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

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1. INTRODUCTION

The NAPRA Model Standards for Pharmacy Compounding of Non-Sterile Preparations have been adapted from standards originally developed by the Ordre des Pharmaciens du Quebec, 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 (NACPP) and involved extensive consultation with experts and stakeholders. The model standards are put in place to ensure patient safety and the safety of personnel involved in compounding non-sterile drugs.

To assist with the implementation of these new standards, this Guidance document has been developed to provide some direction on how to implement these standards. Compounding practices should be reviewed to determine what standards apply. This Guidance document can then be consulted for more details on how these standards can be achieved. The use of other technologies, techniques, materials and procedures may be acceptable, if they are proven to be equivalent or superior to those described in this Guidance document.

2. OBJECTIVES

The aim of this Guidance document is to support the implementation of the 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 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[1, 2], and other policies and guidelines that may be in place in provincial/territorial jurisdictions.

As with all prescriptions, a pharmacist would be expected to review the prescription and use their expertise to determine if this compounded prescription is appropriate for the patient. In addition, the pharmacist and/or pharmacy technician, designated as the compounding supervisor, must determine if they have the appropriate knowledge and resources to develop the formulation and/or the appropriate equipment and competency to compound the preparation. Section 2.1, below, is a guideline which may be helpful in making this determination. Once it has been determined that it is appropriate to compound the preparation, the model standards for pharmacy compounding of non-sterile preparations should be applied.

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

[2] National Association of Pharmacy Regulatory Authorities (NAPRA). *Model standards of practice for Canadian pharmacy technicians.* Ottawa, ON: NAPRA; 2011. Available from: http://napra.ca/pages/PharmacyTechnicians/pharmacytechniciansstandards.aspx

2.1. General Guideline on whether or not to compound a preparation

- Are the active ingredients already available in a manufactured product?
- Do you have a referenced formulation?
- Do you have the BUD/stability data?
- Do you have a clean and uncluttered dedicated space for compounding?
- Do you have the appropriate equipment and ingredients to make the compounded preparation?
- Are your pharmacy personnel competent to perform the compounding of the preparation?
- Can you compound the preparation without interruption?
- Is this a compounded preparation that should be referred to another pharmacy where they have the appropriate facilities, equipment and expertise?

3. REGULATORY FRAMEWORK

While compounded non-sterile preparations are prepared by other health care 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 standards and these guidelines could serve as best practices for other health care practitioners, they pertain specifically to compounding by pharmacy personnel for human or animal use[3] in all pharmacy settings where compounded non-sterile preparations are prepared.

In January 2009, Health Canada developed its "Policy on Manufacturing and Compounding Drug Products in Canada"[4]. It is expected that Health Canada policy will be followed along with these 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 in such a scale, time or frequency.to ensure it is being used within a patient-health care professional relationship. Compounders may also prepare batches of compounded product in limited quantities in anticipation of prescriptions. Requests to compound preparations outside the patient-healthcare professional relationship in bulk quantities for distribution or sale generally fall into the realm of manufacturing, and outside the jurisdiction of pharmacies. The chart below provides general guidelines on differentiating between compounding and manufacturing activities.

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[3] The Canadian Veterinary Medical Association's *Guidelines for the Legitimate Use of Compounded Drugs in Veterinary Practice,* states that the veterinarian is responsible for the safety and efficacy of the prescribed drug and for establishing adequate withdrawal times to avoid residues when it is used in food producing animals.

[4] 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

3.1. General Guideline on Compounding and Manufacturing Activities[5]

1) Is there a demonstrated patient-healthcare professional relationship?

- Compounding - Yes
- Manufacturing - No

2) Is there third-party reselling of the product outside of the patient-healthcare professional relationship?

- Compounding - No
- Manufacturing - Yes

3) Is the activity regulated, and facility possibly inspected, by the province/territory?

- Compounding - Yes
- Manufacturing - No

4) If producing product in anticipation of a prescription, is the amount produced consistent with the history of prescriptions received?

- Compounding - Yes
- Manufacturing - No

5) Is there a large quantity of product produced on a regular basis?

- Compounding - No
- Manufacturing - Yes

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 prior to 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

[5] Modified from Health Canada, Policy on Manufacturing and Compounding Drug Products in Canada (POL-0051), January 26, 2009, Appendix 1.

NAPRA's professional competencies for Canadian pharmacists and pharmacy technicians at entry to practice provide guidance for developing an ethical, legal and professional practice. One of these competencies specifies that a pharmacist or pharmacy technician must seek guidance when uncertain about his or her own knowledge, skills, abilities or scope of practice. Given that pharmacists and pharmacy technicians are expected to maintain competency in basic compounding skills, pharmacists and pharmacy technicians are expected to provide compounded preparations within their level of expertise and within the limitations of available and appropriate facilities and equipment. When individuals do not have the knowledge, training, expertise, facilities or equipment required for compounding complicated non-sterile preparations or hazardous non-sterile preparations, they must refer patients to a colleague who does have the competencies and facilities required to do so or, where permitted by provincial/territorial legislation, ask another pharmacy to compound the preparation for them. The Risk Assessment below in Section 4 and the previously mentioned questions in Section 2.1 provides some information for pharmacists and pharmacy technicians when deciding whether or not to compound.

The Model Standards for Pharmacy Compounding of Non-Sterile Preparations excludes mixing, reconstituting, or any other manipulation that is performed in accordance with the directions for use on the label of a drug approved by Health Canada within the normal practice of pharmacy, as these minor modifications are not classified as "compounding" by Health Canada.[6] However, the minimum conditions for good pharmacy practice should be maintained when performing these activities, and pharmacies are encouraged to follow basic requirements for non-sterile compounding found in this document.

There are federal regulations regarding the compounding of a product that is not a drug such as cosmetics or food, and it is recommended that, in the absence of specific legislation, these model standards be considered best practice for those compounded products.

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. It is essential to consider the accumulated risks of all compounds made in the pharmacy. For example, if small quantities of one preparation are compounded occasionally and it has a low risk then you may be able to mitigate the risk by taking certain steps. However, if small quantities of several different preparations, which individually have a low risk, are compounded within the same timeframe, then the total risk must be considered.

If it is necessary to compound a preparation requiring procedures or processes which are not currently in place in the pharmacy, documentation needs to include what the risks of compounding the product may be, the extra steps which must be taken to mitigate the risks, and the references which state that the steps will actually minimize the risk to the quality of the product and safety of personnel.

For example:

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

- For a complex compound, documentation should include extra measures required, for example, those to ensure uninterrupted workflow, extra verification steps, extra equipment and references.

- If a small quantity of hazardous product is used in compounding, there must be documentation of alternate 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 for each compound. Additional laws and regulations governing the compounding of hazardous preparations and handling of hazardous products exist at the federal/provincial/territorial level and these need to be consulted.

Pharmacies must customize their list of drugs and materials being used, including hazardous drugs and hazardous materials. The requirements for safe compounding of all materials needs be researched, and documented. Some useful references are listed below.

4.1. References for Assessing Risk

References - General
United States Pharmacopeial Convention (USP). *USP pharmacists' pharmacopeia.* Rockville, MD: USP; current version (contains all USP chapters useful to pharmacists, including General Chapter <795>: Pharmaceutical Compounding — Non-Sterile Preparations). https://www.usp.org/compounding
Compounding: Guidelines for Pharmacies, Canadian Society of Hospital Pharmacists, Ottawa, Ontario, 2014. https://www.cshp.ca/compounding-guidelines-pharmacies
PIC/S Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments, Pharmaceutical Inspection Convention, Pharmaceutical Inspection Co-operative Scheme, Geneva, Switzerland, March 2014. https://www.picscheme.org/layout/document.php?id=156
Hazardous Drugs and Hazardous Materials
Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs.* Montréal, QC: ASSTSAS; 2008. Available from: http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html In 2008, the Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS; a joint sector-based association for occupational health and safety in the

health and social services sector in the province of Quebec) published a guide pertaining to the risks associated with handling hazardous drugs and the preventive measures to be applied in a health care facility at the various stages of the preparation, distribution and administration of hazardous drugs.

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

Hazardous Products Act and Regulations
http://laws-lois.justice.gc.ca/eng/regulations/SOR-2015-17/index.html

Schedule 2 of the *Hazardous Products Act* divides hazardous products into two categories of physical hazards (flammable, gas under pressure, explosive) and health hazards. The Health Hazard classes are acute toxicity, skin corrosion/irritation, serious eye damage/eye irritation, respiratory or skin sensitization, germ cell mutagenicity, carcinogenicity, reproductive toxicity, specific target organ toxicity – repeated exposure, aspiration hazard, biohazardous infectious materials, and health hazards not otherwise classified.

NIOSH [2016]. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2016. By Connor TH, MacKenzie BA, DeBord DG, Trout DB, O'Callaghan JP.. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2014-138 (Supersedes 2012-150). https://www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf

The US Department of Health and Human Services, through its Centers for Disease Control and Prevention and the National Institute for Occupational Safety and Health (NIOSH), publishes and updates a list of hazardous drugs. Recognizing that no single approach can cover the diverse potential of occupational exposures to hazardous drugs, NIOSH's approach involves three groups of drugs.

The lists contain the criteria and sources of information for determining whether a drug is hazardous, considering genotoxicity, carcinogenicity, reproductive and developmental effects and organ toxicity. This published list can be used by individual pharmacies to develop their own lists of hazardous drugs that require special handling precautions. A list of hazardous drugs used must be available at the pharmacy. Each of these products needs to be handled and disposed of properly. The NIOSH lists are updated on a regular basis, but all new drugs in the antineoplastic, immunosuppressant and sexual hormones 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.

In addition, NIOSH published an alert on preventing occupational exposure to antineoplastic and other hazardous drugs in 2004.

United States Pharmacopeial Convention (USP). *USP pharmacists' pharmacopeia.* Rockville, MD: USP; 2016(contains many USP chapters useful to pharmacists, including General Chapter <800>: Hazardous Compounding). https://www.usp.org/compounding

Notes: Not all USP chapters are available in the most recent edition. Please reference the more

recent version for the chapter in question. See bibliography for more information on relevant chapter locations.

In February, 2016, USP published 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 July 1, 2018.

Workplace Hazardous Materials Information System (WHMIS) http://www.ccohs.ca/oshanswers/chemicals/whmis_ghs/hazard_classes.html

WHMIS is "a Canada-wide system designed to protect the health and safety of working Canadians by providing information about hazardous materials on the job."[7] It has recently been aligned with the Globally Harmonized System (GHS) for a more uniform world-wide system of hazardous product recognition and information.
In Canada, legislation requires that products used in the workplace that meet the criteria to be classified as hazardous products must be labelled. Labels are the first alert to the user about the major hazards associated with that product, and outline the basic precautions or safety steps that should be taken. There are two main hazardous groups: Physical hazards group based on the physical or chemical properties of the product – such as flammability, reactivity, or corrosivity to metals; and Health hazards group based on the ability of the product to cause a health effect – such as eye irritation, respiratory sensitization (may cause allergy or asthma symptoms or breathing difficulties if inhaled), or carcinogenicity (may cause cancer).
Compounders can refer to WHMIS Safety Data Sheets (SDS) materials. The SDS 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 Safe Handling of Hazardous Drugs,* 2015 Workers' Compensation Board of British Columbia, Available at worksafebc.com

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

4.2. Some of the 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 (ie. allergens)
- Concentration of the ingredients in the product
- Quantity of ingredients being handled

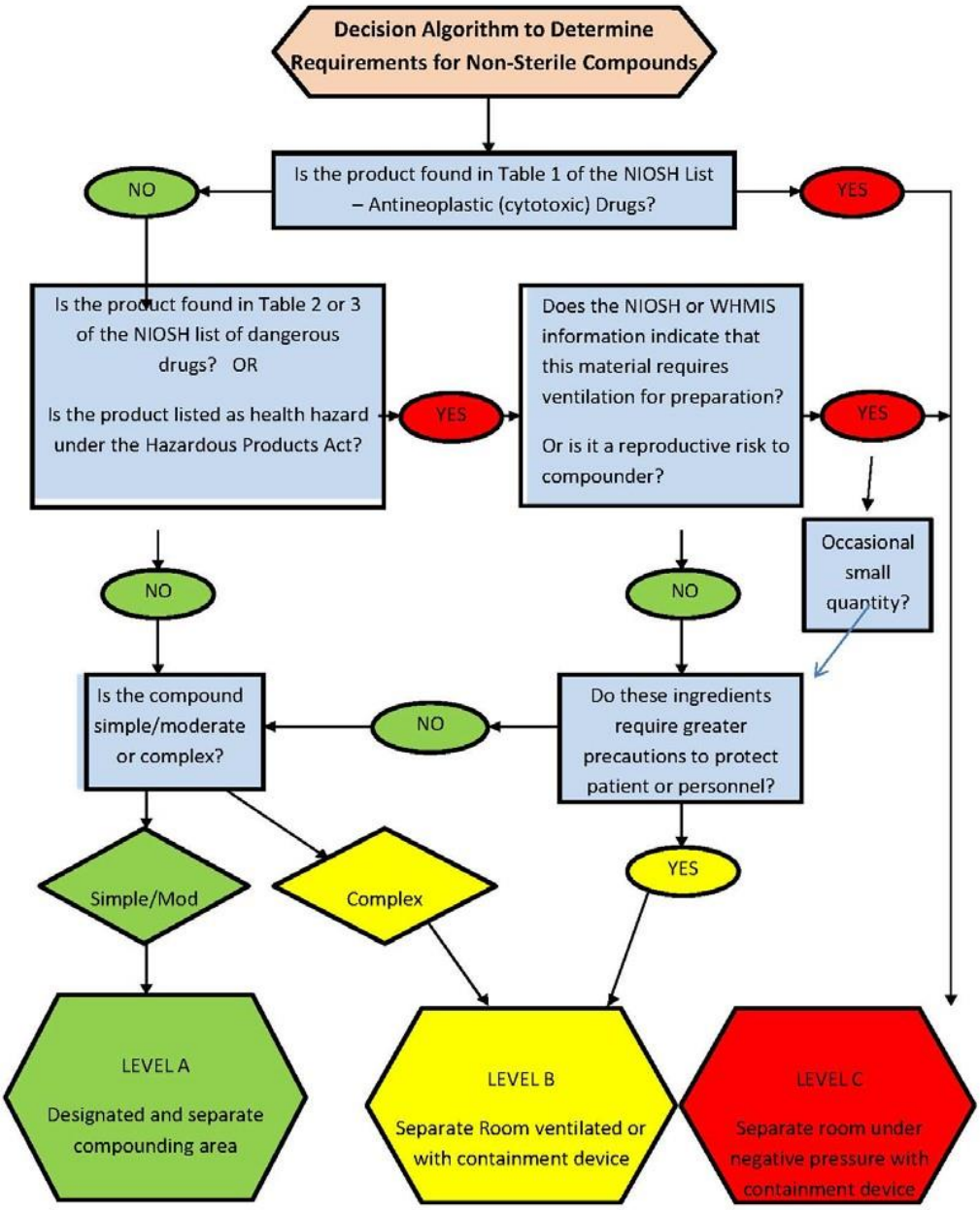
- Physical characteristics of the ingredients such as liquid vs solid vs powders, or water-soluble vs lipid soluble
- Education and competency of compounding personnel
- Availability of appropriate facilities and equipment
- Classification of ingredients as identified by WHMIS[8] as a health hazard or a drug classified by NIOSH as hazardous (See above)
- Type of hazardous drug (ie. anti-neoplastic, non-antineoplastic, reproductive risk only)
- 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)

Assessment of risk 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 below

Note: Occasional small quantities must not be considered in isolation. If you are compounding several different high risk or low risk preparations, then you must consider the cumulative risk, even if they are compounded on different days.

[8] Canadian Centre for Occupational Health and Safety. WHMIS 2015 – Hazard Classes and Categories. Last modified June 17 2016. Available from http://www.ccohs.ca/oshanswers/chemicals/whmis_ghs/hazard_classes.html

4.2.1. Decision Algorithm for Risk Assessment



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

5.1. Compounding Personnel

One pharmacist may be responsible to fulfill all roles and tasks if the pharmacy is small; however, it is best practice to have another person verify calculations and measurements.

5.1.1. Pharmacy manager[9] or pharmacy department head[10]

The pharmacy manager or pharmacy department head is responsible for development, organization and supervision of all activities related to pharmacy compounding of non-sterile preparations. 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 non-sterile preparations as designated 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 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 (ie. personnel training and assessment program) to ensure personnel are competent to perform compounding, which includes training for any specific populations (ie. 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
- Incident/accident reporting and follow-up, as well as recall procedures are in place.
- Policies and procedures covering all activities are developed, regularly reviewed, updated (See Standard 5.3)

[9] In the context of this document, a pharmacy manager in the province of Québec 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.

[10] In the context of this document, the pharmacy department head must be a pharmacist licensed to practice pharmacy by the relevant provincial/territorial pharmacy regulatory authority.

- 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 beyond-use date (BUD) for each non-sterile preparation. (see section 6.1)
- Master Formulation Records are developed, reviewed and updated.
- 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 are also in compliance with provincial/territorial requirements are available. Safety data sheets are available and updated regularly, or 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 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 authority of the pharmacy regulatory authority.

Responsibilities

The compounding pharmacist or pharmacy technician must:

- 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;
- ensure compliance with required rules relating to hygiene, cleanliness and safety;
- ensure that all records related to ongoing activities are completed and 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 preparation prepared including any deviations from the Master Formula;

- ensure the accuracy of calculations and measurements;
- ensure that appropriate equipment and instruments are used for each preparation to be prepared;
- 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 (*see* section 6.6);
- 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 is undertaken by another pharmacy, where 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;
- prior to 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 health care professionals at both facilities to clarify who is responsible for which aspects of patient care and to ensure continuity of care[11].

5.1.4. Non-regulated Pharmacy Personnel

Non-regulated pharmacy personnel with appropriate training[12] can prepare 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 regulatory authority.

Responsibilities

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

[12] Please consult the relevant provincial/territorial pharmacy regulatory authority for any training or supervision requirements defined in each jurisdiction.

The responsibilities of non-regulated pharmacy personnel assigned to prepare 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 person has the appropriate training[13]. 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 for Compounding Personnel

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

Below is a template of skills and abilities to assist in ensuring that personnel have the required competencies. Please use as appropriate in accordance with the regulations and policies in your pharmacy/jurisdiction

#	ELEMENTS TO COVER IN TRAINING OF COMPOUNDING PERSONNEL			
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), 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**
1.8	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	**X**	**X**	**X**

[13] Please consult the relevant provincial/territorial pharmacy regulatory authority for regulatory and/or supervision requirements defined in each jurisdiction.

	used.			
1.9	Be able to recognize errors in the compounding technique of compounding personnel.	**X**	**X**	
1.10	Have a good command of the pharmaceutical calculations required to compound non-sterile preparations.	**X**	**X**	**X**
1.11	Understand the importance of and apply accurate measurements.	**X**	**X**	**X**
1.12	Apply cleaning measures for non-sterile preparation compounding rooms, facilities and materials.	**X**	**X**	**X**
1.13	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**
1.14	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**
1.15	Know and apply quality assurance measures for the various compounded non-sterile preparations.	**X**	**X**	
1.16	Know and follow the verification process.	**X**	**X**	**X**
1.17	Know and use the incident/accident documentation logs.	**X**	**X**	**X**
1.18	Know drug delivery systems.	**X**	**X**	**X**
1.19	Risk Assessment – determine level of risk	**X**	**X**	
1.20	Determine beyond-use date	**X**	**X**	
1.21	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 hazardous products (i.e., receive, unpack, store and deliver hazardous products).	**X**	**X**	
2.8	Know and use the emergency measures to be applied in the case of accidental exposure, accidents or spills.	**X**	**X**	**X**
2.9	Know how to safely destroy hazardous products and the materials used in their preparation.	**X**	**X**	

5.2.1.1. Skills Assessment

A skills assessment program must be established for all personnel involved in non-sterile compounding, which considers the type and complexity of operations performed. Compliance with operating procedures and application of non-sterile compounding techniques must be evaluated regularly and be included in the skills assessment program for compounding personnel. The results of these evaluations and any corrective action taken must be noted in the employee's file. Below is an example of a self-evaluation which personnel could use individually or with each other to assess the compounding process.

Skills Assessment - Compounding Process

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

Compounding steps		**Compliant (✓)**	**Non-compliant (✓)**
1.	Consider if the compounded preparation prescribed is appropriate and safe for the patient, based on the therapeutic intention. (pharmacist)		
2.	Determine if a valid formula exists and if not develop a master formula (pharmacist)in consultation with experts &/or reliable resources. Ensure that the master formula includes instructions regarding special handling considerations		
3.	Calculate and verify the quantities required for each ingredient 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 lab coat or disposable gown		
5.	For preparations that contain hazardous products, ensure 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 prepared 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.	Confirm each ingredient and the quantity with the compounding record through an independent check, before the preparation is compounded.		
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 provincial/territorial regulatory authority:		
a.	All active ingredients and the concentration of each ingredient must be identified on the label.		

b. The BUD 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 is cleaned immediately after use according to manufacturer's directions or standards, and dried		
14. Ensure that the products, ingredients and equipment were put away immediately after use and properly stored.		

5.2.2. Cleaning Personnel

#	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[14, 15]

- Policies and procedures must be established providing detailed descriptions of all activities, including cleaning in the pharmacy's compounding of non-sterile preparations (*see* the following example of policies and procedures). The supervisor must also ensure application of and compliance with these policies and procedures. There is also a Procedure Template below which can be used as a model for developing these procedures.
- All established policies and procedures must be promptly updated whenever there is a change in practice or in standards and any changes are documented. In addition, policies and procedures must be reviewed periodically to ensure currency.

[14] United States Pharmacopeial Convention (USP). General chapter <795>: pharmaceutical compounding — non-sterile preparations. USP 39. Rockville, MD: USP; 2016. pp.31,37.
[15] Pharmacy Compounding Accreditation Board (PCAB). Standard 1.40: Standard operating procedures compliance indicators. In: *PCAB accreditation manual.* Washington, DC: PCAB; 2011. p. 7.

- When compounding hazardous drugs or materials, additional policies and procedures must be developed including the safe receiving, storing, handling, compounding, labelling, transporting and disposal of hazardous drugs and materials. (see Section 9)
- Where 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.).

5.3.1. Examples of policies and procedures

	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/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 and C-PEC	
6.	Deactivation, decontamination and cleaning of the C-PEC	
7.	Receiving, 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	
12.	Storage of products used and final preparations	
13.	Transport and delivery of final preparations (to the patient, to patient care units or to the dispensing pharmacist)	
14.	Recording of preparations in the patient file	
15.	Hazardous waste management (e.g., at the pharmacy, returns from patients or	

		patient care units, instructions to patients)	
	16.	Accidental exposure of personnel to hazardous products (eyewash station, log)	
	17.	Spills and spill management	
	18.	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)	

5.3.2. Procedure Template (included as an example which could be used to develop procedures such as hand hygiene, cleaning compounding areas, storing products etc as found in 5.3.1 above)

Pharmacy name Or Hospital XYZ pharmacy department	**Procedure #** _____ **Revised:** **Yes ☐ No ☐** **Approved by**_____**Date** _____ **Effective date:** _____
Procedure title:	

Aim and objective:

- Describe the objective of the procedure.

Target personnel: Use this section to describe the expected responsibilities for each group that will be affected by this procedure.

- ☐ Non-sterile compounding supervisor
- ☐ Pharmacist
- ☐ Pharmacy technician
- ☐ Non-regulated Personnel
- ☐ Cleaning and disinfecting personnel
- ☐ Other: …….

Required facilities, equipment and material:
Include the following types of information here:

- Facilities and equipment required to apply the procedure, including PPE for compounding personnel.
- Materials (e.g., accessories, instruments) required to apply the procedure.
- APIs 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 compounding should only be used by personnel authorized to compound non-sterile preparations. This space should be designated for compounding, but may also be used in preparing or reconstituting marketed products. When a pharmacy or health care facility compounds 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 compounding.[16]

5.4.1. Facilities for Non-sterile Compounding

5.4.1.1. General

[16] United States Pharmacopeial Convention (USP), General Chapter <797>, Pharmaceutical Compounding- Sterile Preparations, Environmental Quality and Control, 2016.

All compounding must be performed in a separate space specifically designated for compounding of prescriptions. This space shall provide for the orderly placement of equipment and materials to prevent errors.[17] It should be designed and arranged to prevent cross contamination between products, and away from parts of the pharmacy where there is a considerable amount of traffic (aisles, entrance and exit doors, etc.) to avoid contaminating the compounded product with dust and dirt, as well as to avoid interrupting or distracting compounding personnel.[1819] L'Ordre des pharmaciens du Québec produced a video regarding non-sterile compounding which demonstrates, among other things, examples of designated compounding spaces.

Compounding areas must be large enough for personnel to be able to work comfortably and safely, with room to store equipment and products in an orderly manner in ~~a~~ clean and secure surroundings. All components, equipment, and containers shall be stored off the floor, and in a manner to prevent contamination and permit 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 should be conducive to cleaning and contain no areas that are difficult to clean. Special attention should be given to fixtures liable to collect dust (eg. ceiling lamps, plumbing, window frames, wire) and any horizontal surface serving no purpose, which 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 light fixtures should be s located so as to provide a well-lit area to facilitate the compounding process and to allow verification at all stages of compounding.

5.4.1.3. Heating, ventilation and air conditioning system

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

5.4.1.4. Water supply[20]

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

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[17] United States Pharmacopeial Convention (USP) General Chapter <795> pharmaceutical compounding – non-sterile preparations. USP 39. Rockville, MD: USP 2016, p33.

[18] OPQ Non-Sterile Compounded Preparations, Ordre des Pharmaciens du Quebec, Montreal, QC,2011, pg 35. www.opq.org

[19] PIC/S Guide to Good Practices for the Preparartion of Medicinal Products in Healthcare Establishments, Pharmaceutical Inspection Convention, Pharmaceutical Inspection Co-operation Scheme, Geneva, Switzerland, 1 March 2014, p13, www.picscheme.org

[20] United States Pharmacopeial Convention(USP) Chapter <795> Pharmaceutical Compounding – Non-sterile Preparations, USP 39, Rockville, MD, USP 2016; p33.

There should be a sink with hot and cold running water, preferably one made of stainless steel and with touchless controls to supply potable water for hand and equipment washing. The plumbing system shouldl be free of defects that could contribute to contamination of any compounded preparation. Purified water shouldl be used for compounding non-sterile drug preparations when formulations indicate the inclusion of water. Purified water could 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, impermeable 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, should 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 should be established appropriate to the level and type of non-sterile compounding.

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 the compounding instruments and accessories are washed or at least once a day and whenever it appears soiled. The 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 shall 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 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 washed and disinfected between uses, and stored separately to avoid contamination from the cleaning process or equipment.

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 only be used for compounding.

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

5.4.2.1. 1. Routine Maintenance

To ensure their 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 such recommendations.

Equipment, instruments and accessories used for several different preparations must be completely and thoroughly cleaned after compounding to remove all traces of the previous product and any remaining water and solvent, thus preventing any cross-contamination between preparations. After each use and cleaning, the equipment, instruments and other accessories used for compounding should be neatly stored to protect it from contamination. Immediately before compounding operations, equipment should be inspected by the compounder to determine its suitability for use.

All notes made on the maintenance forms should indicate the person doing the maintenance (pharmacist, pharmacy technician, cleaning personnel).

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

5.4.2.2. Cleaning the equipment and instruments

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.

The equipment should be thoroughly cleaned with water and detergent immediately after it has been used for compounding. It is not enough to use only isopropyl alcohol 70% as the cleaning agent. All equipment and accessories should be rinsed with purified water. Cleaning work recommended by the manufacturer should be noted in the maintenance log.

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, and should include the name of the person carrying out the cleaning or calibration**.** This information may also be found in any log used to record information about general pharmacy maintenance (e.g., the dates and times when the temperatures of the refrigerators and freezers used to store drugs are checked, cleaning of the premises and equipment).

6. PRODUCT AND PREPARATION REQUIREMENTS

6.1. Beyond-use date and dating methods

The beyond-use date (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, and therefore their BUDs are assigned on the basis of criteria different from those applied to assigning expiration dates to manufactured drug products. Instead, the compounder shall refer to the manufacturer and the literature for information on stability, compatibility and degradation of ingredients.

Extensive experience in non-sterile compounding and broad scientific knowledge are required to determine a BUD and to interpret the stability data in relation to the actual compounded formulations. The product should be observed at all stages of compounding for signs of instability.

BUDs should be assigned conservatively. When assigning a BUD, compounders shall consult the literature and documentation available on stability in general and on the specific stability of the active pharmaceutical ingredient. When a manufactured drug is used as an active pharmaceutical ingredient, the information provided by the manufacturer may be used as a reference. The manufacturer's expiry date (ED) for a drug should not be used directly as the beyond-use date of the final preparation in which it is an ingredient. As recommended in Table 1 below, the BUD for nonaqueous formulations is not later than the time remaining until the earliest expiration date of any ingredient or 6 months, whichever is earlier. The nature of the ingredient to be used, the compounding method, its degradation mechanisms, compatibility, dosage form, the potential for microbial proliferation in the preparation, the container in which it is packaged, the expected storage conditions, and the intended use and duration of therapy should all be considered and the BUD assigned conservatively.

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, the following table 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 indicated[21]. Drugs or chemicals known to be labile to decomposition will require shorter BUDs.

Table 1

BUD by Type of Formulation*[22]
For Nonaqueous Formulations – The BUD is not later than the time remaining until the earliest expiration date of any API or 6 months, whichever is earlier.
For Water- Containing Oral Formulations – The BUD is not later than 14 days when stored at controlled cold temperatures.
For Water-Containing Topical/Dermal and Mucosal Liquid and Semisolid 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 mold 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

[21] United States Pharmacopeial Convention (USP), Chapter <659> Packaging and Storage Requirements, Rockville, MD, USP 2016.

[22] United States Pharmacopeial Convention (USP), Chapter <795> Pharmaceutical Compounding – Non-sterile Preparations, USP 39, Rockville, MD, USP 2016, p35.

about proper storage. Antimicrobial preservatives should not be used in place of good compounding practices.

6.2. Master Formulation Record

The master formulation record should include all the necessary information to compound a non-sterile preparation.

To ensure preparation quality and safety, the master formulation records should be kept up to date. If any amendment is needed, the change must be made in the master formulation record, provide supporting rationale and references, and compounding personnel must be informed of the change. The development of a new master formulation record must be based on scientific data and appropriate references must be documented.

All master formulation records should be kept together, in hard copy or electronic format, and readily available.

The master formulation record should include all the following information as required to compound the preparation:[23] [24]

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

[23] United States Pharmacopeial Convention (USP), Chapter <795> Pharmaceutical Compounding – Non-sterile Preparations, USP 39, Rockville, MD, USP 2016, p35.
[24] OPQ Non-Sterile Compounded Preparations, Ordre des Pharmaciens du Quebec, Montreal, QC,2011, pg 35. www.opq.org

6.2.1. Template for a Master Formulation Record

TO BE COMPLETED FOR EACH PREPARATION (AS APPLICABLE)

Name of compounded product:	Protocol number and version (e.g., 001-01)
Concentration:	**Effective date:** (dd/mm/yyyy)
Pharmaceutical form:	
	Developed by: _____
Route of administration:	**Verified by:** _____

FORMULA

Ingredients	**Quantities**	**Physical description**	**Other information (e.g. DIN , Lot #, 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 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.

Indicate any requirement for verification by the pharmacist.

Examples:

- 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 pr ocess.

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 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 requirement s of the compounded non-sterile preparation.

Specify the beyond-use date (BUD) for the compounded non-sterile preparation

Indicate the references used to deter mine the BUD.

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:

Sample label

B) When dispensed to a patient In addition to the legally mandated information, ad d: - beyond-use date - precautions and other patient information leaflet	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:	☐ YES	☐ NO
Revised:	(dd/mm/yyyy)	Revised by:		
Change made:		Version number changed:	☐ YES	☐ NO

6.3. Ingredients Used for Non-sterile Compounding– quality and storage

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

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 in 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
- ingredient efficacy
- stability

- compatibility
- toxicity
- information about the patient and disease state
- the prescriber's therapeutic objective
- possible interactions
- treatment duration
- route of administration
- frequency of administration

Purified water[25](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 requires water as an ingredient. A dispenser of bottled water, programmed or unprogrammed and independent of the pharmacy plumbing, cannot currently be recommended for non-sterile compounding because no data is available on whether the quality of the water supplied by these dispensers is maintained during use. Tap water does not meet this standard and must not be used when compounding or reconstituting.

6.3.2. Sources of ingredients

Ingredients used in compounding must come from recognized and reliable sources. Non-sterile preparations should be compounded using approved ingredients that have been assigned a Drug Identification Number (DIN), Active Pharmaceutical Ingredients (APIs) used in a product approved for use in Canada or ingredients that meet the requirements of monographs in a current version of a recognized pharmacopoeia, that is, the United States Pharmacopoeia (USP), European Pharmacopoeia (PhEur), French Pharmacopoeia (PhF), International Pharmacoeia (PhI), British Pharmacopoeia (BP), Canadian Formulary (CF), National Formulary of United States (NF) or Codex-*Schedule B Food and Drugs Act*, in keeping with the recommendations of Health Canada's Policy 0051.[26]

When components of compendial quality are not obtainable, quality ingredients, such as those mentioned in the Food Chemical Codex (FCC) or components of high quality such as those that are chemically pure, analytical reagent grade, or American Chemical Society-certified may be used.[27] However, these components should be used cautiously because the standards for analytical reagents or American Chemical Society-grade materials do not consider whether any impurity present raises human or animal safety concerns.

6.3.3. Quality of ingredients

Quality ingredients (identity, purity) should be chosen for the preparations and documents obtained for this purpose, including the certificates of analysis for the ingredients. The source of all ingredients must be traceable, including lot numbers, expiry dates, and date of receipt in the pharmacy.

If the product is not sourced from a recognized supplier, a qualified laboratory should analyze the product and confirm its identity, purity and quality, based on the requirements of a recognized pharmacopoeia. The analysis results and the certificates should be kept in the

[25] United States Pharmacopeial Convention, Chapter <1231> Water for Pharmaceutical Purposes, USP Compounding Compendium, Feb 2016, p456-462.
[26] Health Canada, Policy on Manufacturing and Compounding Drug Products in Canada, POL-0051, January 26, 2009.
[27] United States Pharmacopeial Convention, Chapter <795> Pharmaceutical Compounding – Non-sterile Preparations, USP 39, Rockville, MD, Feb 2016. p 34.

ingredients log. It should be noted that federal regulations currently prohibit compounding pharmacists in pharmacies from shipping controlled substances ingredients to be analyzed.

Drugs approved by Health Canada (those with a DIN) may be used as active ingredients. When using one of these products, all the ingredients (active and inactive) in the approved drug must be considered.

When components are derived from ruminant animals (eg. bovine, caprine, ovine), the supplier should provide written assurance that the component is in compliance with all federal regulations governing processing, use and importation requirements for these materials. Ingredients that have been recalled or withdrawn from the market for safety reasons should not be used for compounding. Health Canada publishes on its website a list of drugs that have been recalled from the market.

For components that have an expiration date on the container from the manufacturer or distributor, the material may be used in compounding before that expiration date when the material is stored in its original container under conditions to avoid decomposition of the chemicals, when there is minimal exposure of the remaining material each time material is withdrawn from the container, and when any withdrawals from the container are performed by those trained in the proper handling of the material. If the component has been transferred to another container it should be identified with the component name, original supplier, lot or control number, transfer date, and expiration date and shall be at least equivalent integrity to the original container. For ingredients without an expiration date assigned by the manufacturer, the container shall be labelled with the date of the receipt and a conservative expiration date, not to exceed three years after receipt, depending on the nature of the ingredient, the container and storage conditions.[28]

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

6.3.4. Safety Data Sheets

The Safety Data Sheets (formerly known as Material Safety Data Sheets) published by suppliers under the *Hazardous Products Act* are documents providing information about the risks and preventive measures that apply to the use of products and their storage conditions. Safety Data Sheets are available from the supplier or through the Canadian Center for Occupational Health and Safety (CCOHS)[29]. 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 easy to access.

Safety Data Sheets are updated by suppliers every three years. It is therefore important that the dates of the available sheets be verified to ensure that the pharmacy always uses the 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 must be stored and kept safely in conditions

[28] United States Pharmacopeial Convention, General Chapter <795> Pharmaceutical Compounding – Non-sterile Preparations, USP 39, Rockville, MD. Feb 2016. p 34.
[29] For access to Safety Data Sheets, go to: http://ccinfoweb.ccohs.ca/msds/search.html

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, etc.).

The origin of the compounded non-sterile preparation dispensed to the patient should be recorded in the patient file in cases where the preparation was made by another pharmacy, where permitted by provincial/territorial legislation. Any pharmacy (in the health care 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 shall contain:[30]

- official or assigned name, strength, and dosage of the preparation
- Master Formulation Record reference for the preparation
- names and quantities of all components
- sources, lot numbers, and expiration dates of components
- 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 (eg. 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

6.5. Conduct of personnel in compounding areas

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

[30] United States Pharmacopeial Convention (USP), General Chapter <795> Pharmaceutical Compounding – Non-sterile, USP 39, Rockville, MD, USP 2016, p36.

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 soap[31] 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 risk that patients or personnel may be allergic to latex, nitrile or neoprene gloves are preferable.,

✓ wear a clean laboratory coat reserved for compounding. It is highly recommended that a disposable gown be worn for compounding. If a clean laboratory coat is worn for compounding, it should be reserved for making these preparations and not be worn outside the compounding area. When employees leave the compounding area, they should leave their laboratory coats behind. They may put them on again when they return, provided they are clean and unsoiled. Laboratory coats should be changed as soon as they become soiled or according to protocols required. Disposable gowns should be changed every day or as soon as they become soiled.

- ✓ avoid other sources of contaminating the preparation such as hair, long or false nails, jewellery on hands and wrists; chewing gum, having food or drink in the compounding area
- ✓ notify the compounding supervisor if the compounder has an active respiratory tract infection, an eye or skin infection or a hand lesion, etc. to determine the fitness of the person to carry out compounding activities or specific protective measures that should be taken to avoid contamination of the product[32];
- ✓ If indicated on the Master Formulation Record, wear a cap and mask, eye protection and, if applicable, a beard guard.
- ✓ Take any other reasonable measures to prevent cross contamination, and to protect themselves 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 prior to preparation;
- Verify the volume, quantity or weight of the ingredients;
- Verify ingredient information documented on the compounding record
- Review the Master Formulation Record and Compounding Record to ensure errors have not occurred in the compounding process and that the preparation is suitable for useVerify all information on the final label, including beyond-use date, and ensure this information is recorded on the compounding record
- Regularly verify the quality of compounding technique

[31] Hand Hygiene Practices In Healthcare Settings. Public Health Agency of Canada. Tunney's Pasture, Canada. 2012 p33, part C, section 2.2 Available from: http://publications.gc.ca/collections/collection_2012/aspc-phac/HP40-74-2012-eng.pdf

[32] PIC/S Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments, Pharmaceutical Inspection Convention, Pharmaceutical Inspection Co-operation Scheme, Geneva, Switzerland, 1 March 2014, p12, www.picscheme.org

- Verify the integrity of the container and that the container is appropriate for the physical and chemical properties of the compounded preparation to avoid a container-drug interaction[33]
- Approve the final prepared product using factors such as weight, adequacy of mixing, clarity, odor, color, consistency, pH, and analytical testing as appropriate, and sign the compounding record[34]
- 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 the labelling 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 regulatory body.

All active ingredients and the concentration of each active ingredient should be identified on the label. The label should include the BUD, and 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 labeled. In these cases, the dispensing pharmacy should keep all of the records from the compounding pharmacy (such as the 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, 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 should provide all information required for proper use of the drug by the patient or for safe administration by a third party including:

- pharmacy identification (name, address and telephone number of the compounder's or dispenser's pharmacy 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 required by provincial/territorial legislation and regulations regarding the labelling of medications 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

[33] United States Pharmacopeial Convention (USP) General Chapter <795> pharmaceutical compounding – non-sterile preparations, USP 39, Rockville, MD, USP 2016, p36.
[34] ISMP Canada Safety Bulletin Vol 17, Issue 5, May 25, 2017

the refrigerator door"; "Keep out of reach of children");

- any special precautions for disposal or destruction of the preparation;

6.7.3. Packaging process and procedure

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

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., temperature, fragility, safety) and instructions (name and address of patient) on the outside packaging of each item.

6.8. Storage[35,36]

A storage procedure should be developed and followed at all times.

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

Active and inactive ingredients and finished products should always be put away on receipt. They must be handled and put away 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, pharmacy, delivery vehicle, unloading dock for deliveries, carrier, etc.). The temperature of the premises (pharmacy, warehouse, etc.) should be controlled and remain within the limits indicated in the chart below regardless of the season. Information on monitoring of room, refrigerator and other temperatures and controls related to implementation of the storage procedure should be recorded in the general maintenance log[37].

6.8.1. Temperatures for different types of storage

Storage type	Temperature range
Freezing	–25°C to –10°C*
Refrigeration (cold)	2°C to 8°C*

[35] United States Pharmacopeial Convention (USP), General Chapter <797>, Pharmaceutical Compounding- Sterile Preparations. USP 39, Rockville, MD, USP 2016. p65-69

[36] United States Pharmacopeial Convention (USP). General Chapter <1079>: good storage and shipping practices. USP 39, Rockville, MD, USP 2016. p351-360

[37] United States Pharmacopeial Convention (USP). General chapter <1079>: good storage and shipping practices. USP 39, Rockville, MD, USP 2016. p351-360.

Refrigeration (cool)	8°C to 15°C*
Controlled room temperature	15°C to 20°C†
Drug conservation temperature	15°C to 30°C

*United States Pharmacopeial Convention (USP). General notices and requirements. In: *USP pharmacists' pharmacopeia.* Rockville, MD: USP; 2008. p. 29.
†United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

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 expiration 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 transportation and delivery must be developed which meet provincial regulatory requirements, and include any special precautions regarding the transport of compounded non-sterile preparations[38] [39] and their delivery to patient care areas, pharmacists, pharmacies, health care 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 health care facility should also address 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 (temperature, fragility safety) and the information required for delivery to the patient (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.

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Where compounding is undertaken by another pharmacy, where 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.

[38] Transportation of Dangerous Goods Act, 1992 (S.C. 1992, c. 34): http://laws-lois.justice.gc.ca/eng/acts/T-19.01/page-1.html
[39] Transportation of Dangerous Goods Regulations: http://www.tc.gc.ca/eng/tdg/clear-tofc-211.htm

6.10. Product Recalls

When 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 procedure should be in place to:

- identify patients or pharmacies who 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 information about individual units or batches of compounded non-sterile preparations recorded in the patient file and the compounding log should be sufficient to allow users to track recipients of compounded non-sterile preparations.

The pharmacy's procedure for recall should include procedures for recall of compounded non-sterile preparations.

The causes of the problem leading to the recall should be reviewed, and corrective and preventive measures should be identified and implemented, regardless of the location of the pharmacist's or pharmacy technician's practice.

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 health care facilities or community pharmacies, a form developed or selected by the facility or pharmacy may be used. (*see* an example below).

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

6.11.1. Incident / accident reporting and follow-up form

Accident/accident* reporting and follow-up	
Reporting an incident ☐ accident ☐	
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: ☐			
Name of pharmacist responsible for follow-up:			
Analysis of causes			
Causes: (Identify causes of the problem)	Options for corrections or changes: (Assess potential corrections or changes to be made)	Corrections or changes chosen: (Indicate the corrections or changes to be made)	
Action plan			
Actions (Describe the actions to be taken and the steps required to correct the situation, with a specific timeline. Determine who will be responsible for implementation.)	**Responsible**	**Deadline**	✓
Monitoring			
Verifications (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 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 that will affect the quality of 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), facilities and equipment needed, personnel involved, and extent of compounding. Each verification carried out according to the quality assurance program needs to be documented. An example of possible components of a quality assurance program is provided at the end of this section.

7.2. Quality Assurance of equipment and compounding areas

7.2.1. Certification

Equipment that supports compounding activities, especially refrigerators, and air sampling instruments when required, 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., refrigerator, freezer,) is used to review temperatures 24 hours a day, the temperature log of equipment should be checked at least once a day in case of substantial variance with respect to specified parameters, and corrective action taken.

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 and Processes

Compounding personnel need to be trained/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 in the case of contamination.

7.4. Quality assurance - procedures

A 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 federal/provincial/territorial regulations.

- Situations of non-compliance (where action is required), deviations from protocols, and missing documentation should be investigated;
- corrective and preventive actions should be taken; and,
- 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

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

COMPONENT	CONTROLS	FREQUENCY
FACILITIES	Verification of compounding area (Level A) (clean, orderly, good state of repair, appropriate storage, space reserved for compounding etc)	• 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 C) (appropriate ventilation, materials storage, clean, orderly, good state of repair)	• 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 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	• Monthly
EQUIPMENT	Certification of C-PEC (Level B or C)	• 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)	• Verify logs monthly or more often if problems identified

		• Yearly calibration of temperature probes
	Operational indicators of C-PEC and other instruments (ie automated compounding)	• Verify logs monthly
PERSONNEL	Skills assessment (technique, following procedures, appropriate PPE, etc)	• 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)	• Yearly when being used, or when new information becomes available.
	Verification that preparation matches Prescription, protocols are followed, ingredients verified, preparation is assessed for clarity, odor, color, consistency, and labelling/container are appropriate	. Quarterly review of documentation
	Verification that documentation of procedures, compounders initials, entry in logs are being carried out.	• Quarterly review of documentation
DOCUMENTATION	Policies and procedures in place and updated regularly	• Every 3 years, or when new information becomes available
	Compounded prescription records meet all regulatory requirements, all logs current in documentation	• Quarterly
	Current references and safety data sheets available	• Yearly

8. LEVELS OF REQUIREMENTS

USP 795 Categories – Non-sterile Preparations

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 as per Health Canada policy

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

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 into three levels: A, B and C. Many non-sterile preparations in the USP categories simple or moderate can be compounded following Level A requirements for the facilities, equipment and protective wear. Other non-sterile preparations may need additional requirements; therefore, it is necessary to examine many factors in order to assess the associated risk of using a certain substance and determine the appropriate level of requirements. For example, it would be possible to compound a non-sterile simple preparation, which contains a drug categorized by NIOSH as hazardous (ie. clonazepam, carbamazepine), and follow Level A requirements, if the hazardous drug is in a small quantity and has the physical characteristics conducive to minimizing contamination of the immediate area and risk to the personnel. Pharmacists need to undertake a risk assessment and identify the appropriate level of requirements needed to guarantee a quality product and adequate protection for personnel. A summary of requirements has been included for ease of reference.

8.1. Level A

Level A refers to requirements to be met when compounding simple and moderate preparations as defined in USP 795, excluding mixing or reconstituting in accordance with Health Canada's policy on compounding.[40] Requirements for Level A include a separate compounding area as well as the general requirements for procedures and equipment.

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

[40] Health Canada, Health Products and Food Branch Inspectorate. *Policy on manufacturing and compounding drug products in Canada.* POL-051. Ottawa, ON: Health Canada; 2009. Available from: http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/docs/pol_0051-eng.php
United States Pharmacopeial Convention (USP) General Chapter <795> pharmaceutical compounding – non-sterile preparations, USP 39, Rockville, MD, USP 2016, p36.

Many non-sterile preparations can be compounded within Level A requirements. This could also include simple or moderate preparations containing hazardous drugs in NIOSH group 2 or 3, or materials designated as health hazardous by the *Hazardous Products Act* which pose little or no risk for compounding personnel when compounded in occasional small quantities. This would be a small quantity which has been determined to be a low risk to compounders in a particular instance at the pharmacy with appropriate precautions being taken.

USP 795 Categories – Non-sterile Preparations Continued

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 systems] dosage forms, modified-release preparations, and some inserts and suppositories for systemic

8.2. Level B

Level B refers to requirements which should be met when making complex compounded preparations defined in USP 795, or when small quantities of products which require ventilation or other precautions are compounded. These compounded preparations require more specialized equipment, instruments and training.

In addition to the requirements for Level A, Level B requires 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 when certain powders, aromatic products or other hazardous products are compounded. These include drugs such as allergenic products or products which could have unintended effects such as hormones, but may not require the extensive precautions of Level C in small quantities. If a ventilated containment device is used, the pharmacy should follow the same requirement as 9.2.3.1.

As the complexity of the non-sterile preparation increases, so do the requirements for compounding a quality product which 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 little, or preferably, no interruptions. In addition, if ingredients which could be irritating to personnel such as powders are frequently used, or materials which require some hazardous safety measures are used, further requirements are necessary to produce quality products and to protect compounding personnel**.**

8.3. Level C

Level C refers to requirements which should be met when compounding any amount and all dosage forms of hazardous drugs which are classified by NIOSH[41] as Group 1 or hazardous materials classified by WHMIS[42] as a health hazard such as those very irritating to the

[41] National Institute for Occupational Safety and Health (NIOSH), NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2014. Available from : http://www.cdc.gov/niosh/docs/2014-138/

[42] WHMIS at http://www.hc-sc.gc.ca/ewh-semt/occup-travail/whmis-simdut/index-eng.php

United States Pharmacopeial Convention (USP) General Chapter <795> pharmaceutical compounding – non-sterile preparations, USP 39, Rockville, MD, USP 2016, p36.

respiratory tract, the skin and the mucous membrane. It may also apply to NIOSH group 2 and 3 drugs where large quantities of APIs are used routinely, and depending on the risk assessment.

Requirements for Level C include a room under negative pressure, a ventilated containment device and personal protective equipment appropriate for handling hazardous products. These requirements are detailed in section 9

NIOSH [43]

The National Institute for Occupational Safety and Health (NIOSH) has prepared a list of antineoplastic and other hazardous drugs, and divided them into three groups.

Group 1 of the NIOSH list includes antineoplastic drugs (or cytotoxic drugs). The majority are also hazardous to males or females who are actively try to conceive, women who are pregnant or may become pregnant, and women who are breast feeding, because they may be present in breast milk. These drugs represent an occupational hazard to healthcare workers and should always be handled with the use of recommended engineering controls and personal protective equipment (PPE), regardless of their formulation (intravenous, subcutaneous, topical, tablet or capsule). Examples of drugs in this category are chlorambucil, cyclophosphamide, fluorouracil, hydroxyurea, methotrexate, tamoxifen.

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

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

NIOSH performs hazard identification on each of the drugs. The actual risk to health care 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 personal protective equipment (PPE) are used.

[43] National Institute for Occupational Safety and Health (NIOSH), NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2014. Available from : http://www.cdc.gov/niosh/docs/2014-138/

Hazardous Products Act[44]

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 *Hazardous Products Act* divides hazardous products into two categories of physical hazards (flammable, gas under pressure, explosive) and health hazards. The Health Hazard classes are acute toxicity, skin corrosion/irritation, serious eye damage/eye irritation, respiratory or skin sensitization, germ cell mutagenicity, carcinogenicity, reproductive toxicity, specific target organ toxicity – 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, that is, the compounder's exposure to the product. The precautions listed in Level A (separate area, attire) or Level B requirements (attire, room or hood ventilated to the outside, etc.) may, therefore, be adequate for small quantities of hazardous products or those with led hazard risk. However, stricter preventive measures, that is Level C requirements may be necessary to compound very hazardous materials with a health risk such as those that are very irritating to the respiratory tract, the skin, and the mucous membranes.

[44] Government of Canada, *Hazardous Products Act. http://laws-lois.justice.gc.ca/eng/acts/H-3/*

8.4. Summary of requirements for compounded non-sterile preparations

REQUIREMENTS		Level A	Level B	Level C
		Mandatory = ✓		
Personnel:	**Sec 7.1**			
Appoint a non-sterile compounding supervisor		✓	✓	✓
Training:	**Sec 7.2**			
Has received orientation and training during education or on the job concerning the preparations to be compounded and had a skills assessment when hired. The training 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 compounding all non-sterile dosage forms				✓
An annual skills assessment program must be implemented.		✓	✓	✓
Facilities:	**Sec.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 could be simple, moderate or complex, but the level of precautions needed is more dependent on the risk posed by the hazardous product, rather than the complexity of the preparation. Small quantities of simple or moderate preparations containing products classified by NIOSH or WHMIS as hazardous may sometimes be compounded in a pharmacy with Level A requirements, with additional precautions, depending on the risk as determined in section 5 and reviewed annually.

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

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 penetration[45].

Absorption through the skin occurs by direct contact with contaminated surfaces or objects. Ingestion occurs by eating foods that might have been contaminated or by putting contaminated hands or objects, particularly pens, into the mouth[46] [47]. Inhalation of vaporized drugs can also be a source of contamination[48]. Therefore; the compounding of hazardous non-sterile preparations requires the implementation of safety measures to protect personnel and the environment. NIOSH has created a Hierarchy of Controls diagram which depicts the various levels of controls which can be implemented. https://www.cdc.gov/niosh/topics/hierarchy/

In the pharmacy of a health care facility, a hazardous drugs committee[49] should be established when hazardous drugs or materials are compounded. 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, the skin and the mucous membranes requires the precautions of Level C. Level C requires compounding in a closed-off room under negative pressure with filtered air

[45] American Society of Health-System Pharmacists. ASHP guidelines on handling hazardous drugs. *Am J Health Syst Pharm*. 2006;63(12):1172-93.
[46] American Society of Health-System Pharmacists. ASHP guidelines on handling hazardous drugs. *Am J Health Syst Pharm*. 2006;63(12):1172-93.
[47] Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs.* Montréal, QC: ASSTSAS; 2008. Available from: http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html
[48] American Society of Health-System Pharmacists. ASHP guidelines on handling hazardous drugs. *Am J Health Syst Pharm*. 2006;63(12):1172-93.
[49] Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs.* Montréal, QC: ASSTSAS; 2008. Available from: http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html

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 in which there is no risk of cross-contamination with the hazardous materials before compounding other preparations. Detailed requirements for Level C are included in the remainder of this section.

9.1. Facilities for handling hazardous products[50] (Level C)

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, with other applicable standards regulating the construction of government buildings.

In addition to previously stated requirements such as adequate space for compounding and sufficient lighting (section 5), hazardous non-sterile preparations should be compounded in a separate room. For less hazardous products, this could be level B requirements with a well-ventilated room and in some cases, a ventilated containment device and extra PPE, and for hazardous products with greater health risk, this would require Level C precautions of a separate room under negative pressure. The risk assessment 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 worker and environmental hazardous product exposure when directly handling hazardous products. 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:[51]

1. Be externally vented through high-efficiency particulate air (HEPA) filtration
2. Be physically separate from other preparation rooms
3. Have an appropriate air exchange of at least 12 ACPH
4. Have a negative pressure of – 2.5 Pa relative to surrounding areas.

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

Due to the difficulty of cleaning hazardous product contamination, 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 non-shedding.

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

[51] United States Pharmaceopeial Convention, Chapter <800> Hazardous Drugs – Handling in health care settings, USP39, Rockville, MD, USP 2016, p88 (Chapter to become official July 1, 2018)

9.1.2. Heating, ventilation and air conditioning system for controlled rooms

The room should be vented to the outside though HEPA filters, have an air exchange of at least 12 ACPH, and have a negative pressure to contain the hazardous products and minimize the risk of exposure. Consideration should be given to an uninterrupted power source for the ventilation systems to maintain negative pressure in the event of power loss.

An air conditioning system should be included in the HVAC system to help ensure the comfort of personnel wearing personal protective equipment (PPE). The temperature of the room should be less than or equal to 20°C, taking into account employees' comfort once all personal protective equipment has been donned.

9.1.3. Windows and 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. If any doors lead to the outside or to a non-controlled area (other than the doors designated for accessing the room), they should be sealed. An environmental control procedure and a housekeeping procedure, including the cleaning of sealed windows and doors, should be implemented by cleaning personnel.

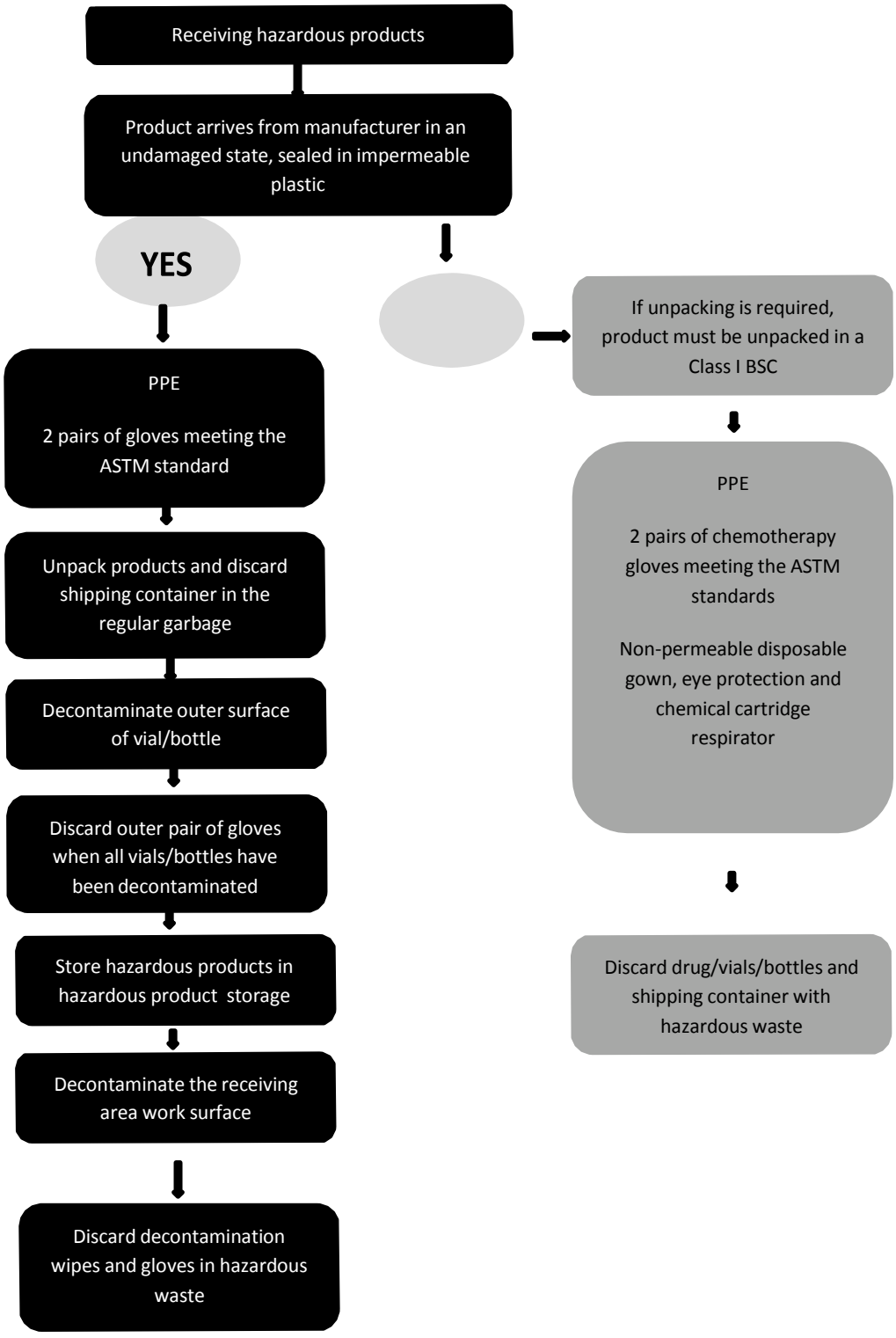
9.1.4. Area for unpacking hazardous products

If a hazardous product arrives from the manufacturer in an undamaged state, sealed in impermeable plastic, then no special precautions are necessary in the area[52], however two pairs of ASTM International–approved gloves should be worn by personnel doing the unpacking.

If a hazardous product arrives in a damaged state and unpacking is required, a C-PEC will be needed. The C-PEC may be used just for unpacking the damaged product, or it could also be used for the compounding of non-sterile hazardous preparations[53]. Personnel should wear PPE recommended in 9.2.3. A procedure for unpacking is included below.

[52] United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings [draft]. USP39, Rockville, MD, USP 2016, p88 (Chapter to become official July1, 2018).
[53] United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings [draft]. USP39, Rockville, MD, USP 2016, p88 (Chapter to become official July1, 2018).

Receiving, unpacking and storing hazardous products



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 exterior[54]. The storage area should have negative pressure relative to the adjacent rooms and should have at least 12 ACPH. It should be identified with the proper signage to indicate the presence of hazardous products[55]. Additional requirements for a hazardous products storage area are listed in the table below.

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[56]
Storage spaces for hazardous products and preparations identified with the proper signage to indicate the presence of hazardous products[57]
Sufficient ventilation to prevent contamination from spreading to adjoining rooms[58]

Alternatively, hazardous non-sterile preparations and the refrigerator in which they are stored may be placed in the room for compounding non-sterile hazardous preparations. This approach

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

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

[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. p. 6-4. Available from: http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html

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

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

ensures that the drugs are stored in a negative pressure room with sufficient ACPH (since the room has 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 (example; pictograms indicating cytotoxicity, the need for special care, hazards, restricted access, dress code, etc)

9.2. Equipment for handling hazardous products

9.2.1. Containment Primary Engineering Control(C-PEC)

The containment primary engineering control (C-PEC) is installed in the compounding room, and should be either externally vented (preferred) 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 personnel and environmental protection such as a Class I Biological Safety Cabinet (BSC) [59, 60, 61, 62] or a Containment Ventilated Enclosure (CVE).[63] 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 compounded.

For occasional non-sterile hazardous product compounding, a C-PEC used for sterile compounding (e.g., Class II BSC or CACI) may be used but 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 non-sterile hazardous product compounding does not require unidirectional airflow because the environment does not need to be ISO classified.[64]

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

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[65] [66]. If there is a loss of power to the C-PEC or moving or repair occurs, all activities occurring in the C-PEC should be

[59] CDC, NIOSH ALERT – Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings, DHHS-CDC (NIOSH), No. 2004-105, September 2004, p.15.
[60] ASHP, ASHP Guidelines on Handling Hazardous Drugs, Am J Health-Syst Pharm. 2006; 63:1172-93.
[61] McElhiney, LF, Preparing Non-sterile & Sterile Hazardous Compounds in an Institutional Setting, IJPC, Vol. 13, No. 4, July/August 2009, p. 303.
[62] ASSTSAS, Prevention Guide – Safe Handling of Hazardous Drugs, ASSTSAS 2008, p. 8-9.
[63] United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings USP 39, Rockville, MD: USP; 2016 Feb (to become official July 1, 2018)
[64] United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings USP 39, Rockville, MD: USP; 2016 Feb (to become official July 1, 2018) p.88
[65] Occupational Safety and Health Administration (OSHA). *OSHA technical manual (OTM): controlling occupational exposure to hazardous drugs*. Section VI, Chapter 2. Washington, DC: US Department of Labor; 1999. Available from: https://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html
[66] United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings USP 39, Rockville, MD: USP; 2016 Feb (to become official July 1, 2018)

suspended immediately. Once the C-PEC can be powered on, decontaminate and clean all surfaces and wait for the manufacturer-specified recovery time before resuming compounding.[67]

The work surface of the C-PEC should be resistant to damage from cleaning, disinfecting, deactivating 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 should be reviewed and corrective measures taken, as appropriate. The supervisor should sign the maintenance form or log.

9.2.2. Other instruments or accessories related to the compounding of hazardous non-sterile preparations

All reusable instruments and accessories used to handle hazardous products should be deactivated, decontaminated, and cleaned.[68] Instruments and accessories to be used in controlled rooms should not be removed without good reason. If they should be removed, they should be decontaminated.

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

9.2.3. Personal protective equipment (PPE)[69]

PPE adapted and approved for the compounding of hazardous non-sterile preparations should 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

[67] United States Pharmacopeial Convention (USP). General Chapter <800>: hazardous drugs — handling in health care settings USP 39, Rockville, MD: USP; 2016 Feb (to become official July 1, 2018)p88

[68] United States Pharmacopeial Convention (USP). General Chapter <800>: hazardous drugs — handling in health care settings USP 39, Rockville, MD: USP; 2016 Feb (to become official July 1, 2018) p94

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

- deactivating, decontaminating and cleaning the C-PEC
- compounding of hazardous preparations
- managing a spill
- disposal of hazardous products

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

Glove changes

Both pairs of gloves should be discarded and replaced at the earliest of; manufacturer limit for permeation of the gloves, every 30 minutes[70] [71] [72][73], immediately if a tear, puncture or contamination has occurred or is suspected.

Gown

When gowns are required, they should be disposable and shown to resist permeability by hazardous products. Gowns should be selected based on the hazardous products handled. 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), be long sleeved and have fitted cuffs at the wrists.

The gown should be discarded and replaced at the earliest of; the manufacturer's time limit of permeation of the gown or after 2–3 hours of continuous[74, 75] compounding work or 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 occurred[76].

Cloth laboratory coats, surgical scrubs, isolation gowns, or other absorbent materials are not appropriate protective outwear because they permit the permeation of hazardous products and can hold spilled products against the skin. Clothing may also retain hazardous residue and may transfer to other healthcare workers or various surfaces. Washing of non-disposable clothing contaminated with hazardous product residue should only be done according to policy as the hazardous product residue may transfer to other clothing. Potentially contaminated clothing should not be taken home under any circumstances.[77]

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

[71] 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.

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

[73] United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings USP 39, Rockville, MD: USP; 2016 Feb (to become official July 1, 2018)

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

[75] United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings [draft]. Rockville, MD: USP; 2016 Feb. (to become official July 1, 2018) p91.

[76] United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings [draft]. Rockville, MD: USP; 2016 Feb. (to become official July 1, 2018) p95.

[77] United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings USP 39, Rockville, MD: USP; 2016 Feb (to become official July 1, 2018) p90

Head, hair, shoe and sleeve covers[78]

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 contaminated[79]. 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 hazardous drug handling areas should not be worn to other areas to avoid spreading hazardous drug contamination and exposing other healthcare workers. Disposable sleeve covers, preferable 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 from hazardous drug exposure is required.

For most activities, a fit-tested N95 or N100 mask (NIOSH approved) will protect against airborne particles; however, N95 or N100 masks offer no protection from vapours, gases and little protection from liquid splashes. A full-facepiece chemical cartridge-type respirator or a powered air-purifying respirator (PAPR) 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 in the process of deactivating, decontaminated and cleaning underneath the work surface of a C-PEC.

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

Eye and Face Protection

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

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 requires 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.

[78] United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings USP 39, Rockville, MD: USP; 2016 Feb (to become official July 1, 2018) p91

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

The compounding area, equipment and accessories should be meticulously cleaned immediately after preparations containing hazardous products or allergenic ingredients (sulfonamides, penicillins, etc.) have been compounded. It is strongly recommended that equipment be set aside especially for compounding each of these classes of products, and if possible, disposable equipment should be used to reduce chances of bioburden and cross- contamination[80].

Policies and procedures for cleaning and 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 contamination[81]. Only trained and qualified cleaning and disinfecting personnel should be allowed to clean controlled rooms.

9.3.1. Surface deactivation, decontamination and cleaning[82]

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

Deactivation

Deactivation renders a compounded preparation inert or inactive. Residue from deactivation should be removed by decontaminating the surface. Products that have known deactivation properties (EPA-registered oxidizing agents that are appropriate for the intended use) should be used when possible. Care should be taken when selecting materials for deactivation due to potential adverse effects such as hazardous by-products or caustic damage to surfaces

Decontamination

Decontamination occurs by 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.

Cleaning

Cleaning is a process that results in the removal of contaminants (e.g., soil, microbial contamination, hazardous product residue) from objects and surfaces using water, detergents, surfactants, solvents, and/or other chemicals. Cleaning agents should not introduce microbial contamination.

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

9.3.2. Garbing of cleaning personnel

Cleaning personnel must comply with the pharmacy's hand hygiene and garbing procedure before entering hazardous product compounding areas and performing housekeeping duties.

[80] United States Pharmacopeial Convention (USP), Chapter <795> Pharmaceutical Compounding – Non-sterile Preparations, USP 39, Rockville MD, USP 2016; p 34.

[81] United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings USP 39, Rockville, MD: USP; 2016 Feb (to become official July 1. 2018) p92

[82] United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings

USP 39, Rockville, MD: USP; 2016 Feb (to become official July 1. 2018)p94-95

9.3.3 Surface deactivation, decontamination and cleaning of the containment primary engineering control [83]

The work surface of the C-PEC must be deactivated, decontaminated and cleaned between compounding 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 voluntary interruption occurs and if the ventilation tool is moved.

C-PECs may have areas under the work tray where contamination can build up and these areas should be deactivated, decontaminated, and cleaned at least monthly to reduce the contamination level in the C-PEC. Deactivate, decontaminate, and clean as much as possible of the C-PEC surfaces before accessing the area under the work tray. When deactivating, decontaminating, and cleaning the area under the work tray of a C-PEC, the containment airflows are compromised by opening the cabinets and respiratory protection may be required to perform this task.

Decontamination, deactivation and cleaning tasks performed should be recorded in the general maintenance log.

9.4. Incident and accident management

9.4.1. Accidental exposure[84]

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 center 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 must be established to prevent spills and to direct the clean up of hazardous product spills, addressing size and scope of the spill, as well as 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.

Spill kits

[83] United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs — handling in health care settings USP 39, Rockville, MD: USP; 2016 Feb (to become official July 1. 2018) p94-95.

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

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

9.4.3. 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 health care facilities or community pharmacies, a form developed or selected by the facility/pharmacy may be used (see section 6.10 for an example).

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

9.5. Hazardous waste management

A procedure for the destruction of pharmaceutical waste must be developed and implemented to ensure that hazardous products are:

- disposed of safely in compliance with the environmental protection laws in force in the jurisdiction; and.
- safely stored in a location separate from other medications in inventory 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 products.[85] A list of hazardous products in use must be available in the pharmacy. The list produced by NIOSH, which is part of the US Centers for Disease Control and Prevention[86] or WHMIS materials can be used to determine if a particular product is hazardous. Each pharmacy should customize a list for their own use as some drugs may be available in Canada and not the US or new drugs may be available after the NIOSH list is published.

Policies and procedures for the management of hazardous waste[87] 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:

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

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

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

- All personnel involved in the management of hazardous product waste should receive appropriate training on destruction procedures to ensure their own protection and to prevent contamination of the premises or the environment[88].
- All equipment, products and vials used in the compounding of hazardous preparations should be discarded in a hazardous waste container.
- Hazardous waste containers should be identified with a self-adhesive label marked "Hazardous waste – cytotoxic"[89]. Containers should be filled to only three-quarters of their capacity[90]. 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 may not be sent for decontamination by autoclave and subsequent burial.

9.6. Verification of controlled rooms and the containment primary engineering control (CPEC)

9.6.1. Certification

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

- at least every 6 months[91];
- during installation of new equipment or a new controlled area;
- during maintenance or repair of equipment (repair of C-PEC, ventilation system, etc.) or a controlled area (repair of hole in a wall, etc.) that might alter environmental or operational parameters;
- when investigation of a contamination problem or a problem involving non-compliance in handling of hazardous products requires exclusion of malfunctioning facilities.

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[88] United States Pharmacopeial Convention (USP). General chapter <800>: hazardous drugs- handling in healthcare settings. USP 39. Rockville, MD: USP; 2018, Feb (to become official July 1, 2018)

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

[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. 12-3. Available from: http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html

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

- The 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 shall 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 reception, 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 compounding 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 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 should the pressure deviate from specifications.

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

Hazardous product contamination/Wipe sampling

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

Sampling should occur in the various sites, 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 on previous monitoring.

A baseline assessment should precede any preventive measure put in place (as described in the ASSTSAS guide[92]), 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 maintenance log.

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

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.

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

10. Abbreviations and Glossary of Terms[93,94,95,96,97,98,99, 100]

Term or Abbreviation	Definition
ACPH	Air changes per hour
Active Pharmaceutical Ingredient (API)	Any substance or mixture of substances intended to be used in the manufacture of a drug (medicinal) product and that, when used in the production of a drug, becomes an active ingredient of the drug product which has a pharmacological activity in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body.
Inactive ingredient excipient	Ingredients that are necessary to compound a preparation but are not intended or expected to cause a pharmacological response in humans if administered alone in the amount or concentration contained in a single dose of the compounded preparation.
ASSTSAS	Association paritaire pour la santé et la sécruité du travail du secteur affaires sociales, a joint sector-based association dedicated to occupational health and safety in the health and social services sector within the province of Quebec
ASTM	American Society for Testing and Materials
Beyond-use date (BUD)	The BUD is the date after which a compounded preparation shall not be used and is determined from the date when the preparation is compounded.
Biological safety cabinet (BSC)	Laminar airflow workbench that is ventilated to protect personnel, hazardous sterile compounded preparations and the immediate environment. The open front of a BSC has the following features: • Air intake, to protect compounding personnel from hazardous sterile preparations;

[93] Health Canada, Policy on Manufacturing and Compounding Drug Products in Canada (POL-0051), January 26, 2009,
[94] Bussières J.F., Législation et système de soins, 5th edition, August 2009, p. 171.
[95] United States Pharmacopeial Convention (USP). General Chapters 795, 797, 800, 1072. USP Rockville, MD: USP; 2016
[96] Commission de la santé et de la sécurité du travail (CSST). *Material safety data sheet user's guide.* CSST; 2010. Available from: http://www.csst.qc.ca/en/prevention/reptox/whmis/material-safety-data-sheet-users-guide/pages/table-contents.aspx
[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. Available from: http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html
[98] National Institute for Occupational Safety and Health (NIOSH). NIOSH alert: preventing occupational exposures to antineoplastic and other hazardous drugs in health care settings. Publ. No. 2004-165. Atlanta, GA: Department of Health and Human Services, Centers for Disease Control and Prevention, NIOSH; 2004 Sep. Available from: http://www.cdc.gov/niosh/docs/2004-165/pdfs/2004-165.pdf
[99] Canadian Nurses Association (CNA). *Joint position statement: Promoting continuing competence for registered nurses.* Ottawa, ON: CNA; 2004. Available from: http://www.cna-aiic.ca/~/media/cna/page-content/pdf-en/ps77_promoting_competence_e.pdf
[100] *Controlled Products Regulations,* SOR/88-66, 1987. Available from: http://laws-lois.justice.gc.ca/eng/regulations/SOR-88-66/

	• Descending air curtain filtered with a high-efficiency particulate air filter to protect the hazardous sterile product; • Air evacuation system equipped with high-efficiency particulate air filters for environmental protection.
Biomedical Refrigerator	Refrigerator designed to refrigerate biological and medical products and drugs. It often comes with an integrated temperature control system and an alarm system.
CACI	Compounding Aseptic Container 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 containment primary engineering control is a ventilated device designed to minimize worker and environmental hazardous product exposure when directly handling hazardous products. For hazardous non-sterile compounding, containment primary engineering controls include biological safety cabinets (BSCs).
Containment Secondary Engineering Control (C-SEC)	A containment secondary engineering control (C-SEC) is the room in which the C-PEC is placed.
Containment system	Arrangement or equipment to contain the particles of hazardous products in the chosen space.
CSST	Commission de la santé et de la sécurité du travail
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 (ex. counter, bag of solution) to a disposable surface (ex. wipe, cloth). The wipe 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, lead to a developmental or reproductive toxicity or damage organs. Drugs are considered hazardous because they involve risks for the worker, because of their effects.

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 *Hazardous Products Regulations*.
Hazardous products	Substances that entail risks for the worker because of their effects. For the purposes of these Model Standards, the term "hazardous product" refers to both hazardous drugs and hazardous materials, depending on the situation.
HEPA	High-efficiency particulate air
HVAC	Heating, ventilation and air conditioning
ISO	International Organization for Standardization
NIOSH	National Institute for Occupational Safety and Health
Non-regulated pharmacy personnel	A person who is employed in a pharmacy to assist the pharmacist or pharmacy technician.
OPQ	Ordre des pharmaciens du Quebec
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	(see USP monograph) Is used as an excipient in the production of nonparenteral 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, reserves osmosis, filtration, or other suitable purification procedures. (Distilled water is a form of Purified Water)
Safety data sheet (SDS)	Data Sheets (SDSs) which were formerly known as material safety data sheets, are summary documents that provide information about the hazards of a product and advice about safety precautions. SDSs are usually written by the manufacturer or supplier of the product. In some circumstances, an employer may be required to prepare an SDS (e.g., when the product is

	produced and used exclusively in that workplace). SDSs provide more detailed hazard information about the product than the label. SDSs tell 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

11. Bibliography

Note to readers: The references cited in these Model Standards reflect the references appearing in the source document, "Préparation de produits non stériles en pharmacie – Norme 2011.04," published by the Ordre des pharmaciens du Québec, 2011. Where possible, certain details have been verified against the source documents. URLs for online documents are current as of June 16, 2016.

ACP, *Standards of Practice for Pharmacists and Pharmacy Technicians*, Standard 10, Alberta College of Pharmacists, July 1, 2011.

ACP, *Patient Self-Care: Helping Your Patients Make Therapeutic Choices*, 2nd edition, ACP, 2010, p. 552.

Agence national de sécurité du médicament et des produits de santé (ANSM), *Bonnes pratiques de préparation*, December 3, 2007.

Allen Jr. LV , Standard Operating Procedure: Basic Compounding Documentation – The Master Form, IJPC, Vol. 11, No. 3, May/June, p 240-241.

ANSI. Z358.1-2014 ***Emergency Eyewash and Shower Equipment. 2014.***

APES*, Recueil des informations en oncologie*, October 2004, 284 pages. Website consulted on May 22, 2008: http://www.apesquebec.org/membres/comites/ronc/GuideFr/GuideComplet200310.pdf.

ASHP, ASHP Technical Assistance Bulletin on Compounding Non-Sterile Products in Pharmacies. *Am J Hosp Phar*.1994;51:1441-8.

ASHP, ASHP Guidelines on Handling Hazardous Drugs. *Am J Health-Syst Pharm*. 2006; 63:1172-93.

ASQ, Quality Assurance and Quality Control, www.asq.org, consulted on June 10, 2016.

ASSTSAS, *Prevention Guide – Safe Handling of Hazardous Drugs*, ASSTSAS, 2008.

BCP, *Professional Practice Policy: Standards for Technician Verification of Non Sterile Products in Hospital Pharmacy Practice*. British Columbia College of Pharmacists, www.bcpharmacists.org, consulted on June 10, 2016..

Bussières J.F., Prot S. Perspectives sur les préparations magistrales en pharmacie au Québec. Pharmactuel, Vol.37, Dossier 1, May/June/July 2004, p 4-15.

Bussières J.F., Législation et systèmes de soins : Recueil de textes choisis et commentés. JF Bussières, August 2009.

Cabaleiro J., Quality Control, Quality Assurance and Quality Improvement – What is the Difference and Why Should Compounding Pharmacies Care. IJPC, Vol. 13, No. 4, July/August 2009, p 318-320.

CCOHS, Canadian Centre for Occupational Health and Safety. Site: www.ccohs.ca, consulted on June 17, 2016

Collectif, Antiseptiques et désinfectants, C.CLIN, Paris Nord, May 2000.

CPBC, Bylaws of the Council of the College of Pharmacists of British Columbia, Bylaw 5, Section 30 – Equipment and References, p. 10. Website: http://www.bcpharmacists.org/library/D-Legislation_Standards/D-2_Provincial_Legislation/5076-HPA_Bylaws.pdf, consulted on June 10, 2016.

CSST, List of Agents Causing Occupational Asthma: (2014): ,http://www.csst.qc.ca/en/prevention/reptox/occupational-asthma/Documents/AgentsAnglais.pdf, Consulted on June 17, 2016.

CSST, List of Agents Causing Occupational Asthma (preliminary draft 2016): http://www.csst.qc.ca/en/prevention/reptox/occupational-asthma/Documents/AgentsAnglais-2015.pdf, Consulted on June 17, 2016

CSST, Notions de toxicologie. http://www.reptox.csst.qc.ca/Documents/PlusEncore/Notions/HTM/Notions.htm, consulted on June 17, 2016.

CSST, Service du répertoire toxicologique, http://www.reptox.csst.qc.ca, consulted in August 2010.

Fillmaster Systems/Flavor Master, website: http://www.fillmastersystems.com, consulted on June 15, 2016.

Fontaine L., Manipulation des produits potentiellement dangereux en pharmacie communautaire, OPQ, Informations professionnelles, No. 138, October 2003.

Government of Canada, *Hazardous Products Act. Hazardous Products Regulations. http://laws-lois.justice.gc.ca/eng/regulations/SOR-2015-17/index.html*

Government of Canada, National Fire Code, Canadian Commission on Building and Fire Codes. National Research Council Canada, Ottawa, 2005.

Government of Ontario, O. Reg. 58/11 under *Drug and Pharmacies Regulation Act, R.S.O. 1990, c. H.4* https://www.ontario.ca/laws/regulation/110058#BK23, consulted on June 17, 2016.

Government of Quebec, *Act respecting Occupational Health and Safety* [R.S.Q., chapter S-2.1]. Éditeur officiel du Québec. (2016). Section 51, 62.1 to 62.6

Government of Quebec, Code of ethics of pharmacists, c. P-10, r. 7 (2016)

Government of Québec, *Hazardous Products Information Regulation,* c. S-2.1, r. 8.1 (2016)

Government of Quebec, Regulation respecting the keeping of records, books and registers by a pharmacist in the practice of his profession, chapter P-10, r. 23 (2016).

Government of Quebec, Regulation respecting the labelling of medications and poisons c. P-10, r. 15 (2016).

Gouvernement of Quebec. *Regulation respecting Occupational Health and Safety*. R.R.Q., c. S-2.1, r. 13 (2016) s. 41, 42, 45, 47, Section VII, Section X

Hildgen P., Que faire quand on n'a pas de recette?. Québec Pharmacie, Vol. 40, No. 7, July/August 1998, p 674-675.

Huffman D.C., Holmes ER, Specialty Compounding for Improved Patient Care: 2006 National Survey of Compounding Pharmacists, IJPC, Vol.12, No. 1, January/February 2008, p 74-82.

IACP, Code of Ethics, International Academy of Compounding Pharmacists, http://www.iacprx.org/?page=6, consulted on June 15, 2016

IJPC, Gap Analysis for US Pharmacopeia 795 – Compounding Non-Sterile Preparations, 2008.

Jeffrey M., Is Your Cleanroom Clean? An In-Depth at Cleaning and Disinfecting Agents, Procedures and Requirements for the Compounding Pharmacist, IJPC, Vol. 10, No. 2, March/April 2006, p113-119

Krochmal L., Considerations before Choosing (Extemporaneously) Compounded Products. Dermatologic Therapy, Vol. 22, 2009, p 225-228.

Kupiec T., Huerta PL, Analytical Testing of Extemporaneously Compounded Preparations, IJPC, Vol. 4, No. 2, March/April 2000, p 105-107.

Larin S., Le matériel de base nécessaire à la formulation de préparations magistrales, Québec Pharmacie, Vol. 40, January/February 1993, p 90-92.

McAteer, F., Points to consider for developing a UPS-797 compliant clieaning and sanitization program, http://electroiq.com/blog/2007/08/points-to-consider-for-developing-a-usp-797-compliant-cleaning-and-sanitization-program/. Consulted on June 16, 2016McElhiney L.F.,

Preparing Non Sterile & Sterile Hazardous Compounds in an Institutional Setting, IJPC, Vol. 13, No. 4, July/August 2009, p 300-310.

McElhiney L.F., Non-sterile Compounding: An Overview of United States Pharmacopeia Chapter <795> & American Society of Health System Pharmacists Guidelines, IJPC, Vol. 13, No. 6, November/December 2009, p 525-530.

McElhiney L.F., Records and Record-Keeping for the Hospital Compounding Pharmacist, IJPC, Vol. 11, No. 2, March/April 2007, p 138-143.

McElhiney L.F., Information Resources and Software for the Hospital Compounding Pharmacist, IJPC, Vol. 11, No. 1, January/February 2007, p 36-41.

MSSS, La qualité des vaccin j'y tiens: Guide des normes et pratiques de gestion des vaccins, Publications Québec, 1999, p 21-25.

MSSS, Guide: La qualité de l'air intérieur dans les établissements du réseau de la santé et des services sociaux. Publications Québec, 2005.

Mullarkey T., Pharmacy Compounding of High-Risk Products and Patient Safety, Am J Health-Syst Pharm, Vol. 66, Sept. 1, 2009, Suppl. 5, p S4-S13.

NAPRA, Guidelines to Pharmacy Compounding, October 2006.

Nahata M.C., Allen Jr. LV, Extemporaneous Drug Formulations, Clinical Therapeutics, Vol. 30, No. 11, 2008, p 2112-2119.

NIOSH, NIOSH Alert – Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings, DHHS/CDC (NIOSH) Publication No. 2004-165, September 2004, 50 pages.

NIOSH, Workplace Solutions: Personal Protective Equipment for Health Care Workers Who Work with Hazardous Drugs, DHHS/CDC (NIOSH), Publication No. 2009-106, October 2008.

NIOSH, Workplace Solutions: Medical Surveillance for Health Care Workers Exposed to Hazardous Drugs. DHHS/CDC (NIOSH), Publication No. 2007-117, April 2007.

NIOSH, NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings 2010, DHHS/CDC (NIOSH), Publication No. 2010-167, September 2010.

http://www.cdc.gov/niosh/docs/2010-167/pdfs/2010-167.pdf, consulted on September 9, 2010.

Okeke C.C., Allen LV, *Basics of Compounding: Considerations for Implementing United States Pharmacopeia Chapter <797> Sterile Preparations, Part 4: Considerations in Selection and Use of Disinfectants and Antiseptics*. IJPC, Vol. 11, No. 6, November/December, 2007, p 492-499.

OPQ, Norme 2012.01, Préparation magistrales non stériles en pharmacie. January 10, 2012

OPQ, Norme 95.01 : La préparation des produits stériles en pharmacie, Informations professionnelles, No. 74, June 1995.

OPQ, Mémoire sur le projet de loi no 38: Loi sur le Commissaire à la santé et au bien-être, February 20, 2004, p 6-8.

OPQ, Norme 89.01 : La détermination de la date de péremption réelle des médicaments servis / vendus en exécution ou non d'une ordonnance (reviewed in November 1994), Informations professionnelles, No. 68, December 1994.

OPQ, Guide des soins et services pharmaceutiques: http://guide.opq.org.

Ordre des chimistes du Québec, The Chemical Institute of Canada Laboratory Health and Safety Guidelines. 4th edition, 2003.

Ordre des chimistes du Québec, Guide de santé et de sécurité au laboratoire. 4th edition. 2002.

OSHA, Controlling Occupational Exposure to Hazardous Drugs. OSHA Technical Manual. Section VI, Chapter 2, www.osha.gov, consulted in October 2009.

PEI, Health Canada Manufacturing and Compounding Drug Products in Canada: A Policy Framework Guidelines for P.E.I. Community and Hospital Pharmacists, October 2001.

Rossington K., Cleaning of Isolators: A Vital Part of a Contamination Control Program, IJPC, Vol. 8, No. 6, November/December 2004, pp 452-45.6.

Health Canada, Policy on Manufacturing and Compounding Drug Products in Canada, Health Products and Food Branch Inspectorate, Pol-0051, January 2009.

Health Canada, Questions and Answers on Bottled Water, website: www.hc-sc.gc.ca, consulted on 2008/06/27.

CSHP, Compounding Guidelines for Pharmacies, Official Publications 2014.

Shematek G, Wood W, Laboratory Safety. CSMLS Guidelines. 6th edition, 2006.

USP, USP Chapter <797> Complete Review of the revisions, Webinar series, February 2008.

USP, Pharmaceutical Compounding – Non-sterile Preparations, USP Pharmacist's Pharmacopeia, General Chapter 795, USP, 16, p 31-38.

USP, Pharmaceutical Compounding – Sterile Preparations, UPS Pharmacist's Pharmacopeia, Supplement 2, General Chapter 797, USP, 2016, p 84.

USP, Good Compounding Practices, USP Pharmacist's Pharmacopeia, General Chapter 1075, second edition, USP, 2008-2009, pp 866-869.

USP, Thermometers, UPS Pharmacist's Pharmacopeia, General Chapter 21, second edition, USP, 2008-2009, p 705.

USP, Volumetric Apparatus, USP Pharmacist's Pharmacopeia, General Chapter 31, USP, 2016. P163-164.

USP, Weights and Balances, UPS Pharmacist's Pharmacopeia, General Chapter 41, USP, 2016, p 164-165

USP, Prescription Balances and Volumetric Apparatus, UPS Pharmacist's Pharmacopeia, General Chapter 1176, second edition, USP, 2008-2009, p 946-947.

USP, Stability Considerations in dispensing Practice, USP Pharmacist's Pharmacopeia, General Chapter 1191, UPS, 2016, p 411-416.

USP, Quality Assurance in pharmaceutical Compounding, USP Pharmacist's Pharmacopeia, General Chapter 1163, second edition, USP, 2008-2009, 943-946.

USP, Disinfectants and antiseptics, UPS Pharmacist's Pharmacopeia, General Chapter 1072, UPS, 2016, p 346-351

USP, Good Storage and Shipping Practices, USP Pharmacist's Pharmacopeia, General Chapter 1079, 2016, p 351-360

USP, Water for Pharmaceutical Purposes, USP Pharmacist's Pharmacopeia, General Chapter 1231, 2016 p 456-482.

USP, General Notices and Requirements, USP Pharmacist's Pharmacopeia, 2016. 17-29

Add a Table of Charts for printing as Appendix