

Model Standards for Pharmacy Compounding of Non-Sterile Preparations

DRAFT 5b

National Association of Pharmacy Regulatory Authorities

(adapted with permission from “Préparation magistrales non stériles en pharmacie – Norme 2012.01,” Ordre des pharmaciens du Québec, 2012)

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Table of Contents

1. INTRODUCTION.....	7
2. OBJECTIVES	7
3. REGULATORY FRAMEWORK.....	8
4. ABBREVIATIONS	9
5. LEVELS OF REQUIREMENTS NECESSARY FOR NON-STERILE COMPOUNDED PREPARATIONS.....	10
5.1 BACKGROUND.....	10
5.2 LEVELS OF REQUIREMENTS	11
5.3 ASSESSING RISK FOR COMPOUNDING NON-STERILE PRODUCTS.....	13
6. REQUIREMENTS FOR ALL LEVELS OF NON-STERILE COMPOUNDING ACTIVITIES	14
6.1 Personnel.....	14
6.1.1 Roles and responsibilities	14
6.1.2 Training and assessment	18
6.2 Policies and procedures'	19
6.3 Facilities and equipment	19
6.3.1 General remarks	19
6.3.2 Physical Layout	20
6.3.3 Equipment for Non-sterile Compounding	21
6.4 General maintenance log	23
7. PRODUCT AND PREPARATION REQUIREMENTS.....	23
7.1 Beyond-use date and dating methods.....	23
7.2 Compounded Non-sterile Preparation Master Formulation Record	25
7.3 Ingredients Used for Non-sterile Compounds– quality and storage	26
7.3.1 Safety Data Sheets	26

7.3.2 Selection of ingredients.....	26
7.3.3 Sources of ingredients.....	27
7.3.4 Quality of ingredients.....	27
7.3.5 Ingredients log.....	28
7.4 Compounding Record.....	28
7.5 Conduct of personnel in compounding areas	29
7.5.1 Verification of final compounded non-sterile preparations.....	30
7.6 Labelling and Packaging	31
7.6.1 Labelling of final compounded non-sterile preparations.....	31
7.6.2 Packaging process and procedure.....	32
7.7 Storage	32
7.7.1 General conditions	32
7.8 Transport and delivery of compounded non-sterile preparations	33
7.9 Product Recalls	34
7.10 Incident and accident management	34
7.11 Veterinary Preparations.....	35
8. QUALITY ASSURANCE PROGRAM.....	36
8.1 Program content	36
8.2. Quality Assurance of equipment and compounding areas	36
8.3 Quality Assurance of Personnel and Processes	37
8.4 Quality assurance of compounded non-sterile preparations.....	37
8.5 Documentation of quality control activities	38
9. SOURCE FOR ADDITIONAL INFORMATION.....	38
10. REQUIREMENTS FOR COMPLEX PREPARATIONS AND HAZARDOUS PREPARATIONS (SIMPLE, MODERATE AND COMPLEX).....	38
10.1 Complex Preparations.....	38
10.2 Hazardous Preparations	39

10.3 Facilities and equipment for handling hazardous products (Level C)	40
10.3.1 Compounding Rooms	40
10.3.2 Heating, ventilation and air conditioning system for controlled rooms	41
10.3.3 Windows and openings	41
10.3.4 Area for unpacking hazardous products	41
10.3.5 Area for storing hazardous products.....	42
10.3.6 Signage	42
10.3.7 Equipment	43
10.4 Deactivating, Decontaminating, Cleaning in areas reserved for the compounding of hazardous non-sterile preparations	47
10.4.1 General	47
10.4.2 Garbing of cleaning personnel	48
10.4.3 Surface deactivation, decontamination and cleaning of the containment primary engineering control ...	48
10.5 Incident and accident management	49
10.5.1 Accidental exposure	49
10.5.2 Spills	49
10.5.3 Incidents and accidents	49
10.6 Hazardous waste management	50
10.7 Verification of controlled rooms and the containment primary engineering control (CPEC)	51
10.7.1 Certification	51
10.7.2 Certificate provided by manufacturer (in factory)	51
10.7.3 Environmental verification	52
10. GLOSSARY	53
11. LIST OF TABLES	57
13. APPENDICES	58
APPENDIX I GENERAL GUIDELINE ON COMPOUNDING AND MANUFACTURING ACTIVITIES.....	58
APPENDIX 2 DECISION ALGORITHM TO DETERMINE REQUIREMENTS FOR NON-STERILE COMPOUNDS	59
APPENDIX 3 SUMMARY OF REQUIRED CONDITIONS FOR NON-STERILE COMPOUNDING PREPARATIONS.....	60
APPENDIX 4 TRAINING OF COMPOUNDING PERSONNEL AND CLEANING PERSONNEL.....	62
APPENDIX 5 POLICIES AND PROCEDURES FOR THE COMPOUNDING OF NON-STERILE PREPARATIONS.....	65
APPENDIX 6 PROCEDURE TEMPLATE.....	67

APPENDIX 7 REFERENCES	69
APPENDIX 8 COMPOUNDING PROCESS (self-evaluation)	71
APPENDIX 9 TEMPLATE FOR A MASTER FORMULATION RECORD TO BE COMPLETED FOR EACH PREPARATION... ..	73
APPENDIX 10 PROCEDURE EXAMPLE	79
APPENDIX 11 TEMPERATURES FOR DIFFERENT TYPES OF STORAGE.....	80
APPENDIX 12 INCIDENT/ACCIDENT REPORTING AND FOLLOW-UP FORM.....	81
APPENDIX 13 EXAMPLE COMPONENTS OF A QUALITY ASSURANCE PROGRAM	83
14. BIBLIOGRAPHY	85

1. INTRODUCTION

The “Guidelines to Pharmacy Compounding” published by the National Association of Pharmacy Regulatory Authorities (NAPRA) in October 2006 have recently been reviewed, resulting in a new set of documents: the NAPRA Model Standards for Pharmacy Compounding of Non-hazardous Sterile Preparations¹; the Model Standards for Pharmacy Compounding of Hazardous Sterile Preparations²; and, the Model Standards for Pharmacy Compounding of Non-Sterile Preparations.

The new 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. These model standards are put in place to ensure patient safety and the safety of staff involved in compounding non-sterile drugs.

2. OBJECTIVES

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

These Model Standards represent the **minimum** requirements to be applied in compounding non-sterile preparations; however, it is always possible to exceed these standards. The use of other technologies, techniques, materials and procedures may be acceptable, if they are proven to be equivalent or superior to those described here.

These Model Standards support NAPRA’s Model Standards of Practice for Canadian Pharmacists and Pharmacy Technicians^{3, 4}, as well as other policies and guidelines that may be in place in provincial/territorial jurisdictions.

¹ National Association of Pharmacy Regulatory Authorities (NAPRA), Model Standards for Pharmacy Compounding of Non-hazardous Sterile Preparations, November 2015. Available from: http://napra.ca/Content_Files/Files/Mdl_Stnds_for_Pharmacy_Compounding_NonHazardous_Sterile_Preparations_Dec2015_FINAL.pdf

² National Association of Pharmacy Regulatory Authorities (NAPRA), Model Standards for Pharmacy Compounding of Hazardous Sterile Preparations, Draft 4, March 2015

³ 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

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

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 of pharmacists. Although these standards could serve as best practices for other health care practitioners, they pertain specifically to pharmacists, pharmacy technicians and pharmacies where compounded non-sterile preparations are prepared.

The preparation of medications by compounding has always been an integral part of the practice of pharmacy. It is essential to the delivery of health care and allows for personalized therapeutic solutions to improve patient care. However, compounding must always be carried out within a prescriber–patient–pharmacist relationship, or in the case of a non-prescription drug, within a pharmacist-patient relationship where the drug is prepared for a particular patient. Provincial/territorial pharmacy regulatory authorities are responsible for regulating a pharmacy’s compounding services in these situations.

In situations involving requests to compound preparations outside of a prescriber–patient–pharmacist relationship, in the absence of a patient-specific prescription, the preparation activities fall under the federal legislative framework. For example, the bulk preparation of non-sterile compounds in the absence of a prescriber–patient–pharmacist relationship would fall under the federal legislative framework, namely *the Food and Drugs Act (FDA)* and *the Controlled Drugs and Substances Act (CDSA)*.

Health Canada is the federal department responsible for the FDA and the CDSA and their associated regulations. In January 2009, Health Canada developed its “Policy on Manufacturing and Compounding Drug Products in Canada”⁵. It is expected that Health Canada policy will be followed along with these Model Standards. At the time these Model Standards were prepared, Health Canada was examining this policy with a view to creating new standards for situations not covered within the practice of pharmacy or under the current federal licensing framework, such as commercial compounding manufacturing. [Appendix 1](#) provides general guidelines on differentiating between compounding and manufacturing activities.

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. There is a basic level of compounding that is expected of all pharmacists and pharmacy technicians. However, individuals who do not have the knowledge, training, expertise, facilities or equipment required for compounding more complex non-sterile preparations or hazardous non-sterile preparations 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.

Pharmacists and pharmacy technicians must also comply with any federal regulations regarding the compounding of any non-drug product such as cosmetics, food or dietary products, and it is recommended that these model standards be considered best practice for those compounded products.

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

In addition, the pharmacy standards for non-sterile compounding also apply to compounded preparations intended for animals. Pharmacists preparing non-sterile compounds for animals are expected to have the background knowledge to provide this service.

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 Level A requirements found in this document.

4. ABBREVIATIONS

The following abbreviations are used in this document.

Abbreviation	Definition
ABHR	Alcohol-based hand rub
ACD	Automated compounding device
ACPH	Air changes per hour
API	Active Pharmaceutical Ingredient
ASSTSAS	Association paritaire pour la sante et la securite 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
BP	British Pharmacopoeia
BSC	Biological safety cabinet
BUD	Beyond-use date
CACI	Compounding Aseptic Container Isolator
CCOHS	Canadian Centre for National Occupational Health and Safety
CF	Canadian Formulary
Codex	Pharmaceutical Codex: Principles and Practice of Pharmaceuticals
C-PEC	Containment Primary Engineering Control
CSST	Commission de la sante et de la securite du travail

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

CVE	Containment Ventilated Enclosure
DIN	Drug Identification Number
CETA	Controlled Environment Testing Association
GMP	Good Manufacturing Practice
HEPA	High-efficiency particulate air
HVAC	Heating, ventilation and air conditioning
ISO	International Organization for Standardization
LAFW	Laminar airflow workbench
NF	National Formulary (United States)
NIOSH	National Institute for Occupational Safety and Health
OPQ	Ordre des pharmaciens du Quebec
PAPR	Powered Air-purifying Respirator
PhEur	European Pharmacopoeia
PhF	French Pharmacopoeia
PPE	Personal protective equipment
USP	United States Pharmacopeia
WHMIS	Workplace Hazardous Materials Information System

5. LEVELS OF REQUIREMENTS NECESSARY FOR NON-STERILE COMPOUNDED PREPARATIONS

5.1 BACKGROUND

Compounded non-sterile preparations* include, but are not limited to the following types of medications:

- oral liquids (solutions, suspensions, emulsions)
- creams and ointments
- other topical products (gels, lotions, powders, emulsions)
- suppositories
- lozenges, mouthwashes, lollipops, troches
- sachets, oral powders

- tablets, capsules

*Some of these products can also be made as sterile products when sterility is necessary, such as in the case of applying ointments to burn patients⁷.

All compounded preparations are for the use of individual patients in a given population upon or in anticipation of a prescription written within the framework of an ongoing pharmacist/patient/prescriber relationship or in the case of non-prescription medications or where provincial legislation permits, within the framework of an ongoing pharmacist/patient relationship.

Non-sterile compounded preparations must be made with approved ingredients that have been assigned a Drug Identification Number (DIN), or active pharmaceutical ingredients (API) used in a product approved for use in Canada or ingredients that meet the requirements of a current version of a recognized pharmacopoeia, that is USP, PhEur, PhF, PhI, BP, CF, NF and Codex-*Schedule B Food and Drugs Act*, in keeping with [Health Canada's Policy 0051](#). In addition, some of these compounded products contain hazardous products (hazardous drugs or hazardous materials that are very irritating to the respiratory tract, the skin and the mucous membranes according to WHMIS⁸). These products require specialized equipment and procedures appropriate for handling hazardous products.

5.2 LEVELS OF REQUIREMENTS

The requirements for compounding activities have been separated into levels in order to implement the conditions required to ensure that non-sterile compounding is completely safe for patients and pharmacy personnel. The levels of requirements have been based on the complexity and risks associated with preparing the compound and handling the substances used to make the compound.

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*). Examples include Captopril Oral Solution, Indomethacin Topical Gel, and Potassium Bromide Oral Solution, Veterinary.

* 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. Examples include Morphine Sulfate Suppositories, diphenhydramine hydrochloride troches, and mixing two or more manufactured cream products when the stability of the mixture is not known.

⁷ National Association of Pharmacy Regulatory Authorities (NAPRA), Model Standards for Pharmacy Compounding of Non-hazardous Sterile Preparations, November 2015 Available from: http://napra.ca/Content_Files/Files/Mdl_Stnds_for_Pharmacy_Compounding_NonHazardous_Sterile_Preparations_Dec2015_FINAL.pdf

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

The levels of requirements for the compounding of non-sterile preparations apply to preparations intended for both humans and animals.

Level A refers to requirements which need to be met when making simple and moderate compounds as defined in USP 795, excluding mixing or reconstituting in accordance with Health Canada's policy on compounding.⁹ 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.

Most non-sterile compounding can be done within Level A requirements. This could also include simple or moderate compounds containing hazardous drugs in NIOSH group 2 or 3, or materials designated as hazardous by WHMIS which pose little or no risk for compounding personnel when compounded in small quantities.

Requirements for Level A include a separate compounding area as well as requirements outlined in [section 6](#).

Level B refers to requirements which must be met when making complex compounds as defined in USP 795. These compounds require more specialized apparatus, instruments and training.

Level B also includes requirements for some hazardous materials as categorized by WHMIS or hazardous drugs such as those included in NIOSH Groups 2 and 3. 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. There may also be some substances included in groups 2 and 3 from NIOSH which may pose a greater risk and need to meet Level C requirements.

USP 795 Categories – Non-sterile Preparations cont.

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 dosage forms, modified-release preparations, and some inserts and suppositories for systemic effects.

NIOSH

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) which may also pose a reproductive risk to susceptible persons.

Group 2 are non-antineoplastic drugs that meet one or more NIOSH criteria for a hazardous drug and may pose a reproductive risk to susceptible persons.

Group 3 drugs primarily pose a reproductive risk.

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.

⁹ 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

Requirements for Level B include a dedicated well ventilated room to provide adequate space for the equipment and procedures, storage of products and to provide an uninterrupted workflow. If hazardous products, are being used, the room must also be ventilated to the outside, or have a ventilated containment device. More requirements are detailed in [section 10](#).

Level C refers to requirements which must be met when compounding any amount and all dosage forms of hazardous drugs which are classified by NIOSH¹⁰ as Group 1 or hazardous materials classified by WHMIS¹¹ as very irritating to the respiratory tract, the skin and the mucous membrane. It may also apply to NIOSH group 2 and 3 drugs 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. Requirements are detailed in [section 10](#)

WHMIS

Whenever any of the hazardous materials or drugs covered by WHMIS are used for compounding, precautions must be taken to protect the compounder. Some products present a physical hazard such as flammability or corrosivity, while other products present a health risk. 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 less hazard risk. However, stricter preventive measures, that is Level C requirements are 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.

5.3 ASSESSING RISK FOR COMPOUNDING NON-STERILE PRODUCTS

The above levels of requirements for compounding non-sterile products need to be assessed and determined by the compounding supervisor in collaboration with the pharmacy manager or the pharmacy department head. The compounding supervisor should ensure that Safety Data Sheets and other applicable references have been consulted, and that appropriate procedures for safe compounding are documented on the Master Formulation Record for each compound

Most non-sterile compounds in the USP categories simple or moderate can be made 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

¹⁰ 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/>

¹¹ WHMIS at <http://www.hc-sc.gc.ca/ewh-semt/occup-travail/whmis-simdut/index-eng.php>

appropriate level of requirements. For example, it would be possible to prepare 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.

Some of the factors to consider in risk assessment:

- concentration of the ingredients in the product
- physical characteristics of the ingredients such as liquid vs solid vs powders, or water soluble vs lipid soluble
- the quantity of ingredients being handled
- frequency of making the compound
- exposure to compounding personnel
- risk of microbial contamination (liquids, creams and ointments may be particularly susceptible to microbial and other contamination)
- education and competency of compounding personnel
- availability of appropriate facilities and equipment
- the classification of ingredients as identified by WHMIS as a hazard or a drug classified by NIOSH as hazardous ([See Section 10](#))

[Appendix 2](#) presents a decision algorithm to assist in determining the level of requirements for non-sterile compounding.

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

The following information is also summarized in a table in [Appendix 3](#).

6.1 Personnel

6.1.1 Roles and responsibilities

6.1.1.1 Pharmacy manager¹² or pharmacy department head¹³

The pharmacy manager or pharmacy department head is responsible for developing, organizing and supervising **all** activities related to pharmacy compounding of non-sterile preparations. This person may share or assign these responsibilities to a pharmacist or pharmacy technician, who will be designated as the non-sterile compounding supervisor. If the designated pharmacist or pharmacy technician chooses not to perform these

¹² 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 authority.

¹³ 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.

activities, the pharmacy manager or pharmacy department head must assume the responsibilities of the non-sterile compounding supervisor and must therefore be qualified to perform compounding of non-sterile preparations in the pharmacy

If these responsibilities are assigned to a pharmacist or pharmacy technician, the pharmacy manager or pharmacy department head must ensure that the non-sterile compounding supervisor fulfills them adequately.

One pharmacist may be responsible to fulfill all roles and tasks.

6.1.1.2 Non-sterile compounding supervisor

Definition

The non-sterile compounding supervisor is a pharmacist or pharmacy technician designated to supervise activities related to the compounding of non-sterile preparations. This person works with the pharmacy manager or pharmacy department head and with the compounding personnel.

The non-sterile compounding supervisor develops, organizes and oversees all activities related to non-sterile preparation compounding. These responsibilities are assigned by the pharmacy manager or pharmacy department head.

In accordance with the appropriate supervision protocol and appropriate quality control measures, the non-sterile compounding supervisor may assign technical tasks related to non-sterile preparation compounding to a pharmacy assistant with the appropriate training, using a formal delegation process or under appropriate supervision that complies with the requirements of the provincial/territorial authority.

Responsibilities

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

- A personnel training and assessment program is implemented.
- Personnel know and fully comply with policies and procedures.
- The existing compounding process yields high-quality non-sterile preparations that are safe for patients.
- Appropriate measures are taken to ensure the safety of personnel during each preparation and that incident/accident reporting and follow-up are in place.
- Policies and procedures covering all activities are developed, regularly reviewed, updated (at least every 3 years or more frequently when standards have changed) and always followed (see Appendix 5)
- 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.
- 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 and continuously evaluated and updated as required.

- Current editions of mandatory and supplementary references and safety data sheets are available and updated regularly. [Appendix 7](#) lists suggestions for references.
- All records required by the Model Standards are completed, maintained and readily available for audit and inspection purposes as required by the provincial/territorial regulatory authority.

6.1.1.3 Compounding personnel

Definition

- a) A pharmacist or pharmacy technician who prepares or supervises the compounding of non-sterile preparations
- for patients of the facility or pharmacy where the pharmacist or pharmacy technician is employed;

OR

- where permitted by provincial/territorial legislation, for patients of another facility or pharmacy upon request.

When more than one pharmacist or pharmacy technician is involved in preparing a compounded 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.

- b) A pharmacy assistant with appropriate training¹⁴, who prepares non-sterile preparations or performs other technical tasks related to non-sterile compounding 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 to the pharmacy assistant, or under appropriate supervision in compliance with the requirements of the provincial/territorial authority.

Responsibilities

- a) The compounding pharmacist or pharmacy technician must
- perform or supervise compounding activities;
 - ensure compliance with policies and procedures related to the compounding of non-sterile preparations, including handling of hazardous drugs and materials where applicable.
 - enforce or ensure compliance with required rules relating to hygiene, cleanliness and safety;

¹⁴ Please consult the relevant provincial/territorial pharmacy regulatory authority for any training or supervision requirements defined in each jurisdiction.

- ensure that all records related to ongoing activities are completed and documentation clearly indicates who completed the 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 produced;
- ensure the accuracy of calculations and measurements;
- ensure that appropriate equipment and instruments are used for each preparation to be produced;
- 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 7.7);
- 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 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 pharmacists and pharmacy technicians at both facilities to clarify who is responsible for which aspects of patient care and to ensure continuity of care¹⁵.

¹⁵ 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

- b) The responsibilities of a pharmacy assistant 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 pharmacy assistant has the appropriate training¹⁶. The non-sterile compounding supervisor must ensure that the pharmacy assistant is supervised by a pharmacist or pharmacy technician according to established supervision protocols and appropriate quality measures.

6.1.2 Training and assessment

6.1.2.1 Skills and training for staff

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

Appendix 4 indicates the skills and abilities on which staff training should focus. Any training, professional development and upgrading programs in the area of compounding taken by staff must be noted in their personnel files.

6.1.2.2 Skills assessment for staff

A skills assessment program must be established for all staff, pharmacists and technical personnel (eg. pharmacy technicians, pharmacy assistants) 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 staff. The results of these evaluations and any corrective action taken must be noted in the employee's file. Appendix 8 is an example of a self-evaluation which staff could use individually or with each other to assess the compounding process.

6.1.2.3 Skills training and assessment for cleaning personnel

The initial training and assessment program needs to include training for cleaning personnel, and there must be written policies covering the maintenance and cleaning of the equipment and the compounding premises or areas, so that all personnel are aware of cleaning activities needed to prevent cross-contamination.

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

¹⁶ Please consult the relevant provincial/territorial pharmacy regulatory authority for regulatory and/or supervision requirements defined in each jurisdiction.

6.2 Policies and procedures^{17, 18}

The quality, purity, safety, efficacy and reproducibility of the final preparation depends upon, among other things, full compliance with compounding procedures. This can be accomplished by having clear policies and procedures which are followed by all staff.

- The non-sterile compounding supervisor must establish the content of policies and procedures, providing detailed descriptions of all activities in the pharmacy's compounding of non-sterile preparations (see Appendix 5 for an example). The supervisor must also ensure application of and compliance with these policies and procedures. Appendix 6 may be used as a model for developing these procedures.
- The non-sterile compounding supervisor must ensure that all established policies and procedures are 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.
- When compounding hazardous drugs or materials, additional procedures must be developed including the safe receiving, storing, handling, compounding, labelling, transporting and disposal of hazardous drugs and materials. (see section 10)
- Where compounding is undertaken by another pharmacy, where permitted by provincial/territorial legislation, the pharmacist or pharmacy technician at 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.).

6.3 Facilities and equipment

This section applies to all levels of non-sterile compounding. Additional requirements are expected for Level B and Level C as described in section 10.

6.3.1 General remarks

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

Areas reserved for compounding must only be used by staff authorized to compound non-sterile preparations. This space must be reserved for compounding, but may also be used in preparing or reconstituting marketed products. When a pharmacy or health care institution 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.¹⁹

¹⁷ United States Pharmacopeial Convention (USP). General chapter <795>: pharmaceutical compounding — non-sterile preparations. USP 39. Rockville, MD: USP; 2016. pp.31,37.

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

¹⁹ United States Pharmacopeial Convention (USP), General Chapter <797>, Pharmaceutical Compounding- Sterile Preparations, Environmental Quality and Control, 2016.

6.3.2 Physical Layout

General

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 mixups among ingredients, containers, labels, in-process materials, and finished preparations.²⁰ 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 staff.^{21 22}

Compounding areas must be large enough for staff to be able to work comfortably and safely, with room to store the required equipment and products neatly in a clean and secure manner. 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.

The layout must be conducive to cleaning and contain no areas that are difficult to clean. Fixtures liable to collect dust (eg. ceiling lamps, plumbing, window frames, wire) and any horizontal surface serving no purpose should be covered, sealed up, modified or removed from the room or 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. There must be an adjacent sink with hot and cold running water, preferably one made of stainless steel.

Lighting

The lighting must be sufficient and fixtures located so as to provide a well lit area to facilitate the compounding process and to allow verification at all stages of compounding.

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 staff safety and comfort. Appropriate temperature and humidity monitoring should be maintained as required for certain components and compounded dosage forms.

Water supply²³

Potable water shall be supplied for hand and equipment washing and facilities shall be easily accessible to the compounding areas. Purified water shall be used for

²⁰ United States Pharmacopeial Convention (USP) General Chapter <795> pharmaceutical compounding – non-sterile preparations. USP 39. Rockville, MD: USP 2016, p33.

²¹ OPQ Non-Sterile Compounded Preparations, Ordre des Pharmaciens du Quebec, Montreal, QC,2011, pg 35. www.opq.org

²² 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, p13, www.picscheme.org

²³ United States Pharmacopeial Convention(USP) Chapter <795> Pharmaceutical Compounding – Non-sterile Preparations, USP 39, Rockville, MD, USP 2016; p33.

compounding non-sterile drug preparations when formulations indicate the inclusion of water. The plumbing system shall be free of defects that could contribute to contamination of any compounded preparation.

Work surfaces

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

Furniture, walls and flooring

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

6.3.3 Equipment for Non-sterile Compounding

The equipment (instruments and apparatus) chosen must be appropriate to the type of preparations to be compounded. It may vary, depending on preparation complexity, quantities compounded and equipment manufacturer's instructions.

The format and precision of the apparatus and instruments also depend on the type and quantity of preparations to be compounded. The apparatus and instruments should only be used for compounding.

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

The non-sterile compounding supervisor is responsible for ensuring that the instruments used will provide the precision required for the preparation being compounded.

6.3.3.1 Equipment maintenance

General remarks

To ensure their precision and reliability, all apparatus, instruments and accessories must all be inspected, maintained, cleaned and calibrated at appropriate intervals, as recommended by the manufacturer, and at least once a year if there are no such recommendations.

After each use and cleaning, the apparatus, instruments and other accessories used for compounding must be neatly stored in the appropriate cabinets.

Instruments and apparatus 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.

All notes made on the maintenance forms must indicate the staff member doing the

maintenance (pharmacist, pharmacy technician, member of the cleaning staff).

Compounding supervisors should follow the requirements of provincial/territorial regulatory authorities for balances/ weights and refrigerator/freezers. In the absence of requirements specific to the provincial/territorial pharmacy regulatory authorities, refer to the following standards.

Balances and weights

The balance must be verified every day or before it is used if it is only used occasionally, to ensure that it is in good working order. Certified weights must be used to verify the balance. It must be verified again if it is knocked or banged and whenever it is moved. The weights used to verify the balance must be certified every year by a qualified firm.

The balance must be calibrated before first use, if it is moved, knocked, dropped or banged, or at least once a year and also if, after verification, it proves to be malfunctioning.

Verification and calibration work on the apparatus and instruments must be documented in the maintenance log.

Refrigerator and freezer

The refrigerator and freezer used to store medications must be purpose-built vaccine refrigerators (also referred to as a pharmacy, lab style or laboratory grade refrigerator) or domestic frost free refrigerators/freezers with appropriate modifications²⁴. Manual and cyclic defrost refrigerators or bar fridge units should not be used due to the significant temperature variations.

Refrigerators and freezers used for storing medications must not be used to store food.

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

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

Accurate temperature probes (gauges or sensors) must be installed to indicate the actual temperature. A continuous temperature recorder built into each unit is the preferred option to be able to monitor minimum and maximum temperatures. Alternately the minimum and maximum temperature inside the fridge can be checked with a calibrated thermometer at least twice each day.

A notification system must be installed in each refrigerator and freezer to alert pharmacy personnel when temperatures deviate from specifications. A procedure should be in place in case of an electrical outage or defective equipment.

6.3.4 Cleaning the premises

²⁴ Health Canada, Health Products and Food Branch Inspectorate. *National Vaccine Storage and Handling Guidelines for Immunization Providers*. Ottawa, ON: Health Canada; 2015. Available from: <http://healthycanadians.gc.ca/publications/healthy-living-vie-saine/vaccine-storage-entreposage-vaccins/index-eng.php#a3d3b>

Cleaning in the areas reserved for non-sterile compounding must be performed in a manner that maintains the cleanliness and hygiene needed to ensure the quality and integrity of the final preparations.

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

To limit the accumulation of dust and particles, packaging and cardboard boxes from products used must be removed from the non-sterile compounding area.

A sufficient number of easy-to-clean waste containers of suitable size and made of materials resistant to damage from cleaning products must be available. The waste shall be collected in plastic bags and removed with minimal agitation. The waste containers must 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 must 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.

Staff responsible for cleaning the premises must be adequately trained for their task. Cleaning work in the premises must be noted on a form or a calendar, and kept in the maintenance log.

Cleaning the apparatus and instruments

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

6.4 General maintenance log

The maintenance log must show the calibration dates for the balances, apparatus and instruments used. 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).

7. PRODUCT AND PREPARATION REQUIREMENTS

7.1 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.

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 an approved drug is used as an active pharmaceutical ingredient, the pharmacist may refer to the information provided by the manufacturer. The manufacturer's expiry date (ED) for an approved drug must 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 compounding pharmacist must also consider 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 duration of therapy, and assign the BUD conservatively.

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.

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 drug preparations that are packaged in air-tight, light-resistant containers and stored at controlled room temperature, unless otherwise indicated. Drugs or chemicals known to be labile to decomposition will require shorter BUDs.

Table 1

BUD by Type of Formulation^{*25}
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

²⁵ United States Pharmacopeial Convention (USP), Chapter <795> Pharmaceutical Compounding – Non-sterile Preparations, USP 39, Rockville, MD, USP 2016, p35.

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

7.2 Compounded Non-sterile Preparation Master Formulation Record

The master formulation record must include all the following information as required to produce the preparation:^{26 27}

- ✓ official or assigned name, strength, and dosage form of the preparation
- ✓ expected yield
- ✓ calculations needed to determine and verify quantities of components and doses of active pharmaceutical ingredients
- ✓ description of all the ingredients, their quantities and source
- ✓ compatibility and stability data, including references when available
- ✓ equipment needed to prepare the preparation
- ✓ special precautions to be observed by the staff (including personal protective equipment)
- ✓ source or origin of the formula
- ✓ references used to write the formula and the consultation date
- ✓ mixing instructions that should 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

The master formulation record should include specific cleaning instructions when these differ from the usual cleaning instructions. See the template of a master formulation record in Appendix 9.

To ensure preparation quality and safety, the non-sterile compounding supervisor must ensure that the master formulation records are updated. If any amendment is needed, the non-sterile compounding supervisor must describe the change made in the master formulation sheet, and also provide supporting rationale and references. The development of a new master formulation must be based on scientific data and appropriate references must be documented.

²⁶ United States Pharmacopeial Convention (USP), Chapter <795> Pharmaceutical Compounding – Non-sterile Preparations, USP 39, Rockville, MD, USP 2016, p35.

²⁷ OPQ Non-Sterile Compounded Preparations, Ordre des Pharmaciens du Quebec, Montreal, QC, 2011, pg 35. www.opq.org

All master formulation records should be kept together in a Master Formulation Log which contains, in hard copy or electronic format, the master formulation records to be used for the pharmacy's non-sterile compounded preparations.

7.3 Ingredients Used for Non-sterile Compounds– quality and storage

The non-sterile compounding supervisor must ensure the purity and quality of the ingredients used in the preparations compounded in the pharmacy. All ingredients (powder, liquids, etc.) that require special precautions when used or stored must be identified. Ingredients and raw materials must be stored and kept safely in conditions that will preserve their quality and purity as directed by the manufacturer or according to pharmacopeia monographs.

7.3.1 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)²⁸. These sheets must be kept together and made available to staff (pharmacists, pharmacy technicians and pharmacy assistants). All employees must 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.

7.3.2 Selection of ingredients

In choosing active or inactive ingredients to be used for compounding, compounders must 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
- level of difficulty in administering the final preparation

²⁸ For access to Safety Data Sheets, go to: <http://ccinfoweb.ccohs.ca/msds/search.html>

Purified water²⁹ 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.

7.3.3 Sources of ingredients

The non-sterile compounding supervisor must ensure that ingredients used come from recognized and reliable sources. Non-sterile preparations must 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 USP, PhEur, PhF,PhI, BP,CF,NF or Codex-*Schedule B Food and Drugs Act*, in keeping with the recommendations of Health Canada's Policy 0051.³⁰

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.³¹ 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.

7.3.4 Quality of ingredients

Reasonable means must be taken to determine the purity and safety of the ingredients used for compounding. These means may include analyzing the batch and verifying the manufacturer's reputation and the supplier's reliability. Compounders must be sure to choose quality ingredients (identity, purity) for the preparations and to obtain the documents needed for this purpose, including the certificates of analysis for the ingredients.

If the product is not sourced from a recognized supplier, a qualified laboratory must analyze the product and confirm its identity, purity and quality, based on the requirements of a recognized pharmacopoeia. The analysis results and the certificates must be kept in the 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, the compounder must consider all the ingredients (active and inactive) in the approved drug.

Compounders must not use any ingredients for compounding that have been recalled or withdrawn from the market by Health Canada for safety reasons. Health Canada publishes on its website a [list of drugs that have been withdrawn from the market](#).

²⁹ United States Pharmacopeial Convention, Chapter <1231> Water for Pharmaceutical Purposes, USP Compounding Compendium, Feb 2016, p456-462.

³⁰ Health Canada, Policy on Manufacturing and Compounding Drug Products in Canada, POL-0051, January 26, 2009.

³¹ United States Pharmacopeial Convention, Chapter <795> Pharmaceutical Compounding – Non-sterile Preparations, USP 39, Rockville, MD, Feb 2016. p 34.

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 must 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.³²

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

7.3.5 Ingredients log

The ingredients log contains information about the ingredients used for the pharmacy's compounded preparations, such as the date of receipt of the ingredients, their source and the certificates of analysis or analysis results. This log must be accessible to all employees who might need to consult the information on hand about a given product.

An additional log must be created and maintained for narcotics, controlled drugs and targeted substances used in compounded preparations, and it must comply with the regulations governing these products.

7.4 Compounding Record

The Compounding Record for non-sterile compounds shall contain:³³

- 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 compounder who approved the preparation
- date of preparation
- assigned preparation batch number or prescription number
- assigned BUD
- duplicate label as described in the Master Formulation Record

³² United States Pharmacopeial Convention, General Chapter <795> Pharmaceutical Compounding – Non-sterile Preparations, USP 39, Rockville, MD. Feb 2016. p 34.

³³ United States Pharmacopeial Convention (USP), General Chapter <795> Pharmaceutical Compounding – Non-sterile, USP 39, Rockville, MD, USP 2016, p36.

- description of final preparation
- 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

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

The rationale for compounding must be documented in the patient's file with the appropriate justification, regardless of the reason, when there is a marketed drug available (e.g., allergy, drug temporarily in short supply, difficult to swallow, etc.).

The origin of the compounded non-sterile preparation dispensed to the patient must 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) must be able to track information related to preparations that it dispenses, even if those preparations were made by another pharmacy.

7.5 Conduct of personnel in compounding areas

Personnel must behave in a professional manner, following all pertinent policies and procedures. The risk of contamination of the product by personnel should be minimized. For reasons of hygiene and safety and to avoid possible contamination, during non-sterile compounding staff must:

- ✓ have short nails and not wear false nails;
- ✓ have long hair tied up;
- ✓ not wear jewellery on their hands or wrists;
- ✓ not chew gum;
- ✓ not consume or keep food, drink, or tobacco in compounding area
- ✓ notify the compounding supervisor if they have 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 product³⁴;
- ✓ wear clean clothing appropriate to the type of compounding being done;
- ✓ wear a clean laboratory coat³⁵ reserved for compounding (preferably a disposable gown), a cap and mask and, if applicable, a beard guard;

³⁴ 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

³⁵ It is highly recommended that a disposable gown be worn for compounding. If a clean laboratory coat is worn for compounding, it must be reserved for making these preparations and not be worn outside the compounding area. When employees leave the compounding area, they must leave their laboratory coats behind. They may put them on again when they return, provided they are

- perform appropriate hand hygiene with regular soap or antimicrobial soap³⁶ and low particle-release paper for drying;
 - ✓ slip on powder-free gloves³⁷ after proper hand hygiene;
 - ✓ Take any other reasonable measures to prevent cross contamination, and to protect themselves from chemical exposure

7.5.1 Verification of final compounded non-sterile preparations

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

- Ensure that all compounded non-sterile preparations comply with compounding protocols;
- Verify the identity of the ingredients;
- Verify the volume, quantity or weight of the ingredients;
- Regularly verify the quality of compounding technique

When compounding a preparation, compounding personnel must undertake the following activities:

- Assess the final preparation using factors such as weight, adequacy of mixing, clarity, odor, color, consistency, pH, and analytical testing as appropriate.
- Verify the information on the label; and ensure this information is recorded on the compounding record.
- 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.³⁸
- 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 use.
- Verify that products requiring refrigeration are stored appropriately pending delivery to the patient.
- Ensure the preparation is delivered to the patient or caregiver with appropriate consultation.

clean and unsoiled. Laboratory coats must be changed as soon as they become soiled or according to protocols required.

Disposable gowns must be changed every day or as soon as they become soiled.

³⁶ 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

³⁷ Powder-free gloves must always be worn for compounding. The compounding pharmacist must select gloves appropriate for the type of compounding to be done, consulting the Safety Data Sheets for the ingredients to be used. Given the risk that patients or staff may be allergic to latex, nitrile or neoprene gloves are preferable. Pharmacists must ask their patients whether they are allergic to latex

³⁸ United States Pharmacopeial Convention (USP) General Chapter <795> pharmaceutical compounding – non-sterile preparations, USP 39, Rockville, MD, USP 2016, p36.

7.6 Labelling and Packaging

7.6.1 Labelling of final compounded non-sterile preparations

7.6.1.1 General

The non-sterile compounding supervisor must establish a procedure for the labelling of compounded non-sterile preparations and ensure that it is followed. The labels for compounded non-sterile preparations must meet the requirements of the applicable legislation and regulations.

Each container for a compounded non-sterile preparation must be labelled. All active ingredients and the concentration of each ingredient must be identified on the label. The label must include the BUD, and storage and handling information. The labeling should indicate that “this is a compounded preparation”.

The compounding pharmacist or pharmacy technician must similarly label non-sterile preparations that have been compounded at the request of another pharmacy, where permitted by provincial/territorial legislation.

As required by the respective provincial/territorial regulatory authority, , another label must be added at the pharmacy where the compounded non-sterile preparations will be dispensed to the patient. Both labels must be retained on the preparations.

7.6.1.2 Label and insert

The computer-generated self-adhesive label printed by the prescription and file management software may be too small to carry all relevant information to ensure safe, appropriate use of the compounded non-sterile preparation by the patient. If this information cannot be included on an auxiliary label, an insert must be prepared. The insert is considered to be an integral part of the label.

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

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

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

The package insert must include the following information:

- all information required by federal/provincial/territorial legislation and regulations

regarding the labelling of medications that could not be included on the main label;

- details concerning mode of administration;
- special precautions related to drug storage (e.g., “Caution: contents must be refrigerated upon receipt — store between 2°C and 8°C. Do not freeze”; “Do not store medication in the refrigerator door”; “Keep out of reach of children”);
- special precautions for disposal or destruction of the preparation;
- emergency contact information of the compounding pharmacy (where compounding has been undertaken by another pharmacy, where permitted by provincial/territorial legislation), provided there is explicit agreement on this matter between the two pharmacies involved.

7.6.2 Packaging process and procedure

Appropriate packaging must 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, the non-sterile compounding supervisor must develop and implement a packaging procedure for final compounded non-sterile preparations.

During packaging, compounding personnel must

- put all final compounded non-sterile preparations in packaging that maintains each preparation’s stability, integrity and storage conditions;
- indicate storage requirements on the final package (e.g., temperature, protection from light);
- indicate additional precautions on the final packaging (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.

7.7 Storage^{39,40}

7.7.1 General conditions

The non-sterile compounding supervisor must develop a storage procedure and this procedure must be followed at all times.

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

⁴⁰ United States Pharmacopeial Convention (USP). General Chapter <1079>: good storage and shipping practices. USP 39, Rockville, MD, USP 2016. p351-360

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 staff.

Active and inactive ingredients and finished products must 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 must be controlled. Product storage conditions must 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.) must be controlled and remain within the limits indicated in [Appendix 11](#) regardless of the season. Information on monitoring of room, refrigerator and other temperatures and controls related to implementation of the storage procedure must be recorded in the general maintenance log⁴¹.

Products that have been stored must 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 must be developed and implemented to ensure that products and compounded non-sterile preparations that have become unusable are quickly discarded.

7.8 Transport and delivery of compounded non-sterile preparations

Policies and procedures must be developed and implemented for the transport of compounded non-sterile preparations^{42 43} and their delivery to patient care units, pharmacists, pharmacies and patients (see Appendix 5). A policy for return and disposal of expired, partially used or unused compounded non-sterile preparations from the patient's home or the patient care unit in a health care facility must also be developed.

Preparations to be delivered must 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.) must always be indicated on the outside of the packaging.

As a rule, extreme temperatures (excessive heat or freezing) must 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 must be indicated in the procedure.

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

When a private carrier is used, the non-sterile compounding supervisor must verify the steps taken to ensure maintenance of stability of the compounded preparation throughout transport

⁴¹ United States Pharmacopeial Convention (USP). General chapter <1079>: good storage and shipping practices. USP 39, Rockville, MD, USP 2016. p351-360.

⁴² 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>

⁴³ Transportation of Dangerous Goods Regulations: <http://www.tc.gc.ca/eng/tdg/clear-tofc-211.htm>

and storage.

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

7.9 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, the pharmacist or pharmacy technician must be able to

- identify patients or dispensers who have received the compounded non-sterile preparation;
- notify patients or their caregivers that there is a problem with the preparation;
- 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 must be sufficient to allow users to track recipients of compounded non-sterile preparations.

The non-sterile compounding supervisor must ensure that a procedure for recall of compounded non-sterile preparations has been developed and approved (see Appendix 5).

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

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

7.10 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 [Appendix 12](#) for an example).

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

7.11 Veterinary Preparations

Compounding of drugs for animals is subject to the same rules as compounding of drugs for human consumption. Compounding of animal drugs in a pharmacy must take place within the framework of a valid veterinarian/client/patient/ pharmacist relationship, the patient being the animal treated and the client being the animal's owner.

Pharmacists who compound products for animals bred, kept or slaughtered specifically for the purpose of producing food for human consumption or for competition animals (e.g., race horses) must understand the legislation specific to the animal population and comply with it in all respects.

To ensure that an animal is fit for human consumption, the time required for the metabolism and elimination of the drug or the "withdrawal period" must be added to the labels of products compounded for animals that are intended for human consumption, along with the other instructions on the subject provided by the veterinary doctor's prescription.

Pharmacists shall be knowledgeable about the individual species' limitations in physiology and metabolic capacity that can result in toxicity when certain drugs or excipients are used in compounded preparations for animals. If formulations specifically developed for animals are not available, extrapolating formulations intended for human use may not be appropriate for animal species and may contribute to negative outcomes.⁴⁴

⁴⁴ United States Pharmacopeial Convention, Chapter <795> Pharmaceutical Compounding – Non-sterile, USP 39, Rockville MD, USP 2016, p 38.

8. QUALITY ASSURANCE PROGRAM

8.1 Program content

The non-sterile compounding supervisor must establish a quality assurance program 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. [Appendix 13](#) provides an example of possible components of a quality assurance program.

8.2. Quality Assurance of equipment and compounding areas

8.2.1 Certification

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

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

8.2.2 Temperature readings

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

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

non-sterile compounding supervisor must record and retain 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 must offer features to record and store temperature readings at the same frequency as specified above (at a minimum). The system must also trigger an alarm if the temperature readings deviate from the acceptable range.

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

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

8.3 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.

8.4 Quality assurance of compounded non-sterile preparations

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

The program must 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.

8.5 Documentation of quality control activities

Written documentation related to the quality assurance program must be verified, analyzed and signed by the non-sterile compounding supervisor and retained for a period as designated by federal/provincial/territorial regulations.

The non-sterile compounding supervisor must

- investigate missing documentation, situations of non-compliance (where action is required) and deviations from protocols;
- take corrective and preventive actions; and,
- document all findings and corrective actions.

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

9. SOURCE FOR ADDITIONAL INFORMATION

For more information on compounding of non-sterile products, please refer to General Chapter <795> in the most recent edition of USP–NF. For more information on compounding hazardous sterile preparations, please refer to Chapter <800> in the most recent edition of the USP-NF which is scheduled to become official July 1, 2018.

10. REQUIREMENTS FOR COMPLEX PREPARATIONS AND HAZARDOUS PREPARATIONS (SIMPLE, MODERATE AND COMPLEX)

10.1 Complex Preparations

As the complexity of the non-sterile compounded product increases, so do the requirements for producing 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.

Level B requirements are needed for the compounding of complex preparations. 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 well ventilated, entirely closed off room or a room with a ventilated containment device is required with the air exhausted to the outside when certain powders, aromatic products or other hazardous products are compounded. If a ventilated containment device is used, the pharmacy should follow the same requirement as [10.2.3.1](#).

Compounding of complex preparations as defined by USP 795, or hazardous products posing less risk can follow Level B requirements.

10.2 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 following Level A requirements, depending on the risk. 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 penetration⁴⁵.

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 contamination⁴⁸. Therefore; the compounding of hazardous non-sterile preparations requires the implementation of safety measures to protect personnel and the environment

Compounding supervisors should consult appropriate references ([Appendix 7](#)) to determine what risk the hazardous drug or hazardous material would be to personnel. In regard to hazardous drugs, USP 800 suggests that at a minimum, the following should be considered: Type of hazardous drug (antineoplastic, non-antineoplastic, reproductive risk only), dosage form, risk of exposure, packaging, manipulation. In addition, there should be documentation of the alternate containment strategies and/or work practices that are being employed for specific dosage forms to minimize occupational exposure, and assessment of risk must be reviewed at least every 12 months.

Additional laws and regulations governing the compounding of hazardous preparations and handling of hazardous products may exist at the federal/provincial/territorial level and would need to be consulted. Pharmacies must customize their list of hazardous drugs and hazardous materials being used, and document the compounding requirements necessary for safe compounding of these products.

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.

In the pharmacy of a health care facility, a hazardous drugs committee⁴⁹ 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 must 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 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 must 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.

10.3 Facilities and equipment for handling hazardous products⁵⁰ (Level C)

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

In addition to previously stated requirements such as adequate space for compounding and sufficient lighting, compounding of hazardous non-sterile preparations should be done in a separate room. For less hazardous products, this could be level B requirements with a well-ventilated room, and for hazardous products with greater health risk, this would require Level C precautions of a separate room under negative pressure.

10.3.1 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 must.⁵¹

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>

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

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 must 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 must 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 must be smooth, impermeable, free from cracks and crevices and non-shedding.

10.3.2 Heating, ventilation and air conditioning system for controlled rooms

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

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

10.3.4 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 area⁵², however two pairs of ASTM International–approved gloves must 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 preparations⁵³. Personnel must wear PPE recommended in [10.2.3.4](#).

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).

10.3.5 Area for storing hazardous products

Hazardous products must be grouped and stored in a properly ventilated room with all air exhausted to the exterior⁵⁴. The storage area must have negative pressure relative to the adjacent rooms and must have at least 12 ACPH. It must be identified with the proper signage to indicate the presence of hazardous products⁵⁵. Additional requirements for a hazardous products storage area are listed in Table 2 below.

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 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.

10.3.6 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)

Table 2

Required conditions for a hazardous products storage area
<ul style="list-style-type: none">• 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 breaking⁵⁶• Storage spaces for hazardous products and preparations identified with the proper signage to indicate the presence of hazardous products⁵⁷• Sufficient ventilation to prevent contamination from spreading to adjoining rooms⁵⁸

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>

10.3.7 Equipment

The compounding area, equipment and accessories must 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-contamination⁵⁹.

10.3.7.1 Containment Primary Engineering Control(C-PEC)

The containment primary engineering control (C-PEC) is installed in the compounding room, and must 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 must be compounded inside a C-PEC that provides personnel and environmental protection such as a Class I Biological Safety Cabinet (BSC)^{60, 61, 62, 63} or a Containment Ventilated Enclosure (CVE).⁶⁴ A Class II BSC or a Compounding Aseptic Containment Isolator (CACI) may also be used. The safety cabinet must 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 must 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.⁶⁵

The non-sterile compounding supervisor must ensure that the C-PEC is installed according to manufacturer's recommendations and that certification is completed according to certification standards currently in force.

The C-PEC must 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^{66 67}. If there is a loss of power to the C-PEC or moving or repair occurs, all activities occurring in the C-PEC

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>

⁵⁹ United States Pharmacopeial Convention (USP), Chapter <795> Pharmaceutical Compounding – Non-sterile Preparations, USP 39, Rockville MD, USP 2016; p 34.

⁶⁰ 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.

⁶¹ ASHP, ASHP Guidelines on Handling Hazardous Drugs, *Am J Health-Syst Pharm*. 2006; 63:1172-93.

⁶² McElhiney, LF, Preparing Non-sterile & Sterile Hazardous Compounds in an Institutional Setting, *IJPC*, Vol. 13, No. 4, July/August 2009, p. 303.

⁶³ ASSTSAS, *Prevention Guide – Safe Handling of Hazardous Drugs*, ASSTSAS 2008, p. 8-9.

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)

⁶⁵ 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

⁶⁶ 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

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)

must be 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.⁶⁸

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

Maintenance of C-PEC

C-PECs must be maintained in accordance with the manufacturer's recommendations.

BSCs must be certified⁶⁹

- every 6 months
- when relocated
- after major repairs
- when viable air sampling indicates that the C-PECSs may not be in compliance with specifications

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

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

Preventive maintenance for C-PECs and other equipment must be performed when no compounding is in progress, before cleaning and disinfection operations.

All C-PEC maintenance must be noted on a form and entered in the general maintenance log (paper-based or computerized). The non-sterile compounding supervisor must ensure that C-PEC maintenance has been performed. The supervisor must review the results or ensure that the results have been reviewed and corrective measures taken, as appropriate. The supervisor must sign the maintenance form or log.

10.3.7.2 Other devices, instruments or accessories related to the compounding of hazardous non-sterile preparations

All reusable equipment and devices used to handle hazardous products must be deactivated, decontaminated, and cleaned.⁷⁰ Devices, instruments and accessories to be used in controlled rooms should not be removed without good reason. If they must be removed, they must be decontaminated.

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

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)p88

⁶⁹ United States Pharmacopeial Convention (USP), General Chapter <797>, Pharmaceutical Compounding- Sterile Preparations. USP 39, Rockville, MD, USP 2016. p54

⁷⁰ 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

10.3.7.4 Personal protective equipment (PPE)⁷¹

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

Gloves

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

- unpacking
- deactivating, decontaminating and cleaning the room
- deactivating, decontaminating and cleaning the C-PEC
- compounding 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 must be discarded and replaced at the earliest of; manufacturer limit for permeation of the gloves, every 30 minutes^{72 73 7475}, immediately if a tear, puncture or contamination has occurred or is suspected.

Gown

When gowns are required, they must be disposable and shown to resist permeability by hazardous products. Gowns must 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 must close in the back (no open front), be long sleeved and have fitted cuffs at the wrists.

The gown must 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^{76, 77} compounding work

⁷¹ 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>

⁷² Buchanan EC, Schneider PJ. *Compounding sterile preparations*. 3rd ed. Bethesda, MD: American Society of Health-System Pharmacists; 2009. p. 85.

⁷³ 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.

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. pp. 4-5. 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 USP 39, Rockville, MD: USP; 2016 Feb (to become official July 1, 2018)

⁷⁶ Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. p. 4-6. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

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 occurred⁷⁸.

Cloth laboratory coats, surgical scrubs, isolation gowns, or other absorbent materials are not appropriate protective outerwear 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 must not be taken home under any circumstances.⁷⁹

Head, hair, shoe and sleeve covers⁸⁰

Disposable head and hair covers (including beard and mustache, if applicable) and shoe covers must be worn during the compounding of hazardous non-sterile preparations. They must be changed after each removal or if they become contaminated⁸¹. 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.

No mask is necessary for unpacking hazardous products that have been received from the supplier in impervious plastic. However, if hazardous products have been damaged

⁷⁷ 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.

⁷⁸ 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.

⁷⁹ 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

⁸⁰ 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

⁸¹ 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>

before receipt, a chemical cartridge respirator is required during unpacking⁸². See [Appendix 10](#) for a procedure example.

The mask must 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 Protections

Goggles and face shield or a full face-piece respirator must 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.

10.4 Deactivating, Decontaminating, Cleaning in areas reserved for the compounding of hazardous non-sterile preparations

10.4.1 General

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

Policies and procedures for cleaning and tasks must be developed, and cleaning personnel must be trained and assessed on correct application of these policies and procedures to protect themselves and the environment from contamination⁸³. Only trained and qualified cleaning and disinfecting personnel must be allowed to clean controlled rooms.

Surface deactivation, decontamination and cleaning⁸⁴

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

Deactivation

Deactivation renders a compound inert or inactive. Residue from deactivation must 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 must be taken when selecting materials for deactivation due to potential adverse effects such as hazardous by-products or caustic damage to surfaces

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) p95.

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) p92

⁸⁴ 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

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.

10.4.2 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.

10.4.3 Surface deactivation, decontamination and cleaning of the containment primary engineering control⁸⁵

The work surface of the C-PEC must be deactivated, decontaminated and cleaned between different compounds. The C-PEC must 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 must 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 must be recorded in the general maintenance log.

⁸⁵ 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.

10.5 Incident and accident management

10.5.1 Accidental exposure⁸⁶

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 must be accessible in the workplace. An eyewash station and sink with hot and cold running water must be available. The phone number of the local poison center should be posted where staff can easily see it.

The exposure must be documented in the appropriate logs.

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

Spill kits

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

10.5.3 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 Appendix 12 for an example).

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

⁸⁶ 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>

10.6 Hazardous waste management

In the performance of assigned duties, the pharmacist/pharmacy technician must⁸⁷

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

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

Hazardous products must be destroyed in accordance with regulations governing such products.⁸⁸ 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 Prevention⁸⁹ or WHMIS materials can be used to determine if a particular product is hazardous. Each pharmacy must 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 waste⁹⁰ must be developed and followed. These policies and procedures must comply with local, provincial and federal requirements.

The policies and procedures must include the following provisions:

- All personnel involved in the management of hazardous product waste must receive appropriate training on destruction procedures to ensure their own protection and to prevent contamination of the premises or the environment⁹¹.
- All equipment, products and vials used in the compounding of hazardous preparations must be discarded in a hazardous waste container.
- Hazardous waste containers must be identified with a self-adhesive label marked "Hazardous waste – cytotoxic"⁹². Containers should be filled to only three-quarters of

⁸⁷ 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

⁸⁸ American Society of Health-System Pharmacists. ASHP guidelines on handling hazardous drugs. *Am J Health Syst Pharm*. 2006;63(12):1172-93.

⁸⁹ 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>

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. 12-2. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

⁹¹ 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)

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. p. 12-2. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

their capacity⁹³. 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 must 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 must be removed inside the C-PEC. The gloves must 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 must be discarded into the hazardous waste container.
- Bins used for hazardous product waste must comply with local, provincial and federal requirements. These bins must be incinerated and may not be sent for decontamination by autoclave and subsequent burial.

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

10.7.1 Certification

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

- at least every 6 months⁹⁴;
- 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.

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

10.7.2 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..

⁹³ 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>

⁹⁴ 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

107.3 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 must be verified and documented at least once a day.

The negative pressure of the compounding room (C-PEC) must be maintained to avoid contamination of adjacent areas. Pressure must be measured continuously, and an alarm system must be in place to immediately advise personnel of non-compliance with specifications and to direct that action be taken, if necessary. A procedure must 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.

The non-sterile compounding supervisor or a delegate should sample 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 guide⁹⁵), 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, must 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 must be filed and retained with other compounding records, as per provincial/territorial pharmacy authorities.

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

⁹⁵ 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. GLOSSARY ^{96, 97, 98, 99, 100, 101, 102, 103}

Term	Definition
Accident	Action or situation in which the risk event occurs and has or could have an impact on the health status or well-being of the user (patient), personnel, professional concerned or third party. An accident differs from an incident, which has no effect on the patient.
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, comes 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.
Added substance (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.
Approved	Refers to a substance, ingredient, product or drug that has received official approval for use from Health Canada.
Assessment	Action of assessing and defining an employee's performance and competency.
Beyond-use date (BUD)	The BUD is the date after which a compounded preparation shall not be use and is determined from the date when the preparation sis 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: <ul style="list-style-type: none"> • air intake, to protect compounding personnel from hazardous sterile preparations; • descending air curtain filtered with a high-efficiency particulate air filter to protect the hazardous sterile product; • air evacuation system equipped with high-efficiency particulate air filters for environmental 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.
Cleaning	Removal of dirt, dust and other substances that may host microorganisms.
Commercial container	Container holding a commercially manufactured drug or sterile nutrient, the consumption and sale of which are authorized in Canada; if the drug or sterile nutrient

⁹⁶ Health Canada, Policy on Manufacturing and Compounding Drug Products in Canada (POL-0051), January 26, 2009,

⁹⁷ Bussières J.F., Législation et système de soins, 5th edition, August 2009, p. 171.

⁹⁸ United States Pharmacopeial Convention (USP). General Chapters 795, 797, 800, 1072. USP Rockville, MD: USP; 2016

⁹⁹ 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>

¹⁰⁰ 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>

¹⁰¹ 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>

¹⁰² Canadian Nurses Association (CNA). *Joint position statement: Promoting continuing competence for registered nurses*. Ottawa, ON: CNA; 2004. Available from: http://www.cna-aicc.ca/~media/cna/page-content/pdf-en/ps77_promoting_competence_e.pdf

¹⁰³ *Controlled Products Regulations*, SOR/88-66, 1987. Available from: <http://laws-lois.justice.gc.ca/eng/regulations/SOR-88-66/>

	is authorized by Health Canada's Special Access Programme, such consumption and sale may be limited.
Competencies	Significant job-related knowledge, skills, abilities, attitudes and judgments required for competent performance of duties by members of a profession,
Compounding	Act of preparing something, through preliminary work, to put it into a usable state. Also refers to the material that has been compounded (e.g., a chemical or pharmaceutical preparation).
Compounding personnel	Pharmacists, pharmacy technicians or pharmacy assistants assigned to the compounding of non-sterile preparations.
Compounding Record	A record of procedure followed including Master Formulation Record used, ingredients used, compounding personnel, calculations, BUD, final product and any quality control measures.
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 system	Arrangement or equipment to contain the particles of hazardous products in the chosen space.
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.
Detergent	Product that eliminates accumulated dirt from a solid medium by resuspension or dissolution.
Disinfectant	A disinfecting agent, typically of a chemical nature, that can destroy microorganisms or other pathogens, but not necessarily bacterial spores or fungal spores. Refers to substances applied to inanimate objects.
Disinfection	Treatment that eliminates most of the pathogens present on an object or surface
Facilities	All devices, rooms and spaces that are organized, arranged and modified to better adapt them to the activities to be conducted therein.
Dispensing a prescription	All activities relating to the validation (including therapeutic appropriateness), preparation and packaging of a patient's medication prepared pursuant to a prescription.
Final non-sterile preparation	A non-sterile preparation ready to be stored and then administered to a patient, which has been prepared according to a preparation-specific master formulation record which respects the prescriber's prescription.
Hand hygiene	All methods related to hand washing that is performed using soap and water, followed by a waterless, alcohol-based hand rub with persistent activity.

Hazardous drug	<p>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.</p> <p>Drugs are considered hazardous because they involve risks for the worker, because of their effects.</p>
Hazardous material	<p>A material that, because of its properties, constitutes a danger to an employee's health, safety or physical integrity. Hazardous materials are dangerous products regulated by a workplace hazardous material information system; as such, they are considered "controlled" products under the <i>Hazardous Products Regulations</i>.</p>
Hazardous products	<p>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.</p>
Incident	<p>An action or situation that has no impact on the health status or well-being of the user (patient), personnel, professional concerned or third party, but which as an unusual result that could, on other occasions, lead to consequences. An incident differs from an accident, which has or could have an impact on the patient.</p>
Insert	<p>Document or leaflet containing information about a drug additional to that written on the computer-generated label produced by the prescription management software; provides the patient with information as required by regulations.</p>
Label (for identifying a non-sterile preparation)	<p>Label that identifies the drugs prepared or sold with or without a prescription. It is usually computer-generated and adhesive. It must bear the information required by federal/provincial/territorial regulations.</p>
Log	<p>Book or notebook in which data are recorded or compiled to demonstrate that the quality of the pharmacy compounding process has been maintained.</p> <p>A log may be in computerized format.</p>
Maintenance of competency	<p>Continued ability to integrate and apply knowledge, know-how, judgment and personal qualities necessary to practise in a safe and ethical fashion in a designated role and framework.</p>
Master Formulation Record	<p>This contains all the information, instructions and procedures required to compound a non-sterile preparation.</p>
Maintenance (of facilities and equipment)	<p>Operations for maintaining the proper functioning of facilities or equipment according to established specifications or for re-establishing the satisfactory operational condition of facilities, including the heating, ventilation and air conditioning system and related equipment.</p>
Safety data sheet (formerly material safety data sheet)	<p>According to the Commission de la santé et de la sécurité du travail: A "document that provides information on a controlled product, namely its toxic effects, the protective measures for avoiding overexposure or chemical hazards, and the procedures to follow in an emergency. The supplier sends the SDS to the employer when the product is sold. It must be ... kept on the premises by the employer in a location known by the workers, and be easily and rapidly accessible to those who are likely to come in contact with the product. The employer should have it before a product is used for the first time".</p>
Non-sterile compounding supervisor	<p>A person assigned by the department head of the health care facility or by the pharmacist owner of a community pharmacy to supervise and organize all activities related to the compounding of non-sterile preparations.</p>

Non prescription drugs	Drugs that can be sold in a pharmacy without a prescription
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 with a degree in pharmacy who is registered in good standing with one of the pharmacy regulatory authorities in Canada.
Pharmacy assistant	An adult who has earned a vocational school diploma for completing a pharmacy assistant course or any adult person who has received proper training that is deemed equivalent.
Pharmacy technician	A person who has earned a college degree or diploma as a pharmacy technician and is registered or authorized by a pharmacy regulatory authority in Canada to practise as a pharmacy technician.
Policy	All the general principles adopted by a private or public organization for conducting its activities. By extension, the term "policy" also refers to the text or document that presents the policy.
Procedure	All steps to be taken, the means to be used and the methods to be followed in performing a task.
Protocol	Document describing in detail all steps to be followed or behaviours to adopt in precise clinical circumstances.
Stability (period of)	Length of time during which a properly compounded non-sterile preparation maintains, within specified limits and throughout the storage and usage period, the properties and characteristics that it had when it was compounded.
Training	Acquisition of a totality of theoretical, technical and practical knowledge concerning pharmacy preparation.
Withdrawal period	The length of time between the last administration of a drug to an animal and the time when tissues or products collected from the treated animal for consumption as food contain a level of residue of the drug that would not likely cause injury to human health. (Food and Drug Regulations C.01.001)

11. LIST OF TABLES

Table 1 Beyond-use dates (BUD) by Type of Formulation

Table 2 Required conditions for a hazardous products storage area

13. APPENDICES

APPENDIX I GENERAL GUIDELINE ON COMPOUNDING AND MANUFACTURING ACTIVITIES¹⁰⁴

- 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 an inordinate amount of product produced or on a regular basis?
 - Compounding - No
 - Manufacturing - Yes

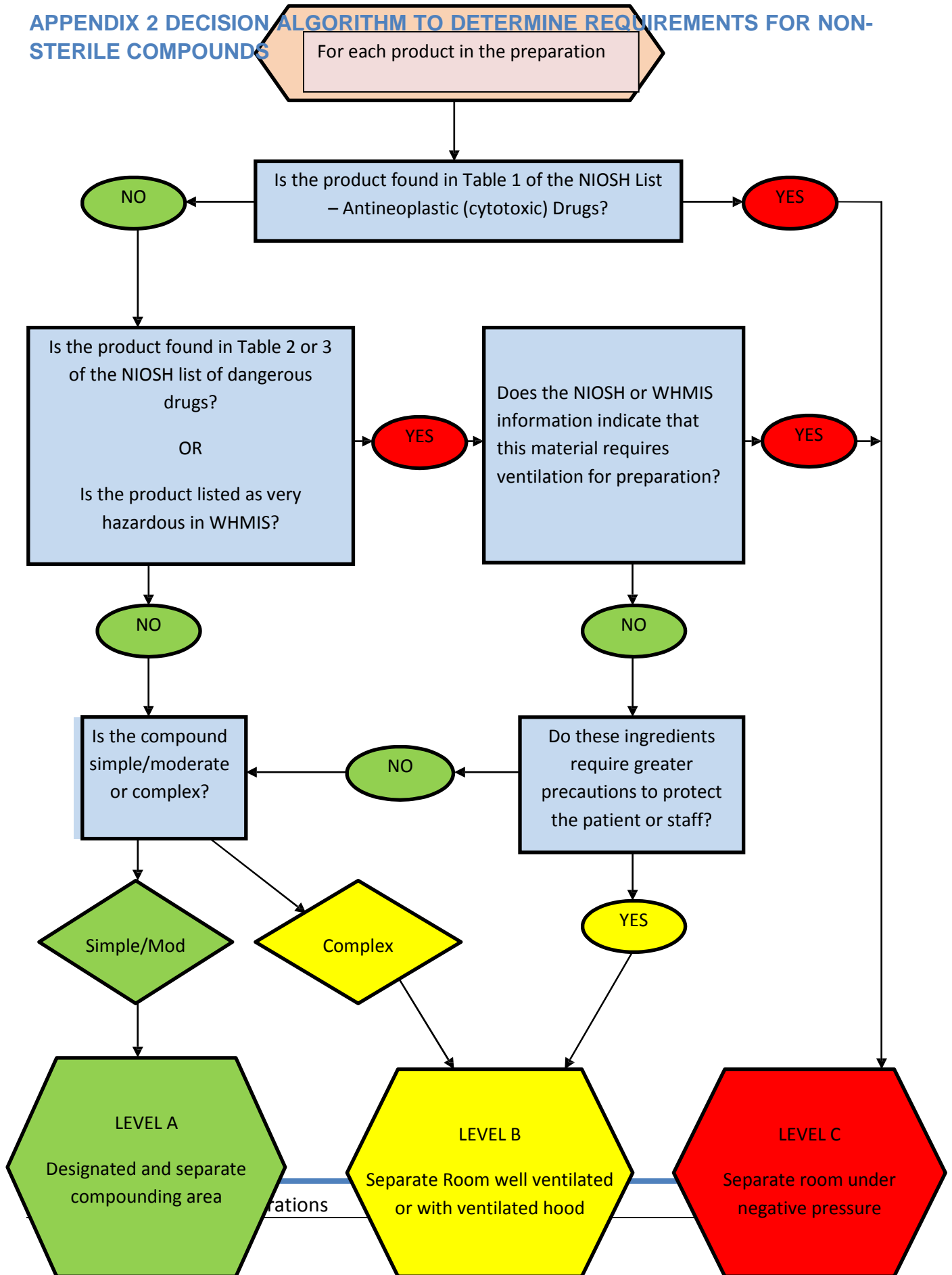
- 6) Is an identical product (e.g. dosage form, strength, formulation) commercially available?
 - Compounding - No
 - Manufacturing - Yes

- 7) Is the product and/or compounding service promoted or advertised to the general public rather than strictly to healthcare professionals?
 - Compounding - No
 - Manufacturing - Yes

- 8) 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

¹⁰⁴ Health Canada, Policy on Manufacturing and Compounding Drug Products in Canada (POL-0051), January 26, 2009, Appendix 1.

APPENDIX 2 DECISION ALGORITHM TO DETERMINE REQUIREMENTS FOR NON-STERILE COMPOUNDS



APPENDIX 3 SUMMARY OF REQUIRED CONDITIONS FOR NON-STERILE COMPOUNDING PREPARATIONS

SUMMARY OF REQUIRED CONDITIONS FOR NON-STERILE COMPOUNDED PREPARATIONS				
REQUIREMENTS		Level A	Level B	Level C
		Mandatory = ✓	Mandatory = ✓	Mandatory = ✓
Personnel:	Sec. 6.1			
Appoint a non-sterile compounding supervisor		✓	✓	✓
Training:	App. 8			
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 staff skills assessment program must be implemented.		✓	✓	✓

Facilities:	Sec. 6.3			
- Designated non-sterile compounding area		✓		
- Dedicated room, entirely closed off, well ventilated or with a ventilated hood. Air exhausted to the outside.			✓	
- Dedicated room under negative pressure to the pharmacy. Filtered air exhausted to the outside.				✓

APPENDIX 4 TRAINING OF COMPOUNDING PERSONNEL AND CLEANING PERSONNEL

A. Training of compounding personnel

#	ELEMENTS TO COVER IN TRAINING			
1.	FOR THE COMPOUNDING OF NON-STERILE PREPARATIONS	PH	PT	PA
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, garbing, 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 disinfecting 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 devices available for the non-sterile preparations to be compounded. Know how to calibrate the devices used.	X	X	X
1.9	Be able to recognize errors in the compounding technique of compounding personnel.	X	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,	X	X	X

	facilities and materials.			
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	Know and establish levels of risk and beyond-use dates.	X		
2.	FOR THE COMPOUNDING OF HAZARDOUS NON-STERILE PREPARATIONS	PH	PT	PA
2.1	Have the competency required to compound non-sterile preparations.	X	X	X
2.2	Identify hazardous products in the composition of 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	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	X

B. Training of cleaning and disinfecting personnel

#	ELEMENTS TO COVER IN TRAINING	PH/PT	PA	C&D
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; PA = pharmacy assistant; C&D = cleaning and disinfecting personnel.				

APPENDIX 5 POLICIES AND PROCEDURES FOR THE COMPOUNDING OF NON-STERILE PREPARATIONS

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 devices, 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 Garbing 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	
	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)	

APPENDIX 6 PROCEDURE TEMPLATE

Pharmacy name Or Hospital XYZ pharmacy department	Procedure # _____ Revised: Yes <input type="checkbox"/> No <input type="checkbox"/> Approved by _____ Date _____ Effective date: _____
Procedure title:	
Aim and objective: ➤ Describe the objective of the procedure.	
Target personnel: Use this section to describe the expected responsibilities for each group that will be affected by this procedure. <input type="checkbox"/> Non-sterile compounding supervisor <input type="checkbox"/> Pharmacist <input type="checkbox"/> Pharmacy technician <input type="checkbox"/> Pharmacy assistant <input type="checkbox"/> Cleaning and disinfecting personnel <input type="checkbox"/> Other:	
Required facilities, equipment and material: Include the following types of information here: ➤ Facilities and equipment required to apply the procedure. ➤ Materials (e.g., devices, instruments) required to apply the procedure. ➤ Products to be used. ➤ Containers to be used. ➤ Logs to be used or completed.	

Procedures

Describe in detail what must be done by each person affected by the procedure, for each step or part of the procedure.

Include examples of labels, symbols, logs, etc., that are to be used.

Attach relevant documents, such as contracts, copies of legislation or regulations, manufacturers' instruction manuals, copies of administrative 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:

APPENDIX 7 REFERENCES

Compounding personnel must be able to consult a wide variety of up-to-date references in the pharmacy at any time.

At a minimum, the non-sterile compounding supervisor must make available the required references, standards guidelines and policies of the relevant pharmacy regulatory authority.

Pharmacies may also find the following references useful.

- 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).
- Compounding: Guidelines for Pharmacies, Canadian Society of Hospital Pharmacists, Ottawa, Ontario, 2014.
- 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.

References for 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”

- NIOSH [2014]. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2014. 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). Available from: <http://www.cdc.gov/niosh/docs/2014-138/pdfs/2014-138.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).

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.

USP has published in February 2016, a chapter describing 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 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."¹⁰⁵ 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, WHMIS 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.

APPENDIX 8 COMPOUNDING PROCESS (self-evaluation)

To avoid errors and maximize the therapeutic effect for the patient, compounding personnel must follow these steps:

Compounding steps	Compliant (✓)	Non-compliant (✓)
1. The compounded preparation prescribed is analyzed by the compounding pharmacist and considered appropriate and safe for the patient, based on the therapeutic intention.		
2. The calculations required to determine the necessary quantities of active ingredients and added substances have been carried out properly and verified.		
3. The instruments and apparatus required for the preparation have been properly selected.		
4. The compounding area and the instruments and apparatus required to compound the preparation have been cleaned.		
5. Staff responsible for compounding the preparation wear the appropriate clothing and wash their hands properly. <ul style="list-style-type: none"> <li data-bbox="296 841 1539 898">▪ Staff are wearing clean clothes appropriate for the tasks they are to perform. They are using the required protective accessories (cap, mask, gloves, etc.). <li data-bbox="296 946 1539 979">▪ A clean laboratory coat or a clean disposable gown is always worn for non-sterile compounding. <li data-bbox="296 1003 1539 1060">▪ For preparations that contain hazardous products, staff wear the appropriate protective clothing: cap, safety goggles, two pairs of gloves, an N95 mask and face protection, a gown and shoe covers, depending on the substance used. 		
6. To avoid microbial contamination of the preparations being compounded, the written procedures include instructions on attire and restrictions on staff working with open lesions or certain diseases.		
7. Compounding personnel compound only one preparation at a time.		
8. The procedures are such that the compounder avoids mixing up preparations to be compounded for different patients (e.g., having a different basket for each patient or a bin system to separate baskets of prescriptions for drug products to be compounded, etc.).		

9. Compounding is in line with the requirements for the various non-sterile compounded preparations.		
10. All the necessary compounding equipment has been assembled and is ready for use.		
11. Compounding of the preparation is in line with the master formulation record and the prescription, as well as with good practice and pharmacy science.		
12. The quality controls stipulated in the procedures have been performed, specifically:		
▪ Verification of the appearance of the final preparation (clarity, odour, colour, consistency, pH, etc.);		
▪ The controls performed are in line with the description in the master formulation record.		
13. Container labelling complies with provincial/territorial regulatory authority		
a. The batch number assigned to the preparation by the pharmacy has been added;		
b. The expiry date has been determined and it is marked on the label;		
c. The storage information has been added.		
14. The required forms have been completed and signed by the compounding personnel		
15. The uniformity, identity and strength of the preparation, as well as its quantity and the purity of the preparation ingredients are as required.		
16. The required information has been noted in the various logs.		
17. A description of the appearance of the finished product can be found in the master formulation record. Conformity of the appearance of the final preparation has been verified.		
18. The equipment was:		
▪ cleaned immediately after use according to manufacturer's directions or standards, and dried;		
▪ properly stored in a cabinet;		
▪ The cabinet is clean and used only for this purpose.		
19. The products and ingredients were put away immediately after use.		

APPENDIX 9 TEMPLATE FOR A MASTER FORMULATION RECORD TO BE COMPLETED FOR EACH PREPARATION

<p>Name of compounded product:</p> <p>Concentration:</p> <p>Pharmaceutical form:</p> <p>Route of administration:</p>	<p>Protocol number and version (e.g., 001-01)</p> <p>Effective date: (dd/mm/yyyy)</p> <p>Authorized by: _____, pharmacist</p>
---	---

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 devices to be carried out and documented before measurements are taken.
- Accuracy of measurement devices.
- Verification and documentation of ingredients, batch numbers and beyond-use dates.
- Type of report required on the compounding form.

Required devices, instruments and materials

Indicate all materials and equipment that were required to compound the non-sterile preparations.

Compounding method

Describe all steps of the non-sterile-product compounding process.

Quality controls

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

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

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

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

Packaging

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

Stability and storage

Specify the preservation requirements of the compounded non-sterile preparation.
Specify the shelf life of the compounded non-sterile preparation (beyond-use date).
Indicate the references used to determine shelf life.

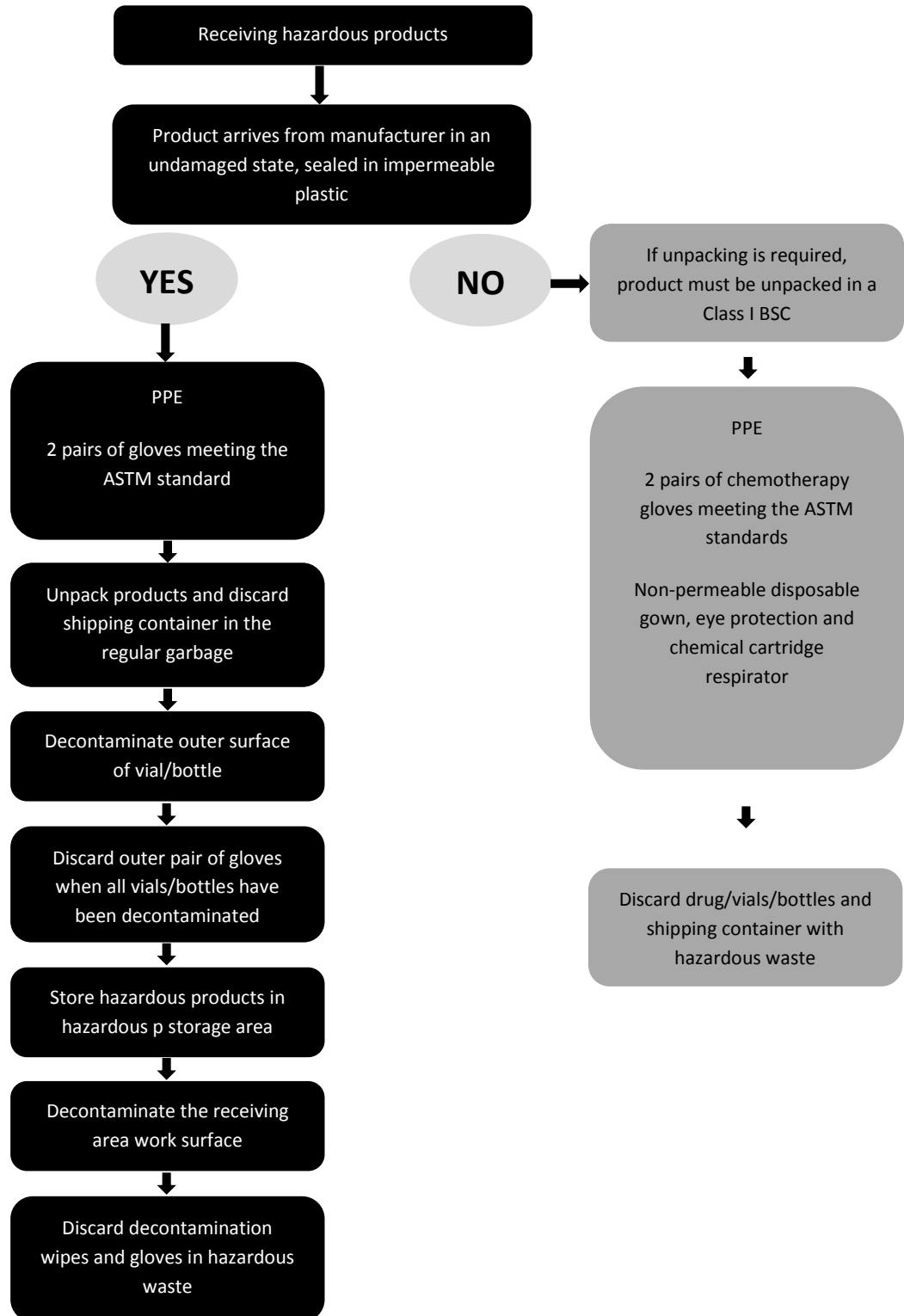
Labelling	Sample label
<p>Indicate mandatory information that must be on the label of the compounded non-sterile preparation.</p> <hr/> <p>A) When kept at the pharmacy or sent to another pharmacy</p>	<hr/> <p>Name of preparation:</p> <p>Date when preparation was made:</p> <p>Lot:</p> <p>Quantity prepared:</p> <p>Beyond-use date:</p> <p>Shelf life:</p> <p>Verified by:</p>

<p>B) When dispensed to a patient</p>	<p>Customer label</p> <p>In addition to the legally mandated information, add:</p> <ul style="list-style-type: none"> - lot number of compounded preparation - beyond-use date - precautions and other patient information leaflet
<p>Training</p> <p>Indicate the training that personnel must undergo before the specific compounding procedure is implemented.</p>	
<p>References consulted:</p> <p>Indicate the source of the specific compounding procedure. Indicate any documentation supporting the stability of the final compounded non-sterile preparation.</p>	
<p>Preparation data sheet history No.:</p>	
<p>Date drafted: (dd/mm/yyyy)</p>	<p>Drafted by:</p>
<p>Revised: (dd/mm/yyyy)</p>	<p>Revised by:</p>

Change made:	Version number changed: <input type="checkbox"/> YES <input type="checkbox"/> NO
Revised: (dd/mm/yyyy)	Revised by:
Change made:	Version number changed: <input type="checkbox"/> YES <input type="checkbox"/> NO

APPENDIX 10 PROCEDURE EXAMPLE See [10.3.4 Area for unpacking hazardous products](#) for more details

Receiving, unpacking and storing hazardous products



APPENDIX 11 TEMPERATURES FOR DIFFERENT TYPES OF STORAGE

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

APPENDIX 12 INCIDENT/ACCIDENT REPORTING AND FOLLOW-UP FORM

Accident/accident* reporting and follow-up			
Reporting an incident <input type="checkbox"/> accident <input type="checkbox"/>			
General information			
Date and time of incident/accident:	Reported by:		
Name of patient affected, if applicable:	Full address:		
	Phone number:		
Pharmacy personnel involved:			
Information about incident/accident			
(Summary of the situation and consequences)			
Disclosed to the patient concerned: <input type="checkbox"/>			
Name of pharmacist responsible for follow-up:			
Analysis of causes			
Causes: (Identify causes of the problem)	Options for corrections or changes: (Assess potential corrections or changes to be made)	Corrections or changes chosen: (Indicate the corrections or changes to be made)	
Action plan			
Actions (Describe the actions to be taken and the steps required to correct the situation, with a specific timeline. Determine who will be responsible for implementation.)	Responsible	Deadline	✓

Monitoring		
Verifications (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.

APPENDIX 13 EXAMPLE 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)	<ul style="list-style-type: none"> • At least every 6 months • When the compounding area is installed • When new equipment is installed • When area or equipment are repaired or maintained • When a contamination problem is identified
	Verification of compounding rooms (for Level B or C) (appropriate ventilation, materials storage, clean, orderly, good state of repair)	<ul style="list-style-type: none"> • At least every 6 months (more frequently at the start of the quality assurance program) • When the controlled room is installed • When new equipment is installed • When the controlled room or equipment is repaired or maintained (e.g., when high-efficiency particulate air filter changed) • When a contamination problem is identified • When investigation of a contamination problem or non-compliance in the preparation process requires exclusion of malfunctioning facilities • According to an internal verification program
	Verification that daily temperature and humidity readings are documented in controlled areas	<ul style="list-style-type: none"> • Monthly
EQUIPMENT	Certification of C-PEC (Level B or C)	<ul style="list-style-type: none"> • Before first use • Every 6 months • When a new C-PEC is installed • When the C-PEC is repaired or maintained • When a contamination problem is identified • When investigation of a contamination problem or non-compliance in the preparation process requires exclusion of malfunctioning equipment

	Temperature verification (e.g., refrigerator, freezer)	<ul style="list-style-type: none"> • Verify logs monthly or more often if problems identified • Yearly calibration of temperature probes
	Operational indicators of C-PEC and other devices used (e.g., automated compounding device)	<ul style="list-style-type: none"> • Verify logs monthly
PERSONNEL	Skills assessment (technique, following procedures, appropriate PPE, etc)	<ul style="list-style-type: none"> • At initial qualification: theoretical and practical aspects • Periodically to ensure compliance with policies and procedures • After extended leave • When assessing incidents and accidents • When a contamination problem is identified
FINAL COMPOUNDED NON-STERILE PREPARATION	Verification of master formulation records (usage and maintenance)	<ul style="list-style-type: none"> • Yearly 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	<ul style="list-style-type: none"> • Quarterly review of documentation
	Verification that documentation of procedures, compounders initials, entry in logs are being carried out.	<ul style="list-style-type: none"> • Quarterly review of documentation
DOCUMENTATION	Policies and procedures in place and updated regularly	<ul style="list-style-type: none"> • Every 3 years, or when new information becomes available
	Compounded prescription records meet all regulatory requirements, all logs current in documentation	<ul style="list-style-type: none"> • Quarterly
	Current references and safety data sheets available	<ul style="list-style-type: none"> • Yearly

14. 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.

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