MODEL STANDARDS FOR PHARMACY COMPOUNDING OF NON-STERILE PREPARATIONS

PUBLISHED WITH THE GUIDANCE DOCUMENT FOR PHARMACY COMPOUNDING OF NON-STERILE PREPARATION

NAPRA ANORP

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

Model Standards for Pharmacy Compounding of Non-sterile Preparations — Published with the Guidance Document for Pharmacy Compounding of Non-sterile Preparations

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

Adapted with permission from "Préparations magistrales non stériles en pharmacie – Norme 2012.01", Ordre des pharmaciens du Québec, 2012

The National Association of Pharmacy Regulatory Authorities (NAPRA)
130 Albert Street, Suite 1800, Ottawa, ON K1P 5G4
E-mail: info@napra.ca | Telephone: 613-569-9658 | Fax: 613-569-9659

ACKNOWLEDGEMENTS

The National Association of Pharmacy Regulatory Authorities (NAPRA) would like to first thank one of its members, the Ordre des pharmaciens du Québec, for having made possible the adaptation of its document entitled "Préparations magistrales non stériles en pharmacie – Norme 2012.01" to create this national document, "Model Standards for Pharmacy Compounding of Non-sterile Preparations," and the accompanying "Guidance Document for Pharmacy Compounding of Non-sterile Preparations."

In addition, NAPRA would like to thank the members of the National Advisory Committee on Pharmacy Practice (NACPP) for their continued diligence in the development of these documents.

Craig Connolly, Chair - Nova Scotia College of Pharmacists
Anjli Acharya - Alberta College of Pharmacists
Guylaine Bertrand/Annie Boulanger - Ordre des pharmaciens du Québec
Heather Christ - New Brunswick College of Pharmacists
Dale Cooney/Jennifer Mosher - Alberta College of Pharmacists
Jeanne Eriksen - Saskatchewan College of Pharmacy Professionals
Melanie Healey - Newfoundland and Labrador Pharmacy Board
Suzanne Solven/David Pavan - College of Pharmacists of British Columbia
Anne Resnick - Ontario College of Pharmacists
Sue Sampson - Nova Scotia College of Pharmacists
Michelle Wyand - Prince Edward Island College of Pharmacists
Todd Mereniuk/Jill Hardy - College of Pharmacists of Manitoba

NAPRA also acknowledges with thanks the support and technical contribution of Della Croteau (consultant) in the preparation of these documents.

CONTENTS

1. INTRODUCTION

The "Guidelines to Pharmacy Compounding" published by the National Association of Pharmacy Regulatory Authorities (NAPRA) in October 2006 have recently been reviewed, a process that has resulted in a new set of documents: the Model Standards for Pharmacy Compounding of Non-hazardous Sterile Preparations[1], the Model Standards for Pharmacy Compounding of Hazardous Sterile Preparations[2], and the Model Standards for Pharmacy Compounding of Non-sterile Preparations with its accompanying document, the Guidance Document for Pharmacy Compounding of Non-sterile Preparations (referred to hereafter as the Guidance Document).

The NAPRA Model Standards for Pharmacy Compounding of Non-sterile Preparations and the accompanying Guidance Document 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 and involved extensive consultation with experts and stakeholders. These Model Standards and the accompanying Guidance Document are intended to ensure the safety of both patients and the personnel involved in compounding non-sterile drugs.

Each standard presented herein has a corresponding section in the Guidance Document with details concerning how the standard can be achieved. The corresponding section is referenced in these Model Standards by using the letters GD (for Guidance Document) and the number of the applicable section, i.e. GD-2.1. The requirements of the applicable pharmacy regulatory authority must also be consulted.

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

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

2. OBJECTIVES

The aim of 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 apply to all non-sterile compounding by pharmacy personnel; however, not every standard will apply in every practice setting. These 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 have been proven to be equivalent or superior to those described in the accompanying Guidance Document.

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.

As for all prescriptions, it is expected that a pharmacist will review the prescription for each non-sterile preparation and use personal expertise to determine whether the compounded preparation is appropriate for the particular patient. In addition, the pharmacist and/or pharmacy technician who is designated as the compounding supervisor must determine whether the appropriate knowledge and resources to develop the formulation and/or the appropriate equipment and competency to compound the preparation are available. See section GD-2.1 in the Guidance Document for a list of questions that may be helpful in making this determination. Once a determination has been made that it is appropriate to compound the preparation, these Model Standards must be applied.

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

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

3. REGULATORY FRAMEWORK

Although compounded non-sterile preparations are sometimes prepared by other healthcare professionals, including nurses, physicians and veterinarians, the majority of non-sterile compounding is performed by pharmacy personnel under the supervision or direction of pharmacists. Although these Model Standards could serve as best practices for other healthcare practitioners, they pertain specifically to compounding by pharmacy personnel for human or animal use[5] in all pharmacy settings where non-sterile preparations are compounded.

In January 2009, Health Canada developed its "Policy on Manufacturing and Compounding Drug Products in Canada"[6]. It is expected that this Health Canada policy will be followed, along with these Model Standards. Compounding must always occur within the context of a patient–healthcare professional relationship or, in the case of a compounded veterinary product, within a veterinarian–client–patient relationship. In the absence of a patient-specific prescription, and with a prescriber's order for office use, compounders may prepare a compounded product at an appropriate scale, time or frequency to ensure it is being used within a patient–healthcare professional relationship. Compounders may also prepare batches of compounded product in limited quantities in anticipation of future prescriptions. Requests to compound preparations in bulk quantities for distribution or sale outside a patient–healthcare professional relationship generally fall into the realm of manufacturing and are thus outside the jurisdiction of pharmacies. Section GD-3.1 in the Guidance Document provides general guidance 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. Given that pharmacists and pharmacy technicians are expected to maintain competency in basic compounding skills, they are also expected to provide compounded preparations within their level of expertise and within the limitations of available and appropriate facilities and equipment. When individuals do not have the knowledge, training, expertise, facilities or equipment required for compounding complicated non-sterile preparations or hazardous non-sterile preparations, they must refer patients to a colleague who does have the competencies and facilities required to do so or, where permitted by provincial/territorial legislation, ask another pharmacy to compound the preparation. The sections in the Guidance Document on risk assessment (GD-4) and determining capacity for compounding (GD-2.1) provide information for pharmacists and pharmacy technicians to consider when deciding whether or not to compound a particular preparation.

The Model Standards for Pharmacy Compounding of Non-sterile Preparations exclude 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 such, minor modifications are not classified as "compounding" by Health Canada[7]. However, the minimum conditions for good pharmacy practice should be maintained when performing these activities, and pharmacies are encouraged to follow basic requirements for non-sterile compounding found in these Model Standards.

Pharmacists and pharmacy technicians must also comply with any federal regulations regarding the compounding of a product that is not a drug, such as a cosmetic or food. It is recommended that, in the absence of specific legislation, these Model Standards be considered best practice for such compounded products.

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

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

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

4. ASSESSING RISK FOR COMPOUNDING NON-STERILE PREPARATIONS

A risk assessment must be undertaken to identify the appropriate level of requirements to minimize contamination of each compounded product and to provide adequate protection for personnel. In addition to assessing the risk associated with compounding of individual products, the compounding supervisor must also consider the cumulative risk of all preparations compounded in the pharmacy.

Steps in conducting a risk assessment

Conduct a risk assessment for compounding non-sterile preparations, covering risk to preparation and risk to person(s). (sections GD-4.1 factors to consider, GD-4.2 decision algorithm, and GD-4.3 references)	**Risk to preparation** The preparation must be compounded in an area free of interruption from other activities in the surrounding space The area must be large enough for compounding equipment and ingredients The compounder must ensure that nothing in the surrounding area (either personnel, objects or materials) contaminates the preparation being compounded
	Risk to person(s) The compounder must be protected from materials that may be hazardous or harmful The compounding area must be contained, so that it does not create a hazardous environment for others
Document the risk assessment, clearly explaining how risk to preparation and risk to person(s) have been mitigated.	Rationale for risk assessment and mitigation must be documented on the Master Formulation Record Procedures for mitigating risk must be documented on the Master Formulation Record Rationale and procedures must be referenced Rationale and procedures must be clear to all Rationale and procedures must be reviewed at least every 12 months
Implement the level of requirements commensurate with the risk. See Section 8 in this document and the Guidance Document	**Level A** Simple and moderate compounds, as defined in USP *General chapter <795>* and in accordance with Health Canada POL-0051[8]
	Level B Complex compounds, as defined in USP *General chapter <795>* Small quantities of ingredients or preparations that require ventilation and are compounded occasionally
	Level C Hazardous drugs classified by National Institute for Occupational Safety and Health (NIOSH)[9] as Group 1 Hazardous materials classified by Workplace Hazardous Materials Information System (WHMIS)[10] as representing a health hazard, such as those that are very irritating to the respiratory tract, the skin or the mucous membranes NIOSH Group 2 and 3 drugs for which large quantities of active pharmaceutical ingredients (APIs) are used routinely

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

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

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

5. REQUIREMENTS FOR ALL LEVELS[11] OF NON-STERILE COMPOUNDING ACTIVITIES

5.1 Compounding personnel

All personnel are responsible for knowing and performing their roles and responsibilities in accordance with these Model Standards and the requirements of the applicable pharmacy regulatory authority.

Pharmacy manager Pharmacy department head	Responsible for the development, organization and supervision of all activities related to compounding of non-sterile preparations in the pharmacy (section GD-5.1.1)
Non-sterile compounding supervisor (pharmacist or pharmacy technician)	Develops, organizes and oversees all activities related to compounding of non-sterile preparations in the pharmacy (section GD-5.1.2)
	Ensures that personnel are fully trained and know policies and procedures
	Ensures that a risk assessment is performed for each preparation
	Ensures that appropriate facilities, equipment and references are available for use
	Ensures that the master formula and beyond-use date (BUD) are developed using scientific references and are reviewed appropriately
	Ensures that a quality assurance program is in place
	Ensures that all records of decisions, activities and specifications are complete and appropriately documented
Regulated pharmacy personnel (pharmacist or pharmacy technician)	Compounds non-sterile preparations in accordance with approved formulas (section GD-5.1.3)
	Complies with established policies and procedures
	Clearly documents decisions, completed activities and verifications before dispensing (pharmacist) or releasing (pharmacy technician) a compounded product
	Ensures that all compounding standards and standards of practice have been met
Non-regulated pharmacy personnel	Compounds non-sterile preparations under appropriate supervision in compliance with the requirements of the provincial/territorial pharmacy regulatory authority (section GD-5.1.4)

5.2 Training and skills assessment

Expertise must be commensurate with responsibilities for compounding personnel	A training program must be in place for all compounding personnel, and a record of all training must be kept (section GD-5.2.1 for a template of elements to be covered during training)
	A skills assessment program must be established, administered and documented for all personnel involved in non-sterile compounding (see section GD-5.2.1.1 for example of a skills assessment)
	A record must be maintained of the results of skills assessments and any corrective action taken
Cleaning personnel	Those involved in the cleaning of compounding areas must be properly trained so they are aware of the importance of cleaning activities required to prevent cross-contamination (see section GD-5.2.2 for a template of elements to be covered during training)

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

5.3 Policies and procedures[12, 13]

Policies and procedures for all activities related to compounding must be established (see section GD-5.3.1 for a table listing possible policies and procedures and section GD-5.3.2 for a template)	Must be clear and provide detailed descriptions of all activities, including cleaning
	Must be reviewed at least every 3 years, or more frequently if there is a change in practice or standards
	Must be updated promptly when there is a change affecting practice
	Additional procedures must be developed if staff are also handling hazardous products

5.4 Facilities and equipment

This section applies to all levels of non-sterile compounding. Additional requirements are expected for Level B and Level C compounding, as described in section 9.

5.4.1 Facilities for non-sterile compounding

Compounding must be performed in a separate, specifically designated space	Compounding areas must be large enough for compounding personnel to work comfortably and safely; there must be room to store equipment and products in an orderly manner, in clean and secure surroundings (section GD-5.4.1.1)
	All components, equipment and containers must be stored off the floor, in a manner that prevents contamination and allows for appropriate cleaning and inspection
	The compounding area must be conducive to necessary cleaning and must be maintained in sanitary condition and in good repair; adequate systems must be in place to ensure appropriate and sanitary waste disposal
	Lighting fixtures must be located such that they provide sufficient light for all compounding activities (section GD-5.4.1.2)
	The heating, ventilation and air conditioning systems must be controlled to avoid decomposition and contamination of chemicals, to maintain the quality of products and to ensure the safety and comfort of compounding personnel (section GD-5.4.1.3)
	A clean water supply, with hot and cold running water, must be available in or close to the compounding area (section GD-5.4.1.4)
	Work surfaces and furniture, as well as floor and wall surfaces, must be designed to facilitate repeated cleaning (section GD-5.4.1.5)
	Compounding areas must be maintained with the cleanliness and hygiene needed to ensure the quality and integrity of the final preparations (section GD-5.4.1.6)

5.4.2 Equipment for non-sterile compounding

Equipment, instruments and accessories	Must be appropriate for the type of preparations to be compounded
	Must not negatively affect the purity or quality of the preparation being compounded
	Must be cleaned well after each use

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

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

Equipment, instruments and accessories must be maintained to ensure proper performance (section GD-5.4.2.1)	Must be routinely inspected and calibrated, if applicable, at appropriate intervals, as recommended by the manufacturer, or at least once a year if there are no manufacturer recommendations
	Equipment (e.g., fridges, balances) must meet any requirements established by the provincial/territorial pharmacy regulatory authority
	Records of calibration dates for equipment and instruments must be maintained
Specialized equipment must be clean	Must be cleaned regularly, as recommended by the manufacturer (section GD-5.4.2.2)
	A log must be kept recording each cleaning session (section GD-5.4.2.3)

6. PRODUCT AND PREPARATION REQUIREMENTS

BUD and dating methods (see section GD-6.1.1 for guidelines on assigning BUD)	Must be determined by regulated pharmacy personnel with adequate experience and broad scientific knowledge
	Must be assigned after consulting the manufacturer's documentation and literature on the stability, compatibility and degradation of ingredients
	Compounded preparations must be monitored for signs of instability and/or degradation
Master Formulation Record (see section GD-6.2 for requirements and template)	Must be developed for each non-sterile compound by regulated pharmacy personnel with adequate experience and broad scientific knowledge
	Must include all necessary information to compound the non-sterile preparation
	Must contain supporting rationale and references
	Must be kept in a format that is readily accessible to compounding personnel
Ingredients used for compounding (see section GD-6.3)	Must be pure and of good quality (section GD-6.3.1)
	Purified water or water of equivalent or superior quality must be used whenever the formula specifies water as an ingredient (section GD-6.3.1)
	Must be obtained from recognized and reliable sources (section GD-6.3.2)
	The sources of ingredients (as well as lot numbers, expiry dates and date of receipt in the pharmacy) must be traceable (section GD-6.3.3)
	Ingredients for compounding that have been recalled or withdrawn from the market for safety reasons must not be used (section GD-6.3.3)
	Current safety data sheet must be readily accessible for all ingredients (section GD-6.3.4)
	Must be stored under conditions that will preserve their purity and quality (section GD-6.3.5)
Compounding record (section GD-6.4)	Must be kept (in paper-based or electronic form) for each individual prescription and for non-sterile preparations made in batches
Conduct of personnel (section GD-6.5)	Must behave in a professional manner, following all pertinent policies and procedures
	Must perform good hand hygiene
	Must wear a clean laboratory coat that is reserved for compounding
	Must wear powder-free gloves
	Must use any other personal protective equipment (PPE) or equipment indicated on the Master Formulation Record
	Must not store or consume food or drink, or use tobacco, in the compounding area
	Must take any other reasonable measures to prevent cross-contamination and to protect themselves from chemical exposure
Verification (section GD-6.6)	Must be performed at each stage of the compounding process
	Final verification must take place before the preparation is dispensed

Labelling and packaging (section GD-6.7)	A policy for labelling and packaging must be established that is consistent with the requirements of the applicable pharmacy regulatory authority (section GD- 6.7.1)
	The label and supplementary label must provide all information required for proper use of the compounded preparation by the patient or for safe administration by a third party (section GD-6.7.2)
	Packaging appropriate to maintain the integrity of the compounded preparation must be used (section GD-6.7.3)
Storage (section GD-6.8)	A storage procedure must be established that is consistent with any requirements of the applicable pharmacy regulatory authority
	Active and inactive ingredients must be stored according to manufacturers' recommendations, in a manner that prevents cross-contamination (see section GD-6.8.1 for a chart of recommended storage temperatures)
	Each finished product must be stored according to the requirements outlined in its Master Formulation Record
Transport and delivery	Policies for transport and delivery must meet regulatory requirements and address any special precautions for non-sterile compounded products (section GD-6.9)
Product recalls	Procedures for recall of products must include documentation to ensure traceability of all ingredients included in non-sterile compounded products (section GD-6.10)
Incidents and accidents	An event report must be completed for any incident or accident involving a compounded non-sterile product (see section GD-6.11.1 for an example of an incident / accident reporting and follow-up form)

7. QUALITY ASSURANCE

Quality assurance program (see section GD-7.6 for example components of a quality assurance program)	Must be developed and implemented to ensure the clear definition, application and verification of all activities affecting the quality of the final product and the protection of personnel (section GD-7.1)
Equipment and compounding areas (section GD-7.2)	Equipment must be certified at installation and regular intervals, according to the manufacturers' recommendations (section GD-7.2.1)
	Temperature readings must be taken at regular intervals to ensure the integrity of products stored in refrigerators, in freezers or at room temperature (section GD-7.2.2)
Compounding personnel (section GD-7.3)	Must be trained, certified and reassessed at regular intervals to ensure maintenance of competency
Compounding procedures (section GD-7.4)	Compliance with compounding procedures must be monitored
Documentation (section GD-7.5)	Must be verified, signed and retained as per requirements of the applicable pharmacy regulatory authority
	Non-compliance with the quality assurance (QA) program and corrective actions must be documented

8. LEVELS OF REQUIREMENTS

The requirements for non-sterile compounding are based on the complexity and risks associated with preparing the compound and handling the substances used to make the compound. These requirements have been categorized into three levels. A summary-of-requirements chart can be found in section GD-8.4. See sections 4, 5 and 6 above and sections GD-4, GD-5 and GD-6 for more detail.

8.1 Level A

What is included	Requirements
Simple and moderate compounds, as defined in USP *General chapter <795>*[14]	Separate space designated for compounding

8.2 Level B

What is included	Requirements
Complex compounds, as defined in USP *General chapter <795>*[14]	Separate, well-ventilated room
	Larger workspace and appropriate equipment
	Environment conducive to few or no interruptions
	Greater protection from cross-contamination
Small quantities of ingredients or preparations that require ventilation and are compounded occasionally	May require a ventilated containment device when certain powders, aromatic products or hazardous products are compounded

8.3 Level C

What is included	Requirements
Hazardous drugs classified by NIOSH[15] as Group 1 drugs	Separate room
Hazardous materials classified by WHMIS[16] as representing a health hazard, such as those that are very irritating to the respiratory tract, the skin or the mucous membranes	Well-ventilated room with appropriate air exchange and negative pressure
NIOSH Group 2 and 3 drugs for which large quantities of APIs are used routinely	Appropriate containment device (i.e., Containment Primary Engineering Control [CPEC]) for materials being compounded

14 United States Pharmacopeial Convention (USP). General chapter <795>: pharmaceutical compounding — nonsterile preparations. In: *USP compounding compendium.* Rockville, MD: USP; 2016
Excludes reconstituting and mixing as per Health Canada, Health Products and Food Branch Inspectorate. *Policy on manufacturing and compounding drug products in Canada (POL-0051).* Ottawa, ON: Health Canada; 2009. Available from: http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/docs/pol_0051-eng.php

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

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

9. REQUIREMENTS FOR HAZARDOUS PREPARATIONS

Risk assessment for hazardous materials (section GD-5)	Must be reviewed at least every 12 months

9.1 Facilities for handling hazardous products (Level C)

Facilities (section GD-9.1)	Must be constructed to minimize the risk of exposure to compounding personnel and other pharmacy staff
Compounding room (section GD-9.1.1)	Must be ventilated through high-efficiency particulate air (HEPA) filtration, have appropriate air exchange and have negative pressure relative to surrounding rooms
	Must contain an eyewash station and any other emergency or safety equipment required
	Must be constructed with smooth impermeable surfaces to promote adequate cleaning and decontamination
	The heating, ventilation and air conditioning system must be constructed to prevent contamination of the areas surrounding the compounding room and to ensure the comfort of personnel wearing PPE (section GD-9.1.2)
	Windows and other openings must not lead directly outside or to a non-controlled area (section GD-9.1.3)
	There must be an appropriate area for unpacking hazardous products, and a C-PEC must be available for unpacking hazardous products that appear to be damaged (section GD-9.1.4)
Storage of hazardous products	Hazardous products must be stored in a room with appropriate ventilation (section GD-9.1.5)
	Areas for storing and preparing hazardous products must be identified with appropriate signage (section GD-9.1.6)

9.2 Equipment for handling hazardous products

Equipment (section GD-9.2)	A C-PEC that provides appropriate personal and environmental protection must be installed and maintained (section GD-9.2.1)
	All reusable equipment and devices must be adequately deactivated, decontaminated and cleaned (section GD-9.2.2)
	PPE approved for the compounding of hazardous non-sterile preparations must be worn during compounding activities (section GD-9.2.3): - chemotherapy gloves - disposable, impermeable gown - head, hair, shoe and sleeve covers - respiratory protection - eye and face protection

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

Cleaning of premises and equipment	Compounding area, equipment and accessories must be meticulously cleaned (section GD-9.3)
	Cleaning must also eliminate chemical contamination, specifically by deactivating, decontaminating and cleaning the premises and equipment (section GD-9.3.1)
	Cleaning personnel must comply with the pharmacy's hand hygiene and garbing procedure for handling hazardous products (section GD-9.3.2)
	The work surface of the C-PEC must be deactivated, decontaminated and cleaned before starting the compounding of a different preparation (section GD-9.3.3)

9.4 Incident and accident management

Incidents and accidents	Policies and procedures must be developed and followed for cases of accidental exposure of personnel to hazardous products (section GD-9.4.1)
	Personnel must receive training to prevent spills, as well as training on appropriate procedures to clean up spills, including use of a spill kit (section GD-9.4.2)
	Must be documented and followed up to prevent recurrence (section GD-9.4.3)

9.5 Hazardous waste management

Hazardous waste (section GD-9.5)	Procedures must be in place for the destruction and/or disposal of pharmaceutical waste in compliance with environmental protection legislation
	All personnel involved in the management of hazardous product waste must receive appropriate training and have access to all necessary PPE and cleaning supplies

9.6 Verification of controlled rooms and the containment primary engineering control (C-PEC)

Environmental verification (section GD-9.6)	The controlled room and C-PEC must be examined and certified every 6 months according to manufacturer's recommendations, as appropriate (and more often in the case of new equipment installation, repairs or a contamination problem) (section GD-9.6.1)
	Manufacturers' factory-issued certificates for all HEPA filters and C-PECs must be retained for the service life of the equipment (section GD-9.6.2)
	An environmental verification program must be established to ensure safety standards (section GD-9.6.3)
	All completed documentation concerning components of testing of controlled rooms and equipment for hazardous product contamination must be filed and retained with other compounding records, as per requirements of the applicable pharmacy regulatory authority (section GD-9.6.4)

10. GLOSSARY OF TERMS (WITH ABBREVIATIONS)[17, 18, 19, 20, 21, 22, 23]

Term and/or abbreviation	Definition
ACPH	Air changes per hour
Active pharmaceutical ingredient (API)	Any substance or mixture of substances intended to be used in the compounding or manufacturing of a drug (medicinal) product that, when used in this manner, becomes an active ingredient of the drug product, where the drug product so created has pharmacological activity in the diagnosis, cure, mitigation, treatment or prevention of disease or acts to affect the structure and function of the body. (see also *inactive ingredient excipitent)*
ASSTSAS	Association paritaire pour la santé et la sécruité du travail du secteur affaires sociales, a joint sector-based association dedicated to occupational health and safety in the health and social services sector in the province of Quebec.
ASTM	American Society for Testing and Materials; now known as ASTM International
Beyond-use date (BUD)	Date after which a compounded preparation shall not be used; determined from the date when the preparation is compounded.
Biological safety cabinet (BSC)	Laminar airflow workbench that is ventilated to protect personnel, hazardous compounded preparations and the immediate environment. The open front of a BSC has the following features: • air intake, to protect compounding personnel from hazardous preparations; • descending air curtain filtered with a high-efficiency particulate air filter, to protect the hazardous product; • air evacuation system equipped with high-efficiency particulate air filters for environmental protection.
Biomedical refrigerator	Refrigerator designed to refrigerate biological and medical products and drugs. Such refrigerators often come with an integrated temperature control system and an alarm system.
CACI	Compounding aseptic containment isolator
Competencies	Significant job-related knowledge, skills, abilities, attitudes and judgments required for competent performance of duties by members of a profession.
Containment primary engineering control (C-PEC)	A ventilated device designed to minimize exposure of personnel and the environment to hazardous products when such products are being handled directly. For hazardous non-sterile compounding, containment primary engineering controls include biological safety cabinets (BSCs).
Containment secondary engineering control (C-SEC)	The room in which the C-PEC is placed.
Containment system	Arrangement of equipment to contain the particles of hazardous products in the chosen space.

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

18 Bussières JF. Législation et système de soins : recueil de textes choisi et commentés. 5th edition. JF Bussières; 2009. p. 171.

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

20 Commission de la santé et de la sécurité du travail (CSST). *Material safety data sheet user's guide.* Québec, QC. CSST; 2010.

21 Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs.* Montréal, QC: ASSTSAS; 2008. Available from: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf

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

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

Deactivation	Treatment of a hazardous product to create a less hazardous agent. One method is chemical deactivation.
Decontamination	Transfer of a hazardous product contaminant from a fixed surface (e.g., counter, bag of solution) to a disposable surface (e.g., wipe, cloth). The wipe or cloth is then contained and discarded as hazardous waste.
DIN	Drug Identification Number
Hazardous drug	A drug for which research on humans or animals has shown that any exposure to the substance has the potential to cause cancer, leads to a developmental or reproductive toxic effect, or damage organs.
Hazardous material	A material that, because of its properties, constitutes a danger to an employee's health, safety or physical integrity. Hazardous materials are dangerous products regulated by a workplace hazardous material information system; as such, they are considered "controlled" products under the *Hazardous Products Regulations*.
Hazardous product	A substance that entails risks for the worker because of its effects. For the purposes of these Model Standards and the accompanying Guidance Document, the term "hazardous product" refers to both hazardous drugs and hazardous materials, depending on the situation.
HEPA	High-efficiency particulate air
Inactive ingredient excipient	Ingredient that is necessary to compound a preparation but that is not intended or expected to cause a pharmacological response in humans or animals if administered alone in the amount or concentration contained in a single dose of the compounded preparation.
NIOSH	National Institute for Occupational Safety and Health (US)
Non-regulated pharmacy personnel	A person who is employed in a pharmacy to assist the pharmacist or pharmacy technician.
Personal protective equipment (PPE)	All garb and accessories, such as mask, gloves, gown and safety goggles, that protect the non-sterile preparation and the worker. It enables compliance with the expected specifications of a controlled environment and protects the worker from exposure to physical or chemical risks.
Pharmacist	A person who is registered by a pharmacy regulatory authority in Canada to practise as a pharmacist.
Pharmacy technician	A person who is registered or authorized by a pharmacy regulatory authority in Canada to practise as a pharmacy technician.
Purified water	Used as an excipient in the production of non-parenteral preparations and in other pharmaceutical applications, such as cleaning of certain equipment. Purified water must meet the requirements for ionic and organic chemical purity and must be protected from microbial contamination. The source water may be purified by deionization, distillation, ion exchange, reserves osmosis, filtration or other suitable purification procedures. Distilled water is a form of purified water. (*see* USP monograph)[24]
Safety data sheet	Formerly known as a material safety data sheet, the safety data sheet is a summary document providing information about the hazards of a product and advice about safety precautions. It is usually written by the manufacturer or supplier of the product. In some circumstances, an employer may be required to prepare a safety data sheet (e.g., when the product is produced and used exclusively in that workplace). The safety data sheet provides more detailed hazard information about the product than the label. It tells users what the hazards of the product are, how to use the product safely, what to expect if the recommendations are not followed, how to recognize symptoms of exposure and what to do if emergencies occur.
WHMIS	Workplace Hazardous Materials Information System

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

11. BIBLIOGRAPHY

Note to readers: Many, but not all, references cited in this Guidance Document reflect the references appearing in the source document, "Préparations magistrales non stériles en pharmacie – Norme 2012.01," published by the Ordre des pharmaciens du Québec, 2012. Where possible, certain details have been verified against the source documents. URLs for online documents are current as of November 23, 2017.

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

Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide—safe handling of hazardous drugs.* Montréal, QC: ASSTSAS; 2008. Available from: https://asstsas.qc.ca/sites/default/files/publications/documents/Guides_Broch_Depl/GP65A_hazardous_drugs.pdf

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

Bussières JF. *Législation et système de soins : recueil de textes choisi et commentés.* 5th edition. JF Bussières; 2009.

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

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

Canadian Society of Hospital Pharmacists (CSHP). *Compounding: guidelines for pharmacies.* Ottawa, ON: CSHP; 2014. Available from: https://www.cshp.ca/compounding-guidelines-pharmacies

Canadian Veterinary Medical Association (CVMA). *Guidelines for the legitimate use of compounded drugs in veterinary practice.* Ottawa, ON: CVMA; 2006.

Commission de la santé et de la sécurité du travail (CSST). *Material safety data sheet user's guide.* Québec, QC: CSST; 2010.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Ordre des pharmaciens du Québec (OPQ). *Préparations magistrales non stériles en pharmacie – Norme 2012.01*. Montréal, QC: OPQ; 2012. Available from: www.opq.org

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

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

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

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

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

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

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

United States Pharmacopeial Convention (USP). General chapter <1072>: disinfectants and antiseptics. In: *USP compounding compendium*. Rockville, MD: USP; 2016.

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

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

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.

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