should be similarly labelled. In these cases, the dispensing pharmacy should keep all of the records from the compounding pharmacy (e.g., ingredients, quantity, lot number and BUD) readily accessible.

6.7.2 Label and supplementary label

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 and appropriate use of the compounded non-sterile preparation by the patient. If this information cannot be included on an auxiliary label, a supplementary label should be prepared. The supplementary label is considered to be an integral part of the label.

Together, the label and supplementary label must provide all information required for proper use of the compounded preparation by the patient or for safe administration by a third party, including the following elements:

- pharmacy identification (name, address and telephone number of the compounder’s or dispenser’s pharmacy, as per regulatory requirements)
- drug identification (active ingredients, concentration, form, route of administration, amount prepared)
- special precautions (e.g., if product is an irritant)
- BUD
- all information that is required by provincial/territorial legislation and regulations regarding the labelling of medications but 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”)
- any special precautions for disposal or destruction of the preparation

³⁸ United States Pharmacopeial Convention (USP). General chapter <795>: pharmaceutical compounding — nonsterile preparations. USP 39. Rockville, MD: USP; 2016. p. 36.

³⁹ Institute for Safe Medication Practices Canada (ISMP Canada). Death due to pharmacy compounding error reinforces need for safety focus. *ISMP Canada Safety Bulletin*. 2017; 17(5): 1-5. Available from: <https://www.ismp-canada.org/download/safetyBulletins/2017/ISMPCSB2017-05-Tryptophan.pdf>



6.7.3 Packaging process and procedure

Appropriate packaging should be used for all preparations to be delivered to patients or other healthcare providers. To maintain the integrity of compounded non-sterile preparations and the safety of patients and delivery personnel, a packaging procedure should be developed and implemented for final compounded non-sterile preparations.

The packaging should

- maintain each preparation's stability, integrity and storage conditions;
- indicate storage requirements (e.g., temperature, protection from light);
- indicate additional precautions (e.g., if product is an irritant);
- indicate transport precautions (e.g., related to temperature, fragility, safety) and instructions (name and address of patient) on the outside packaging of each item.

6.8 Storage^{40, 41}

A storage procedure must be established that is consistent with any requirements of the applicable pharmacy regulatory authority, as applicable.

Active and inactive ingredients and finished products must be stored according to the manufacturers' recommendations or the relevant monographs published in recognized pharmacopoeias (with regard to temperature, light, humidity, etc.) and in a place that is inaccessible to the public and unauthorized personnel.

Active and inactive ingredients and finished products should be stored upon receipt and handled in a manner that prevents cross-contamination and incompatibilities.

To ensure the quality and stability of raw materials and final preparations, storage conditions in stockrooms should be controlled. Product storage conditions should be stringently respected, regardless of the storage location (warehouse, quarantine area, pharmacy, delivery vehicle, unloading dock for deliveries, carrier, etc.). The temperature of the premises (pharmacy, warehouse, etc.) should be controlled and should remain within the limits indicated in section 6.8.1, regardless of the season. Information on monitoring of room and refrigerator, as well as other temperatures and controls related to implementation of the storage procedure, should be recorded in the general maintenance log⁴².

6.8.1 Temperatures for different types of storage⁴³

Table 5

Storage type	Temperature range
Freezer	-25 °C to -10 °C*
Refrigerator	2 °C to 8 °C* (cold: not exceeding 8 °C)
Cool	8 °C to 15 °C* (alternatively may be refrigerated, unless otherwise specified)
Controlled room temperature	20 °C to 25 °C

Each finished product must be stored according to requirements outlined in the Master Formulation Record.

40 United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. In: *USP compounding compendium*. Rockville, MD: USP; 2016. pp. 39-84.

41 United States Pharmacopeial Convention (USP). General chapter <1079>: good storage and distribution. In: *USP compounding compendium*. Rockville, MD: USP; 2016. pp. 351-360.

42 United States Pharmacopeial Convention (USP). General chapter <1079>: good storage and distribution. In: *USP compounding compendium*. Rockville, MD: USP; 2016. pp. 351-360.

43 United States Pharmacopeial Convention (USP). General chapter <659>: packing and storage requirements. In: *USP compounding compendium*. Rockville, MD: USP; 2016. pp. 245-249.



Products that have been stored should be inspected before use to detect any signs of deterioration. A procedure for verifying the BUDs of stored compounded non-sterile preparations and the expiry dates of commercial products should be developed and implemented, to ensure that products and compounded non-sterile preparations that have become unusable are quickly discarded.

6.9 Transport and delivery of compounded non-sterile preparations

Policies and procedures for transport and delivery must be developed that meet provincial/territorial regulatory requirements and address any special precautions regarding the transport of compounded non-sterile preparations^{44,45} and their delivery to patient care areas, pharmacists, pharmacies, healthcare professionals and patients. The pharmacy's policy for return and disposal of expired, partially used or unused products from the patient's home or the patient care unit in a healthcare facility should also cover non-sterile compounded products.

Preparations to be delivered should be packed and labelled in a manner that ensures the safety of patients and delivery persons. Transport conditions (related to temperature, fragility and safety) and the information required for delivery to the patient or other recipient (name, address, etc.) should always be indicated on the outside of the packaging.

As a rule, extreme temperatures (excessive heat or freezing) should be avoided, or procedures developed to check the min/max thermometer during transport. The steps to be followed in the event of non-maintenance of target storage temperature during transport should be indicated in the procedure.

The transport and delivery procedures should include any precautions to be taken by the delivery person or private carrier, especially during delivery (e.g., personal delivery of the compounded preparation, rather than delegation to another person) and during return of medications. These steps should be verified to ensure maintenance of stability throughout transport and storage.

When compounding is undertaken by another pharmacy, as permitted by provincial/territorial legislation, the compounding personnel should ensure that the preparation is transported to the dispensing pharmacy under conditions that maintain stability of the preparation. The receiving pharmacy should then ensure that transport conditions are maintained until the product is delivered to the patient.

6.10 Product recalls

For cases in which information obtained by a community or hospital pharmacy as a result of internal control, a complaint or a product recall shows that the grade or quality of a product or preparation does not meet requirements, a recall will be required. The compounding pharmacy should have in place a recall procedure to

- identify patients or pharmacies that have received the compounded non-sterile preparation;
- notify patients or their caregivers of the recall;
- perform the necessary follow-up if the preparation has been administered.

The pharmacy's overall recall procedure should include procedures for recall of compounded non-sterile preparations. The information about individual units or batches of compounded non-sterile preparations recorded in the patient file and the compounding record should be sufficient to allow users to track recipients of compounded non-sterile preparations.

The causes of the problem leading to the recall should be reviewed, and corrective and preventive measures identified and implemented.

⁴⁴ Government of Canada. *Transportation of Dangerous Goods Act*, (S.C. 1992, c. 34), 1992. Available from: <http://laws-lois.justice.gc.ca/eng/acts/T-19.01/page-1.html>

⁴⁵ Government of Canada. *Transportation of Dangerous Goods Regulations*. Available from: <http://www.tc.gc.ca/eng/tdg/clear-tofc-211.htm>



6.11 Incident and accident management

When an incident or accident involving a compounded non-sterile preparation occurs, the compounding personnel must complete an event report and explanation form. In healthcare facilities or community pharmacies, a form developed or selected by the facility or pharmacy may be used (*see* section 6.11.1 for an example).

Complaints, accidents, incidents and reported side effects should be evaluated to determine their cause, and the necessary steps taken to prevent recurrence. Each organization should have a process for this activity and should maintain a log of such events. The information in the log is used to investigate deviations from protocol and to improve processes.

6.11.1 Example of a template for incident/accident reporting and follow-up form

Template 3

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	Responsible	Deadline	✓
(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.)			



Monitoring		
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 or a 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 or any third party, but that does have an unusual result that could, on other occasions, lead to adverse consequences.



7. QUALITY ASSURANCE

7.1 Program content

A quality assurance program must be developed and implemented to ensure the clear definition, application and verification of all activities affecting the quality of final compounded non-sterile preparations and the protection of personnel.

The quality assurance program is intended to generate information showing that the organization's personnel, facilities and equipment attain and maintain the conditions required for quality compounding of non-sterile preparations and that non-sterile preparations are being compounded in compliance with established procedures. This information is made available to and is used by personnel and other responsible individuals.

The verifications required by the quality assurance program help personnel to acquire data and identify trends, which in turn allow corrective and preventive actions to be taken, if necessary. The quality assurance program for each pharmacy will vary depending on the level of requirements (A, B or C), (*see* section 8) the facilities and equipment needed, the personnel involved and the extent of compounding. Each verification carried out according to the quality assurance program should be documented. An example of possible components of a quality assurance program is provided in section 7.6.

7.2 Quality assurance of equipment and compounding areas

7.2.1 Certification

Equipment that supports compounding activities, especially refrigerators and air sampling instruments, must be certified with respect to its installation and operation and should be calibrated before being put into service and thereafter as recommended by the manufacturer.

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

7.2.2 Temperature readings

If an integrated recording instrument (e.g., in a refrigerator or freezer) is used to monitor temperatures 24 hours a day, the temperature log of the equipment should be checked at least once a day in case of substantial variance with respect to specified parameters, and corrective action taken if required.

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

Temperature readings will include the actual temperature, the minimum temperature and the maximum temperature.

If a computerized temperature monitoring system is used, the system should offer features to record and store temperature readings at the same frequency as specified above (at a minimum). The system should also trigger an alarm if the temperature readings deviate from the acceptable range.



Refrigerator and freezer temperature readings should 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 should also be verified and stored.

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

7.3 Quality assurance of personnel

Compounding personnel must be trained and certified and their work routinely observed to ensure compliance with procedures/standards and maintenance of competency. More frequent observations may be needed in cases such as return from extended leaves or contamination.

7.4 Quality assurance related to processes and procedures

The quality assurance program ensures that preparations are compounded in compliance with established procedures.

The program should monitor, among other things,

- the presence of a Master Formulation Record for each compounded non-sterile preparation;
- compliance of the preparation with the prescription issued;
- compliance of labels affixed to containers with legislation and regulations;
- compliance with required documentation in the compounded non-sterile preparations record for individual patients and the batch compounded non-sterile preparations record, ensuring the performance of all verification steps required during and after compounding.

7.5 Documentation of quality control activities

Written documentation related to the quality assurance program must be verified, analyzed, signed and retained for a period of time as designated by the applicable pharmacy regulatory authority.

Situations of non-compliance (where action is required), deviations from protocols, and missing documentation should be investigated, with corrective and preventive actions taken as appropriate. All findings and corrective actions should be documented.

All completed documentation concerning the quality assurance program for personnel involved in the compounding of non-sterile preparations should be retained and made accessible.

7.6 Example of components of a quality assurance program

The quality assurance program outlined below does not include daily operational activities such as checking individual prescriptions and temperatures; rather, it entails a periodic check and documentation that all non-sterile compounding activities are being carried out according to the standards.



Table 6

COMPONENT	CONTROLS	FREQUENCY
FACILITIES	Verification of compounding area for Level A requirements (clean, orderly, good state of repair, appropriate storage, space reserved for compounding)	<ul style="list-style-type: none"> • At least every 6 months • When the compounding area is installed • When new equipment is installed • When area or equipment are repaired or maintained • When a contamination problem is identified
	Verification of compounding rooms for Level B or Level C requirements (appropriate ventilation, suitable materials storage, clean, orderly, good state of repair)	<ul style="list-style-type: none"> • At least every 6 months (more frequently at the start of the quality assurance program) • When the controlled room is installed • When new equipment is installed • When the controlled room or equipment is repaired or maintained (e.g., when high-efficiency particulate air filter is changed) • When a contamination problem is identified • When investigation of a contamination problem or non-compliance in the preparation process requires exclusion of malfunctioning facilities • According to an internal verification program
	Verification that daily temperature and humidity readings are documented in controlled areas	<ul style="list-style-type: none"> • Monthly
EQUIPMENT	Certification of C-PEC (Level B or Level C requirements)	<ul style="list-style-type: none"> • Before first use • Every 6 months • When a new C-PEC is installed • When the C-PEC is repaired or maintained • When a contamination problem is identified • When investigation of a contamination problem or non-compliance in the preparation process requires exclusion of malfunctioning equipment
	Temperature verification (e.g., refrigerator, freezer)	<ul style="list-style-type: none"> • Verify logs monthly (more often if problems are identified) • Calibrate temperature probes yearly
	Operational indicators of C-PEC and other instruments (e.g., those for automated compounding)	<ul style="list-style-type: none"> • Verify logs monthly



PERSONNEL	Skills assessment (technique, following procedures, appropriate PPE, etc.)	<ul style="list-style-type: none"> • At initial qualification: theoretical and practical aspects • Periodically, to ensure compliance with policies and procedures • After extended leave • When assessing incidents and accidents • When a contamination problem is identified
FINAL COMPOUNDED NON-STERILE PREPARATION	Verification of Master Formulation Records (usage and maintenance)	<ul style="list-style-type: none"> • Yearly or when new information becomes available
	Verification that preparation matches prescription; protocols have been followed; ingredients have been verified; preparation has been assessed for clarity, odour, colour and consistency; and labelling/container are appropriate	<ul style="list-style-type: none"> • Quarterly review of documentation
	Verification that documentation of procedures, compounder's initials and entry in logs are being carried out	<ul style="list-style-type: none"> • Quarterly review of documentation
DOCUMENTATION	Policies and procedures are in place and updated regularly	<ul style="list-style-type: none"> • Every 3 years, or when new information becomes available
	Compounding records meet all regulatory requirements, and all logs are kept up to date	<ul style="list-style-type: none"> • Quarterly
	Current references and safety data sheets are available	<ul style="list-style-type: none"> • Yearly
C-PEC = containment primary engineering control; PPE = personal protective equipment.		



USP <795> Categories of non-sterile compounding *

Simple—Making a preparation that has a United States Pharmacopeia (USP) compounding monograph or that appears in a peer-reviewed journal article that contains specific quantities of all components, compounding procedure and equipment, and stability data for that formulation with appropriate BUDs (or reconstituting or manipulating commercial products that may require the addition of one or more ingredients as directed by the manufacturer~*)

~* Not considered compounding by Health Canada

Moderate—Making a preparation that requires special calculations or procedures (such as calibration of dosage unit mold cavities) to determine quantities of components per preparation or per individualized dosage units; or making a preparation for which stability data for that specific formulation are not available.

8. LEVELS OF REQUIREMENTS

The requirements for non-sterile compounding are based on the complexity and risks associated with compounding the preparation and handling the substances used to make the preparation. These requirements apply to preparations intended for both humans and animals.

The requirements have been categorized, by NAPRA, into three levels: A, B and C. Many non-sterile preparations in the USP categories for simple or moderate compounding can be compounded following Level A requirements for facilities, equipment and protective wear. Other non-sterile preparations may have additional requirements; therefore, it is necessary to examine many factors in assessing the risk associated with using a certain substance and determining the appropriate level of requirements. For example, it would be possible to compound a non-sterile simple preparation that contains a drug categorized by NIOSH as hazardous (e.g., clonazepam, carbamazepine) following Level A requirements, provided that the hazardous drug is used in a small quantity and has physical characteristics conducive to minimizing both contamination of the immediate area and risk to personnel. Pharmacists should undertake a [risk assessment](#) (see section 4) and identify the appropriate level of requirements needed to guarantee a high-quality product and adequate protection for personnel. A [summary of requirements](#) has been included for ease of reference (see section 8.4).

8.1 Level A

Level A refers to requirements to be met when compounding simple and moderate preparations, as defined in USP *General chapter <795>*, excluding mixing or reconstituting (in accordance with Health Canada's policy on compounding⁴⁶). Requirements for Level A include a separate compounding area and the general requirements for procedures and equipment.

Although mixing and reconstituting are not considered to constitute compounding in Canada, personnel are encouraged to use the compounding area and follow Level A requirements for these activities as well.

Many non-sterile preparations can be compounded within Level A requirements. These preparations could include simple or moderate preparations containing hazardous drugs in NIOSH Group 2 or 3, or materials designated as health hazards by the *Hazardous Products Act* but that pose little or no risk for compounding personnel when compounded in occasional small quantities (i.e., quantities determined to represent a low risk to compounders in a particular instance at the pharmacy, with appropriate precautions being taken [[see section 4.2 for risk assessment](#)]).

⁴⁶ Health Canada, Health Products and Food Branch Inspectorate. *Policy on manufacturing and compounding drug products in Canada (POL-0051)*. Ottawa, ON: Health Canada; 2009. Available from: http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/docs/pol_0051-eng.php

* United States Pharmacopeial Convention (USP). General chapter <795>: pharmaceutical compounding — nonsterile preparations. In: *USP compounding compendium*. Rockville, MD: USP; 2016. p. 31.



USP <795> Categories of non-sterile compounding *

Complex—Making a preparation that requires special training, environment, facilities, equipment, and procedure to ensure appropriate therapeutic outcomes. Examples of possible complex preparation types include transdermal [delivery system] dosage forms, modified-release preparations, and some inserts and suppositories for systemic effects.

8.2 Level B

Level B refers to requirements to be met when compounding complex preparations, as defined in USP *General Chapter <795>*, or when compounding small quantities of products that require ventilation. These compounded preparations require more specialized equipment, instruments and training.

In addition to the Level A requirements, Level B requirements include a dedicated room that is separate from the rest of the pharmacy, to provide for a larger work space, storage of materials and equipment, uninterrupted workflow and greater protection from cross-contamination. A ventilated, entirely closed off room or a room with a ventilated containment device is required for compounding of certain powders, aromatic products and other hazardous products, including allergenic products or products that could have unintended effects, such as hormones, but that may not require the extensive precautions of Level C requirements if prepared in small quantities and risk can be mitigated (*see section 4.2 for risk assessment*). (Risk mitigation must be documented in the risk assessment.) If a ventilated containment device is used, the pharmacy should follow the same requirements as outlined in section 9.2.3.

As the complexity of the non-sterile preparation increases, so do the requirements for compounding a high-quality product that is safe for the patient, in an environment that is safe for the compounding personnel. Complex preparations require more training and equipment and an environment conducive to few (preferably no) interruptions. In addition, if ingredients that could be irritating to personnel (such as powders) are used frequently, or materials that require some hazardous safety measures are used either occasionally or frequently, further requirements (*see section 8.3*) are necessary to produce high-quality products and to protect compounding personnel.

8.3 Level C

Level C refers to requirements to be met when compounding hazardous drugs that are classified by NIOSH⁴⁷ as Group 1 or hazardous materials that are classified by WHMIS⁴⁸ as a health hazard, such as those very irritating to the respiratory tract, skin or mucous membranes. This level of requirements may also apply to NIOSH Group 2 and 3 drugs involving routine use of large quantities of APIs, according to the risk assessment.

Level C requirements include a room under negative pressure, a ventilated containment device and PPE appropriate for handling hazardous products. These requirements are detailed in [section 9](#).

National Institute for Occupational Safety and Health⁴⁹

NIOSH has prepared a list of antineoplastic and other hazardous drugs, and divided them into three groups.

Group 1 consists of antineoplastic drugs (or cytotoxic drugs). The majority of these are also hazardous to men and women who are actively trying to conceive, women who are pregnant or may become pregnant, and women who are breastfeeding (because they may be present in breast milk). These drugs represent an occupational hazard for healthcare workers and should always be handled with recommended engineering controls and PPE, regardless

⁴⁷ National Institute for Occupational Safety and Health (NIOSH). *NIOSH list of antineoplastic and other hazardous drugs in healthcare settings, 2016*. Cincinnati, OH: Department of Health and Human Services, Centers for Disease Control and Prevention, NIOSH; 2016. Available from: https://www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf

⁴⁸ Health Canada. *Workplace Hazardous Materials Information System (WHMIS)*. Ottawa, ON: Health Canada; 2016. Available from: <http://www.hc-sc.gc.ca/ewh-semt/occup-travail/whmis-simdut/index-eng.php>

⁴⁹ National Institute for Occupational Safety and Health (NIOSH). *NIOSH list of antineoplastic and other hazardous drugs in healthcare settings, 2016*. Cincinnati, OH: Department of Health and Human Services, Centers for Disease Control and Prevention, NIOSH; 2016. Available from: https://www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf

* United States Pharmacopeial Convention (USP). General chapter <795>: pharmaceutical compounding — nonsterile preparations. In: *USP compounding compendium*. Rockville, MD: USP; 2016. p. 31.



of their formulation (intravenous, subcutaneous, topical, tablet or capsule). Examples of drugs in this category are chlorambucil, cyclophosphamide, fluorouracil, hydroxyurea, methotrexate and tamoxifen.

Group 2 consists of non-antineoplastic drugs that meet one or more NIOSH criteria for a hazardous drug and that may pose an occupational risk to men and women who are actively trying to conceive, women who are pregnant or may become pregnant, and women who are breastfeeding (because they may be present in breast milk). Examples of drugs in this category are carbamazepine, azathioprine, cyclosporine, estrogens, risperidone and spironolactone.

Group 3 drugs consists of non-antineoplastic drugs that primarily pose a reproductive risk. They represent a potential occupational hazard to men and women who are actively trying to conceive, women who are pregnant or may become pregnant, and women who are breastfeeding (because they may be present in breast milk). Examples of drugs in this category are clonazepam, fluconazole, misoprostol, testosterone, tretinoin and valproate/valproic acid.

NIOSH performs a hazard identification for each of the drugs on its list. The actual risk to healthcare workers depends on what is done with the drugs: how they are manipulated, how often they are handled, and what type of engineering controls and PPE are used.

Hazardous Products Act⁵⁰

Whenever any of the hazardous materials or drugs listed under the *Hazardous Products Act* are used for compounding, precautions should be taken to protect the compounder. Schedule 2 of the Act divides hazardous products into two categories: physical hazards (flammable, gas under pressure, explosive) and health hazards. The health hazard class includes agents causing acute toxicity, skin corrosion/irritation, serious eye damage/eye irritation, respiratory or skin sensitization, germ cell mutagenicity, carcinogenicity, reproductive toxicity, specific target organ toxicity through repeated exposure, aspiration hazard, biohazardous infectious materials and health hazards not otherwise classified. Compounders should consult safety data sheets and manufacturer's recommendations for precautions. The precautions vary, depending on the hazardous product used and the quantity handled, which together determine the compounder's exposure to the product. The precautions listed in Level A (separate area, attire) or Level B (attire, room or hood ventilated to the outside, etc.) requirements may therefore, be adequate for small quantities of hazardous products or those with low health risk. However, stricter preventive measures (i.e., Level C requirements) may be necessary for compounding very hazardous materials with a known health risk, such as those that are very irritating to the respiratory tract, skin and mucous membranes.

50 Government of Canada. *Hazardous Products Act* (R.S.C., 1985, c. H-3). Available from: <http://laws-lois.justice.gc.ca/eng/acts/H-3/>



8.4 Summary of requirements for compounded non-sterile preparations

Table 7

REQUIREMENTS		Level A	Level B	Level C
		Mandatory = ✓		
Personnel	Section 7.1			
Appoint a non-sterile compounding supervisor		✓	✓	✓
Training	Section 7.2			
Has received orientation and training during education or on the job concerning the preparations to be compounded and underwent a skills assessment at the time of hiring; training has included learning and assimilating workplace operating procedures		✓	✓	✓
Has been trained in techniques appropriate for the compounding of complex preparations and some hazardous products			✓	
Has received hazardous products training and has relevant training and experience in compounding all non-sterile dosage forms				✓
Participates in annual skills assessment program		✓	✓	✓
Facilities	Section 7.3			
Designated non-sterile compounding area		✓		
Dedicated room, entirely closed off, well ventilated or with a ventilated hood			✓	
Dedicated room under negative pressure to the pharmacy; containment device				✓



9. REQUIREMENTS FOR HAZARDOUS PREPARATIONS

Hazardous preparations may be simple, moderate or complex, but the level of precautions needed depends more on the risk posed by the hazardous product than on the complexity of the preparation. Small quantities of simple or moderate preparations containing products classified as hazardous by NIOSH or WHMIS may sometimes be compounded in a pharmacy meeting Level A requirements, with certain additional precautions, depending on the risk determined as described in [section 4](#) and reviewed annually.

Some hazardous products may require compounding using Level B requirements, and yet others may need Level C requirements. Those drugs listed in the NIOSH Group 1 (antineoplastics) and those categorized by WHMIS as very irritating to the respiratory tract, skin and mucous membranes would require the greater precautions of Level C requirements.

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 penetration⁵¹.

Absorption through the skin occurs by direct contact with contaminated surfaces or objects. Ingestion occurs by eating foods that have been contaminated or by putting contaminated hands or objects, particularly pens, into the mouth^{52, 53}. Inhalation of vaporized drugs can also be a source of contamination⁵⁴. Therefore; the compounding of hazardous non-sterile preparations requires safety measures to protect personnel and the environment. NIOSH has created a “hierarchy of controls” diagram depicting the various levels of controls that can be implemented (<https://www.cdc.gov/niosh/topics/hierarchy/>).

In the pharmacy of a healthcare facility that will be compounding hazardous drugs or materials, a hazardous drugs committee⁵⁵ 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 or pharmacy technician should be designated to support hazardous products management.

Handling hazardous drugs with greater risk or certain hazardous materials that are very irritating to the respiratory tract, skin and mucous membranes should meet Level C requirements specifically a closed-off room under negative pressure, with filtered air exhausted to the outside to avoid contaminating the environment. This room should be dedicated to the compounding of preparations containing hazardous drugs or materials or, as a minimum, there should be assurances that the area is meticulously cleaned in a manner preventing any risk of cross-contamination with the hazardous materials before other preparations are compounded. The remainder of this section presents detailed specifications for Level C requirements.

9.1 Facilities for handling hazardous products⁵⁶ (Level C requirements)

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

In addition to previously stated requirements for non-sterile compounding, such as adequate space and sufficient lighting (*see* section 5.4), compounding of hazardous non-sterile preparations should occur in a separate room. For less hazardous products, this room could meet level B requirements: a well-ventilated room with, for some

51 American Society of Health-System Pharmacists (ASHP). ASHP guidelines on handling hazardous drugs. *Am J Health Syst Pharm*. 2006;63(12):1172-91.

52 American Society of Health-System Pharmacists (ASHP). ASHP guidelines on handling hazardous drugs. *Am J Health Syst Pharm*. 2006;63(12):1172-91.

53 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: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf

54 American Society of Health-System Pharmacists (ASHP). ASHP guidelines on handling hazardous drugs. *Am J Health Syst Pharm*. 2006;63(12):1172-91.

55 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: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf

56 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: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf

preparations, a ventilated containment device and extra PPE. For hazardous products with greater health risks, Level C precautions would be required, specifically a separate room under negative pressure. The risk assessment outlined in section 4 should contain documentation to justify the level of requirements needed for each preparation.

9.1.1 Compounding rooms

Engineering controls for containment are required to prevent the cross-contamination of preparations during all phases of the compounding process. A containment primary engineering control (C-PEC) is a ventilated device designed to minimize the exposure of workers and the environment to hazardous products when such products are being handled directly. The containment secondary engineering control (C-SEC) is the room in which the C-PEC is placed.

The room used for compounding hazardous preparations needing Level C requirements should have the following features⁵⁷:

1. external venting through high-efficiency particulate air (HEPA) filtration
2. physical separation from other preparation rooms
3. appropriate air exchange (at least 12 air changes per hour [ACPH])
4. negative pressure (–2.5 Pa relative to surrounding areas)

A sink with hot and cold running water should be available for handwashing, along with an eyewash station and/or other emergency or safety features that meet applicable laws and regulations. Water sources and drains should be located at least 1 meter away from the C-PEC.

Because of the difficulty of removing hazardous product contamination, the surfaces of ceilings, walls, floors, fixtures, shelving, counters and cabinets in the non-sterile compounding area should be smooth, impermeable, free from cracks and crevices, and made of non-shedding material.

9.1.2 Heating, ventilation and air conditioning system for controlled rooms

Controlled rooms should be vented to the outside through HEPA filters, should have an air exchange of at least 12 ACPH and have negative pressure, to contain the hazardous products and minimize the risk of exposure. Consideration should be given to having an uninterrupted power supply for the ventilation systems to ensure that negative pressure is maintained in the event of power outages.

Air conditioning helps to ensure the comfort of personnel wearing PPE. The temperature of the room should be less than or equal to 20 °C, taking into account employees' comfort once all PPE has been donned.

9.1.3 Windows and other openings

Controlled rooms must not have windows or doors opening directly to the exterior of the building. If any windows are present, they should be sealed. Any doors leading to the outside or to a non-controlled area (other than the doors designated for accessing the room) should also be sealed. An environmental control procedure and a housekeeping procedure, including the cleaning of sealed windows and doors, should be implemented by cleaning personnel.

9.1.4 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 necessary in the area⁵⁸; however, two pairs of ASTM International–approved gloves should be worn by personnel doing the unpacking.

57 United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in healthcare settings [draft]. USP 39. Rockville, MD: USP; 2016. p. 88. (To become official December 1, 2019.)

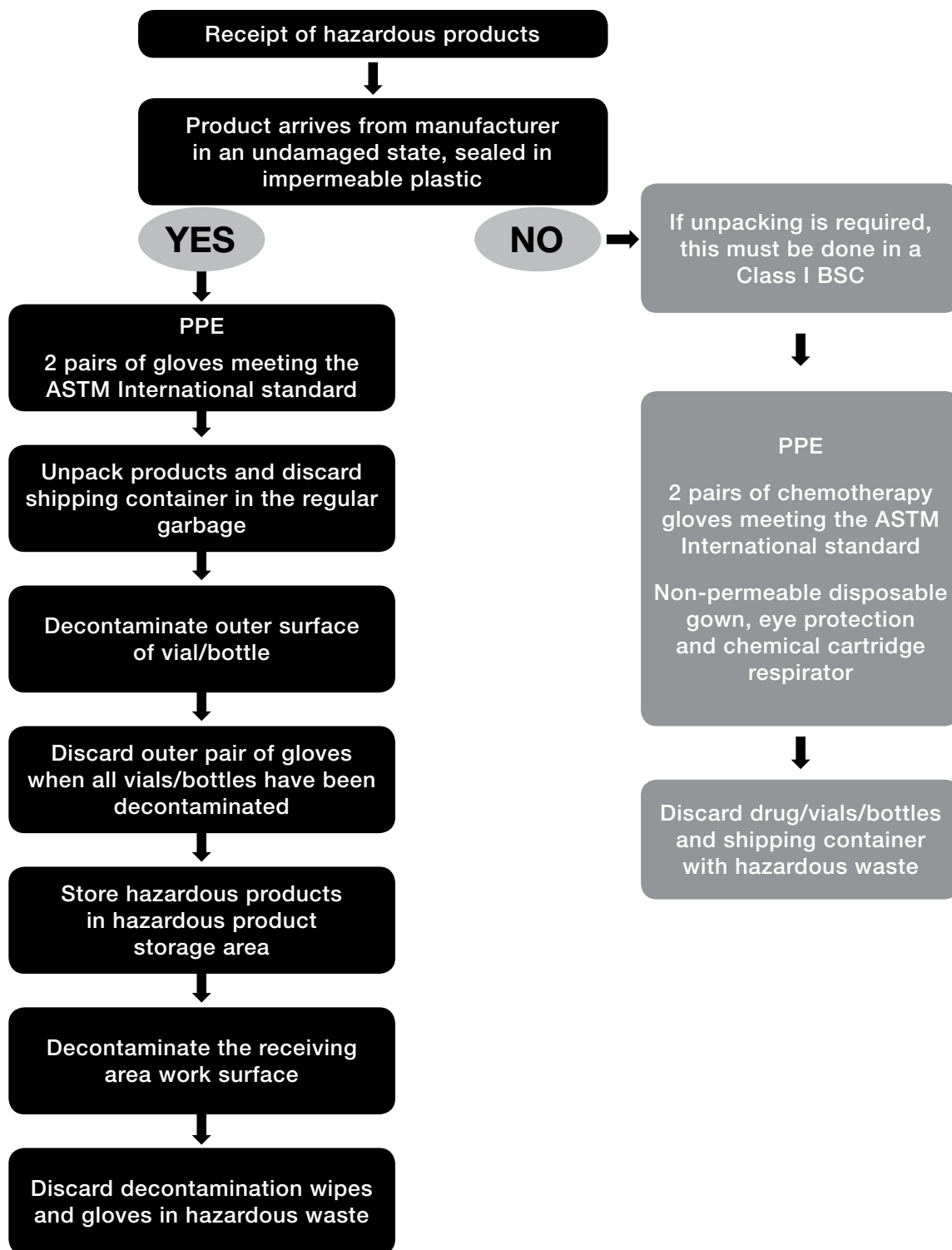
58 United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in healthcare settings [draft]. USP 39. Rockville, MD: USP; 2016. p. 88. (To become official December 1, 2019.)



If a hazardous product arrives in a damaged state and unpacking is required, a C-PEC or other Class I Biological Safety Cabinet (BSC) will be needed. The C-PEC may be reserved for unpacking the damaged product, or it may also be used for the compounding of non-sterile hazardous preparations⁵⁹. Personnel should wear the PPE recommended in section 9.2.3. A procedure for unpacking is presented below.

Receiving, unpacking and storing hazardous products

Diagram 2



⁵⁹ United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in healthcare settings [draft]. USP 39. Rockville, MD: USP; 2016. p. 88. (To become official December 1, 2019.)

9.1.5 Area for storing hazardous products

Hazardous products should be grouped and stored in a properly ventilated room with all air exhausted to the exterior⁶⁰. The storage area should have negative pressure relative to the adjacent rooms and should have at least 12 ACPH. The storage area should be identified with appropriate signage (section 9.1.6) to indicate the presence of hazardous products⁶¹. These and other requirements for a hazardous products storage area are listed in the table below.

Table 8

Required conditions for a hazardous products storage area
Area separate from the unpacking area
Dedicated room
Negative pressure (–2.5 Pa) relative to surrounding areas
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 breaking ⁶²
Storage spaces for hazardous products and preparations identified with appropriate signage to indicate the presence of hazardous products ⁶³
Sufficient ventilation to prevent contamination from spreading to adjoining rooms ⁶⁴

Alternatively, hazardous non-sterile preparations and the refrigerator in which they are stored, if appropriate, may be placed in the room used for compounding such preparations. This approach ensures that the drugs are stored in a negative-pressure room with sufficient ACPH (given that the room will have at least 12 ACPH), with the air being completely exhausted to the exterior.

9.1.6 Signage

Areas for storing hazardous products and facilities for preparing non-sterile hazardous preparations must be identified with appropriate and informative signs (e.g., pictograms indicating cytotoxicity, need for special care, hazards, restricted access, dress code).

9.2 Equipment for handling hazardous products

9.2.1 Containment primary engineering control

The C-PEC is installed in the compounding room and should either be externally vented (the preferred option) or have redundant HEPA filters in a series. Hazardous non-sterile preparations, such as volatile, liquid or powder forms of cytotoxic products, should be compounded inside a C-PEC that provides protection for personnel and the

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. 6-4. Available from: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf

61 Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). Chapter 4: general preventive measures. In: *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. pp. 4-1 to 4-11. Available from: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf

62 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: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf

63 Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). Chapter 4: general preventive measures. In: *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. pp. 4-1 to 4-11. Available from: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf

64 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: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf



environment, such as a Class I biological safety cabinet (BSC)^{65, 66, 67, 68} or a containment ventilated enclosure⁶⁹. A Class II BSC or a compounding aseptic containment isolator (CACI) may also be used. The safety cabinet should be chosen according to the volume of preparations and products to be compounded.

For occasional compounding of non-sterile hazardous products, a C-PEC used for sterile compounding (e.g., Class II BSC or CACI) may be used, but it should be decontaminated, cleaned and disinfected before compounding the non-sterile product and again before resuming sterile compounding in that C-PEC. A C-PEC used only for the compounding of non-sterile hazardous products does not require unidirectional airflow because the environment does not require International Standards Organization (ISO) classification⁷⁰.

The C-PEC should be installed according to the manufacturer's recommendations and certified according to current certification standards.

The C-PEC should operate continuously if it supplies some or all of the negative pressure in the C-SEC or if it is used for sterile compounding 24 hours a day^{71, 72}. If there is a loss of power to the C-PEC, or if moving or repair occurs, all activities occurring in the C-PEC should be suspended immediately. Once the C-PEC can be powered on, all surfaces should be decontaminated and cleaned, and the manufacturer-specified recovery time allowed to elapse before compounding resumes⁷³.

The work surface of the C-PEC should be resistant to damage from cleaning, disinfecting, deactivation and decontamination and should be changed if it is damaged.

Maintenance of C-PEC

C-PECs should be maintained in accordance with the manufacturer's recommendations. The C-PEC's pre-filters should be accessible. They should be inspected every 6 months and replaced if necessary or as recommended by the manufacturer. Washable pre-filters should 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 maintenance for C-PECs and other equipment should be performed when no compounding is in progress, before cleaning and disinfection operations.

All C-PEC maintenance should be noted on a form or entered in the general maintenance log (paper-based or computerized) and signed. Maintenance of the C-PEC should be performed regularly, the results reviewed and corrective measures taken, as appropriate.

65 National Institute for Occupational Safety and Health (NIOSH). *NIOSH list of antineoplastic and other hazardous drugs in healthcare settings, 2016*. Cincinnati, OH: Department of Health and Human Services, Centers for Disease Control and Prevention, NIOSH; 2016. Available from: https://www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf

66 American Society of Health-System Pharmacists (ASHP). ASHP guidelines on handling hazardous drugs. *Am J Health Syst Pharm*. 2006; 63(12):1172-91.

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

68 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. 8-9. Available from: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf

69 United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in healthcare settings [draft]. USP 39. Rockville, MD: USP; 2016. (To become official December 1, 2019.)

70 United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in healthcare settings [draft]. USP 39. Rockville, MD: USP; 2016. p. 88. (To become official December 1, 2019.)

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

72 United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in healthcare settings [draft]. USP 39. Rockville, MD: USP; 2016. (To become official December 1, 2019.)

73 United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in healthcare settings [draft]. USP 39. Rockville, MD: USP; 2016. p. 88. (To become official December 1, 2019.)



9.2.2 Other instruments, devices and accessories related to the compounding of hazardous non-sterile preparations

All reusable instruments, devices and accessories used to handle hazardous products must be deactivated, decontaminated and cleaned⁷⁴. Instruments and accessories to be used in controlled rooms should not be removed without good reason. If they are removed, they should be decontaminated before use elsewhere.

Maintenance of instruments and accessories should be recorded in the general maintenance log.

9.2.3 Personal protective equipment⁷⁵

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

Gloves

For the following activities, personnel should wear *two pairs of chemotherapy gloves* meeting the ASTM International standard D6978 (or its successor):

- unpacking
- deactivating, decontaminating and cleaning the room
- deactivating, decontaminating and cleaning the C-PEC
- compounding hazardous preparations
- managing spills of hazardous products

Gloves should be inspected before use and should be worn over top of the fitted cuff of the gown.

Both pairs of gloves should be discarded and replaced at the earliest of the following: manufacturer time limit for permeation of the gloves; every 30 minutes^{76, 77, 78, 79}; or immediately if a tear, puncture or contamination has occurred or is suspected.

Gown

When gowns are required, they should be disposable and have demonstrated resistance to permeability by hazardous products. Gowns should be selected according to the hazardous products handled in the pharmacy. Disposable gowns made of polyethylene-coated polypropylene or other laminate materials offer better protection than those made of uncoated materials. The gown should close in the back (no open front) and should have long sleeves with fitted cuffs at the wrists.

74 United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in healthcare settings [draft]. USP 39. Rockville, MD: USP; 2016. p. 94. (To become official December 1, 2019.)

75 Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). Section 4.1.7: protective equipment. In: *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 4-5 to 4-11. Available from: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf

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

77 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.

78 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. Available from: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf

79 United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in healthcare settings [draft]. USP 39. Rockville, MD: USP; 2016. (To become official December 1, 2019.)



The gown should be discarded and replaced at the earliest of the following: the manufacturer's time limit for permeation of the gown; after 2–3 hours of continuous^{80, 81} compounding work; after each removal; or after a contamination has occurred or is suspected. A gown is required if the employee is unpacking a damaged hazardous product or if a spill has occurred⁸².

Laboratory coats, surgical scrubs and isolation gowns made of cloth or other absorbent materials are not appropriate as protective outerwear, because they permit the permeation of hazardous products and can hold spilled products against the skin. Clothing may also retain hazardous residue, which may subsequently be transferred to other healthcare workers or various surfaces. Washing of non-disposable clothing contaminated with hazardous product residue should only be done according to established policy, to prevent transferring hazardous product residue to other clothing. Potentially contaminated clothing should not be taken home under any circumstances⁸³.

Head, hair, shoe and sleeve covers⁸⁴

Disposable head and hair covers (including beard and mustache, if applicable) and shoe covers should be worn during the compounding of hazardous non-sterile preparations. They should be changed after each removal or if they become contaminated⁸⁵. When compounding hazardous drugs, a second pair of shoe covers should be donned before entering the C-SEC and doffed when exiting the C-SEC. Shoe covers worn in areas where hazardous drug are handled should not be worn to other areas of the facility, to avoid spreading hazardous drug contamination and exposing other healthcare workers. Disposable sleeve covers, preferably made of polyethylene-coated polypropylene or other laminate materials, may be used to protect areas of the arm that may come in contact with hazardous products.

Respiratory protection

Surgical masks do not provide respiratory protection against drug exposure and therefore should not be used when respiratory protection against hazardous drug exposure is required.

For most activities, a fit-tested N95 or N100 mask (NIOSH-approved) will protect against airborne particles; however, these masks offer no protection from vapours or gases and little protection from liquid splashes. A full face-piece chemical cartridge respirator or a powered air-purifying respirator should be worn in the presence of vapours or gases; if there is a danger of liquid splashes; if there has been a spill; or for deactivating, decontaminating and cleaning beneath the work surface of a C-PEC.

The mask should be changed at the earliest of the following: after 3.5 hours of continuous compounding work, after each removal or if contamination has occurred or is suspected.

Eye and face protection

Goggles and a face shield or full face-piece respirator should be worn when working at or above eye level; when deactivating, decontaminating and cleaning beneath the work surface of a C-PEC; when cleaning up a spill; and when there is risk of splashes to the face and eyes, such as may occur when unpacking suspected damaged drugs. Eyeglasses alone or safety glasses with side shields do not adequately protect the eyes from splashes.

80 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: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf

81 United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in healthcare settings [draft]. USP 39. Rockville, MD: USP; 2016. p. 91. (To become official December 1, 2019.)

82 United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in healthcare settings [draft]. USP 39. Rockville, MD: USP; 2016. p. 95. (To become official December 1, 2019.)

83 United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in healthcare settings [draft]. USP 39. Rockville, MD: USP; 2016. p. 90. (To become official December 1, 2019.)

84 United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in healthcare settings [draft]. USP 39. Rockville, MD: USP; 2016. p. 91. (To become official December 1, 2019.)

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. 4.6. Available from: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf



9.3 Deactivating, decontaminating and cleaning in areas reserved for the compounding of hazardous non-sterile preparations

The room used for non-sterile compounding of hazardous products should be kept clean at all times, which entails periodic washing of the walls, ceiling and storage areas (at least once a year and more frequently if necessary). The floors should be washed at least once a day when the room is in use.

The compounding area, equipment and accessories must be meticulously cleaned immediately after compounding of preparations containing hazardous products or allergenic ingredients (sulfonamides, penicillins, etc.). It is strongly recommended that equipment be set aside especially for compounding each of these classes of products; alternatively, disposable equipment should be used, if possible, to reduce the chances of bioburden and cross-contamination⁸⁶.

Policies and procedures for cleaning tasks should be developed, and cleaning personnel should be trained and assessed on correct application of these policies and procedures, to protect themselves and the environment from contamination⁸⁷. Only trained and qualified cleaning and disinfecting personnel should be allowed to clean controlled rooms.

9.3.1 Garbing of cleaning personnel

Cleaning personnel must comply with the pharmacy's hand hygiene and garbing procedure before they enter areas reserved for compounding hazardous products to perform housekeeping duties.

9.3.2 Surface deactivation, decontamination and cleaning⁸⁸

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

The safety data sheets for products used in the facility for deactivation, decontamination and cleaning must be available on site and readily accessible.

Deactivation

Deactivation renders a compounded preparation inert or inactive. Residue from deactivation should be removed by decontaminating the surface. Whenever possible, products that have known deactivation properties (oxidizing agents registered with the US Environmental Protection Agency that are appropriate for the intended use) should be used. Care should be taken in selecting materials for deactivation because of their potential adverse effects (e.g., hazardous by-products or caustic damage to surfaces).

Decontamination

Decontamination involves inactivating, neutralizing or physically removing the hazardous product residue from non-disposable surfaces and transferring it to absorbent, disposable materials (e.g., wipes, pads or towels) appropriate to the area being cleaned. When choosing a product for decontaminating hazardous products, consideration should be given to surface compatibility and facility requirements.

86 United States Pharmacopeial Convention (USP). General chapter <795>: pharmaceutical compounding — nonsterile preparations. In: *USP compounding compendium*. Rockville, MD: USP; 2016. p. 34.

87 United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in healthcare settings [draft]. USP 39. Rockville, MD: USP; 2016. p. 92. (To become official December 1, 2019.)

88 United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in healthcare settings [draft]. USP 39. Rockville, MD: USP; 2016. pp. 94-95. (To become official December 1, 2019.)



Cleaning

Cleaning is a process that uses water, detergents, surfactants, solvents and/or other chemicals to remove contaminants (e.g., soil, microbial contamination, hazardous product residue) from objects and surfaces. Cleaning agents should not themselves introduce microbial contamination.

9.3.3 Surface deactivation, decontamination and cleaning of the containment primary engineering control⁸⁹

The work surface of the C-PEC must be deactivated, decontaminated and cleaned before starting the compounding of different preparations. The C-PEC should be deactivated, decontaminated and cleaned at least daily when in use, any time a spill occurs, before and after certification, any time that voluntary interruption occurs and if the ventilation is moved.

Certain C-PECs have areas under the work tray where contamination can build up; these areas should be deactivated, decontaminated and cleaned at least monthly to reduce the contamination level in the C-PEC. As many of the C-PEC surfaces as possible should be deactivated, decontaminated and cleaned before the area under the work tray is accessed. The opening of cabinets during deactivation, decontamination and cleaning of this area compromises the containment airflows; respiratory protection may be required while performing this task.

Deactivation, decontamination and cleaning tasks performed should be recorded in the general maintenance log.

9.4 Incident and accident management

9.4.1 Accidental exposure⁹⁰

Policies and procedures to be followed in case of accidental exposure of personnel to hazardous products must be established. For products that have safety data sheets, those documents should be accessible in the workplace. An eyewash station and sink with hot and cold running water should be available. The phone number of the local poison centre should be posted where employees can easily see it.

The exposure should be documented in the appropriate logs.

9.4.2 Spills

Policies and procedures

Policies and procedures and training programs should be established to prevent spills and to direct the cleanup of hazardous product spills, addressing size and scope of the spill and specifying who is responsible for spill management.

Training and garb

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

⁸⁹ United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in healthcare settings [draft]. USP 39. Rockville, MD: USP; 2016. pp. 94-95. (To become official December 1, 2019.)

⁹⁰ 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: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf



Spill kits

Spill kits should be available in locations where hazardous products are handled and should be present when 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*⁹¹, published by the ASSTSAS, which describes the content and use of spill kits.

9.4.3 Documentation for incidents and accidents

When an incident or accident involving a hazardous compounded non-sterile preparation occurs, the compounding personnel must complete an event report and explanation form. In healthcare facilities or community pharmacies, a form developed or selected by the facility or pharmacy may be used (*see* section 6.11.1 for an example).

Complaints, accidents, incidents and reported side effects should be evaluated to determine their cause, and the necessary steps taken to prevent recurrence. Each organization must have a process for this activity and must maintain a log. Information in the log is used to investigate any deviations and improve processes.

9.5 Hazardous waste management (see standard for cross reference)

Procedures for the destruction and/or disposal of pharmaceutical waste should be developed and implemented to ensure that hazardous products are disposed of safely, in compliance with the environmental protection legislation in force in the jurisdiction; and safely stored in inventory, in a location separate from other medications, until they are used or destroyed.

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

Hazardous products should be destroyed in accordance with regulations governing such products⁹². A list of hazardous products in use must be available in the pharmacy. The NIOSH list⁹³ or WHMIS documentation can be used to determine whether a particular product is deemed hazardous in the United States or Canada, respectively. Each pharmacy should customize a list for its own use, as some drugs may be available in one country and not the other, or new drugs may become available after an update of the NIOSH list is published.

Policies and procedures for the management of hazardous waste⁹⁴ must be developed and followed. These policies and procedures should comply with local, provincial and federal requirements.

The policies and procedures should 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 environment⁹⁵.
- All equipment, products and vials used in the compounding of hazardous preparations should be discarded in a hazardous waste container.

91 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: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf

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

93 National Institute for Occupational Safety and Health (NIOSH). *NIOSH list of antineoplastic and other hazardous drugs in healthcare settings, 2016*. Cincinnati, OH: Department of Health and Human Services, Centers for Disease Control and Prevention, NIOSH; 2016. Available from: https://www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf

94 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: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf

95 United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in healthcare settings [draft]. USP 39. Rockville, MD: USP; 2016. (To become official December 1, 2019.)



- Hazardous waste containers should be identified with a self-adhesive label marked “Hazardous waste – cytotoxic”⁹⁶. Containers should be filled to only three-quarters of their capacity⁹⁷. Once a bin is three-quarters full, it should be sealed. Personnel should never attempt to compress the contents of a hazardous waste bin.
- Waste used in the compounding of hazardous preparations should be placed in a hazardous waste container inside the C-PEC or placed in a sealable plastic bag before removal from the C-PEC and then discarded in a hazardous waste container.
- Outer gloves should be removed inside the C-PEC. The gloves should be placed in a hazardous waste container inside the C-PEC or placed in a sealable plastic bag before removal from the C-PEC and then discarded in a hazardous waste container.
- All PPE should be discarded into the hazardous waste container.
- Bins used for hazardous product waste should comply with local, provincial and federal requirements. These bins should be incinerated and not be sent for decontamination by autoclave and subsequent burial.

9.6 Verification of controlled rooms and the containment primary engineering control

9.6.1 Certification⁹⁸

The controlled room (the C-SEC) and the C-PEC must be certified

- at least every 6 months;
- during installation of new equipment or a new controlled area;
- during maintenance or repair of equipment (e.g., repair of C-PEC or ventilation system) or a controlled area (e.g., repair of hole in a wall) that might alter environmental or operational parameters;
- when investigation of a contamination problem or a problem involving non-compliance in the handling of hazardous products requires exclusion of malfunctioning facilities.

The program for monitoring facilities and the C-PEC should include a plan for sampling for hazardous product residue (e.g. wipe sampling).

9.6.2 Certificate provided by manufacturer (in factory)

The non-sterile compounding supervisor must retain, for all HEPA filters and for the C-PEC, the manufacturers’ certificates issued in the factory.

9.6.3 Environmental verification

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

The program should include verification for chemical contamination by hazardous products on surfaces used for receipt, storage, preparation and verification of product and preparations.

The temperature of controlled rooms should be verified and documented at least once a day.

The negative pressure of the controlled room (C-SEC) should be maintained to avoid contamination of adjacent areas. Pressure should be measured continuously, and an alarm system should be in place to immediately advise

96 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: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf

97 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: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf

98 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. 7-5. Available from: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf



personnel of non-compliance with specifications and to direct that action be taken, if necessary. A procedure should be developed to outline and explain the actions to be taken if the pressure deviates from specifications.

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

Hazardous product contamination and wipe sampling

The level of hazardous product contamination should be measured at least once every 6 months, more frequently if there has been a major change in placement of furniture, compounding processes or cleaning practices.

Sampling should be performed at the various sites used for compounding, especially those most likely to be contaminated (e.g., outside the C-PEC, floor surrounding the C-PEC). The sites sampled and the frequency of monitoring should be established on the basis of results obtained with previous monitoring.

A baseline assessment should precede any preventive measure put in place (as described in the ASSTSAS guide⁹⁹), and monitoring should be repeated after implementation of such measures to determine their effectiveness.

Surface contamination by hazardous drugs or hazardous materials, as determined by environmental monitoring, should be recorded in the general maintenance log.

9.6.4 Documentation

All completed documentation concerning aspects of testing controlled rooms, the C-PEC and supporting equipment for hazardous product contamination should be filed and retained with other compounding records, as per requirements of the provincial/territorial pharmacy regulatory authority.

Documents concerning purchase, organization and certification of the C-PEC should be accessible throughout the entire service life of the facility and the C-PEC.

⁹⁹ 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: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf



10. GLOSSARY OF TERMS (WITH ABBREVIATIONS)^{100, 101, 102, 103, 104, 105, 106}

Term and/or abbreviation	Definition
ACPH	Air changes per hour
Active pharmaceutical ingredient (API)	Any substance or mixture of substances intended to be used in the compounding or manufacturing of a drug (medicinal) product that, when used in this manner, becomes an active ingredient of the drug product, where the drug product so created has pharmacological activity in the diagnosis, cure, mitigation, treatment or prevention of disease or acts to affect the structure and function of the body. (see also <i>inactive ingredient excipient</i>)
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 in the province of Quebec.
ASTM	American Society for Testing and Materials; now known as ASTM International
Beyond-use date (BUD)	Date after which a compounded preparation shall not be used; determined from the date when the preparation is compounded.
Biological safety cabinet (BSC)	Laminar airflow workbench that is ventilated to protect personnel, hazardous compounded preparations and the immediate environment. The open front of a BSC has the following features: <ul style="list-style-type: none"> • air intake, to protect compounding personnel from hazardous preparations; • descending air curtain filtered with a high-efficiency particulate air filter, to protect the hazardous product; • air evacuation system equipped with high-efficiency particulate air filters for environmental protection.
Biomedical refrigerator	Refrigerator designed to refrigerate biological and medical products and drugs. Such refrigerators often come with an integrated temperature control system and an alarm system.
CACI	Compounding aseptic containment isolator
Competencies	Significant job-related knowledge, skills, abilities, attitudes and judgments required for competent performance of duties by members of a profession.
Containment primary engineering control (C-PEC)	A ventilated device designed to minimize exposure of personnel and the environment to hazardous products when such products are being handled directly. For hazardous non-sterile compounding, containment primary engineering controls include biological safety cabinets (BSCs).
Containment secondary engineering control (C-SEC)	The room in which the C-PEC is placed.
Containment system	Arrangement of equipment to contain the particles of hazardous products in the chosen space.

100 Health Canada, Health Products and Food Branch Inspectorate. *Policy on manufacturing and compounding drug products in Canada (POL-0051)*. Ottawa, ON: Health Canada; 2009. Available from: http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpff/docs/pol_0051-eng.php

101 Bussi eres JF. *L egislation et syst eme de soins : recueil de textes choisis et comment es*. 5th edition. JF Bussi eres; 2009. p. 171.

102 United States Pharmacopeial Convention (USP). General chapters 795, 797, 800, 1072. USP 39. Rockville, MD: USP; 2016.

103 Commission de la sant e et de la s ecurit e du travail (CSST). *Material safety data sheet user's guide*. Qu ebec, QC: CSST; 2010.

104 Association paritaire pour la sant e et la s ecurit e du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montr eal, QC: ASSTSAS; 2008. Available from: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf

105 National Institute for Occupational Safety and Health (NIOSH). *NIOSH list of antineoplastic and other hazardous drugs in healthcare settings, 2016*. Cincinnati, OH: Department of Health and Human Services, Centers for Disease Control and Prevention, NIOSH; 2016. Available from: https://www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf

106 Canadian Nurses Association (CNA). *Joint position statement: promoting continuing competence for registered nurses*. Ottawa, ON: CNA; 2004. Available from: https://cna-aicc.ca/~media/cna/page-content/pdf-en/promoting-continuing-competence-for-registered-nurses_position-statement.pdf?la=en

Deactivation	Treatment of a hazardous product to create a less hazardous agent. One method is chemical deactivation.
Decontamination	Transfer of a hazardous product contaminant from a fixed surface (e.g., counter, bag of solution) to a disposable surface (e.g., wipe, cloth). The wipe or cloth is then contained and discarded as hazardous waste.
DIN	Drug Identification Number
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, leads to a developmental or reproductive toxic effect, or damage organs.
Hazardous material	A material that, because of its properties, constitutes a danger to an employee's health, safety or physical integrity. Hazardous materials are dangerous products regulated by a workplace hazardous material information system; as such, they are considered "controlled" products under the <i>Hazardous Products Regulations</i> .
Hazardous product	A substance that entails risks for the worker because of its effects. For the purposes of this Guidance Document and the accompanying Model Standards, the term "hazardous product" refers to both hazardous drugs and hazardous materials, depending on the situation.
HEPA	High-efficiency particulate air
Inactive ingredient excipient	Ingredient that is necessary to compound a preparation but that is not intended or expected to cause a pharmacological response in humans or animals if administered alone in the amount or concentration contained in a single dose of the compounded preparation.
NIOSH	National Institute for Occupational Safety and Health (US)
Non-regulated pharmacy personnel	A person who is employed in a pharmacy to assist the pharmacist or pharmacy technician.
Personal protective equipment (PPE)	All garb and accessories, such as mask, gloves, gown and safety goggles, that protect the non-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.
Pharmacist	A person who is registered by a pharmacy regulatory authority in Canada to practise as a pharmacist.
Pharmacy technician	A person who is registered or authorized by a pharmacy regulatory authority in Canada to practise as a pharmacy technician.
Purified water	Used as an excipient in the production of non-parenteral preparations and in other pharmaceutical applications, such as cleaning of certain equipment. Purified water must meet the requirements for ionic and organic chemical purity and must be protected from microbial contamination. The source water may be purified by deionization, distillation, ion exchange, reverse osmosis, filtration or other suitable purification procedures. Distilled water is a form of purified water. (see USP monograph) ¹⁰⁷
Safety data sheet	Formerly known as a material safety data sheet, the safety data sheet is a summary document providing information about the hazards of a product and advice about safety precautions. It is usually written by the manufacturer or supplier of the product. In some circumstances, an employer may be required to prepare a safety data sheet (e.g., when the product is produced and used exclusively in that workplace). The safety data sheet provides more detailed hazard information about the product than the label. It tells users what the hazards of the product are, how to use the product safely, what to expect if the recommendations are not followed, how to recognize symptoms of exposure and what to do if emergencies occur.
WHMIS	Workplace Hazardous Materials Information System

107 United States Pharmacopeial Convention (USP). General chapter <1231>: water for pharmaceutical purposes. In: *USP compounding compendium*. Rockville, MD: USP; 2016. pp. 456-482.



11. LIST OF DIAGRAMS, TABLES, CHECKLIST AND TEMPLATES

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MONITORING FREQUENCY:
MONITORING METHOD:
REVIEW FREQUENCY:
RESPONSIBILITY:



12. BIBLIOGRAPHY

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