

**Model Standards for Pharmacy Compounding of Non-hazardous  
Sterile Products**

**DRAFT 2 A**

**National Association of Pharmacy Regulatory Authorities**

**(adapted with permission from “Préparation de produits stériles non dangereux  
en pharmacie – Norme 2014.01,” Ordre des pharmaciens du Québec, 2014)**

## ACKNOWLEDGEMENTS

The National Association of Pharmacy Regulatory Authorities 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 “Préparation de produits stériles non dangereux en pharmacie – Norme 2014.01” to create this national document, “Model Standards for Pharmacy Compounding of Non-hazardous Sterile Products.”

This adaptation would not have been possible without the work and dedication of the members of the National Association of Pharmacy Regulatory Authorities ad hoc Committee on Pharmacy Compounding. Special thanks are extended to these individuals: (list of members will be added).

## CONTENTS

1. INTRODUCTION
2. OBJECTIVES
3. REGULATORY FRAMEWORK
4. ABBREVIATIONS
5. CORE REQUIREMENTS FOR A STERILE COMPOUNDING SERVICE
  - 5.1 Personnel
  - 5.2 Policies and procedures
  - 5.3 Facilities and equipment
  - 5.4 General maintenance log
6. PRODUCT AND PREPARATION REQUIREMENTS
  - 6.1 Beyond-use date and dating methods
  - 6.2 Compounded sterile preparation protocols
  - 6.3 Compounded sterile preparation log
  - 6.4 Patient file
  - 6.5 Conduct of personnel in areas reserved for the compounding of sterile products
  - 6.6 Aseptic compounding of non-hazardous sterile products
  - 6.7 Packaging
  - 6.8 Storage
  - 6.9 Transport and delivery of final compounded sterile preparations
  - 6.10 Recall of sterile products or final compounded sterile preparations
  - 6.11 Incident and accident management
  - 6.12 Waste management
7. QUALITY ASSURANCE PROGRAM
  - 7.1 Program content
  - 7.2 Results and action levels
  - 7.3 Verification of equipment and facilities
  - 7.4 Quality assurance of personnel involved in aseptic compounding
  - 7.5 Quality assurance of compounded sterile preparations
  - 7.6 Documentation of quality control activities
8. SOURCE FOR ADDITIONAL INFORMATION
9. GLOSSARY

## 10. LIST OF TABLES

## 11. APPENDICES

Appendix 1 Policies and procedures for the compounding of non-hazardous and hazardous sterile products

Appendix 2 Mandatory and supplemental documentation

Appendix 3 Training of compounding personnel and cleaning and disinfecting personnel

Appendix 4 Procedure template

Appendix 5 Best practice indicators for certification of controlled rooms, laminar airflow workbenches and biological safety cabinets

Appendix 6 Certification of controlled rooms, laminar airflow workbenches and biological safety cabinets

Appendix 7 Template for the drafting of compounding protocols to be completed for each drug

Appendix 8 Examples of sterile preparations that must be verified at each stage of compounding

Appendix 9 Examples of sterile preparations that do not require verification during the compounding process

Appendix 10 Temperatures for different types of storage

Appendix 11 Incident/accident reporting and follow-up form

Appendix 12 Components of a quality assurance program

## 12. BIBLIOGRAPHY

## 1. INTRODUCTION

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

Evolving practice and increased awareness of the inherent dangers of compounding sterile products for the health of both patients and compounding personnel<sup>1, 2, 3, 4</sup> led to the need to review the “Guidelines to Pharmacy Compounding” published by the National Association of Pharmacy Regulatory Authorities (NAPRA) in October 2006.

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

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

## 2. OBJECTIVES

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

The Model Standards represent the minimum requirements to be applied in compounding sterile preparations; however, it is always possible to exceed these standards. The use of other technologies, techniques, materials and procedures may be acceptable, so long as they are proven to be equivalent or superior to those described here. Such other technologies, techniques, materials and procedures require prior approval from the provincial/territorial regulatory authority.

---

<sup>1</sup> Bussi eres JF, Prot S. Perspectives sur les pr eparations magistrales en pharmacie au Qu ebec. *Pharmactuel*. 2004;37(3):File 1.

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

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

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

### 3. REGULATORY FRAMEWORK

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

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

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

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

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

Compounded sterile preparations include the following types of medications:

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

---

<sup>5</sup> 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](http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/docs/pol_0051-eng.php)

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

## 4. ABBREVIATIONS

The following abbreviations are used in this document.

Abbreviation	Name
ABHR	Alcohol-based hand rub
ACD	Automated compounding device
ACPH	Air changes per hour
BUD	Beyond-use date
CAI	Compounding aseptic isolator
CFU	Colony-forming unit
GFTS	Gloved fingertip sampling
HEPA	High-efficiency particulate air
HVAC	Heating, ventilation and air conditioning
LAFW	Laminar airflow workbench
NF	National Formulary (United States)
NIOSH	National Institute for Occupational Safety and Health (United States)
PPE	Personal protective equipment
TSP	Technical support personnel
USP	United States Pharmacopeia

## 5. CORE REQUIREMENTS FOR A STERILE COMPOUNDING SERVICE

### 5.1 Personnel

#### 5.1.1 Roles and responsibilities

##### 5.1.1.1 Pharmacist owner or pharmacy manager

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

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

##### 5.1.1.2 Sterile compounding supervisor

###### Definition

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

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

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

###### Responsibilities

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

- A personnel training and assessment program is implemented.
- Personnel know and fully comply with policies and procedures.
- Appropriate measures are taken to ensure the safety of personnel during each

preparation.

- Policies and procedures covering all activities are developed, regularly updated and always followed (see Appendix 1).
- The facilities and equipment used to compound sterile products meet requirements and are maintained, calibrated or certified according to specifications.
- The existing compounding process yields high-quality final preparations that are safe for patients.
- The available recognized scientific literature is used to determine stability and to establish the beyond-use date (BUD) for each sterile preparation.
- A quality assurance program, designed to ensure that preparation activities are performed in accordance with standards of practice, scientific standards, existing data and relevant information, is implemented and followed.
- Mandatory and supplementary documentation is available and updated regularly. Appendix 2 lists required publications and suggestions for supplementary documentation.
- All records required by the Model Standards are completed.

### **5.1.1.3 Compounding pharmacist or pharmacy technician**

#### **Definition**

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

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

**OR**

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

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

#### **Responsibilities**

The compounding pharmacist or pharmacy technician must

- perform or supervise compounding activities;
- ensure compliance with policies and procedures related to the compounding of non-hazardous sterile products;
- enforce or ensure compliance with required aseptic, hygienic, cleanliness and safety rules;



- ensure that all records related to ongoing activities are completed and initialled;
- ensure that all data required for monitoring and reproducing the preparation are recorded or digitized;
- ensure that the equipment, instruments and space used are properly cleaned and maintained;
- ensure application of and compliance with existing compounding procedures;
- ensure that there is a compounding protocol for each preparation produced;
- ensure the accuracy of calculations and measurements;
- use appropriate equipment and instruments for the preparation to be produced;
- follow the compounding process defined in the compounding protocol;
- perform verification during the various stages of compounding and verify the final preparation, or delegate such verification in accordance with the appropriate delegation procedure;
- ensure that all required verification and quality control measures are performed to ensure quality and sterility of each preparation;
- ensure that preparations are packaged and labelled in accordance with provincial/territorial requirements and that a BUD is included on the label (see section 6.1);
- where appropriate, provide the patient care (dispensing) pharmacist, orally or in writing, the information required for storing and transporting any medication prepared at the dispensing pharmacist's request (storage method, precautions, suggested BUD, etc.);
- ensure that the final preparation is properly stored until delivery to the patient or to the pharmacist who ordered it (where compounding is undertaken by another pharmacy, as permitted by provincial/territorial legislation);
- where appropriate, notify the patient care (dispensing) pharmacist when a preparation must be recalled;
- if a sterile preparation has been compounded for an external patient care (dispensing) pharmacist (where permitted by provincial/territorial legislation), ensure that each patient management activity is performed by the dispensing pharmacist and/or the compounding pharmacist or pharmacy technician, to ensure continuity of care<sup>6</sup>;
- where appropriate, collaborate with the patient care (dispensing) pharmacist and share information on the preparation for the patient's benefit and to optimize treatment results;
- ensure that patient management is adequate and consistent with agreements among the various stakeholders.

---

<sup>6</sup> 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](http://napra.ca/Content_Files/Files/Model_Standards_of_Prac_for_Cdn_Pharm_March09_Final_b.pdf)

#### 5.1.1.4 Patient care (dispensing) pharmacist

##### **Definition**

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

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

##### **Responsibilities**

When providing patient care that includes dispensing medications or medication therapies, the patient care (dispensing) pharmacist must follow the standards of practice for Canadian pharmacists.<sup>7</sup>

#### 5.1.1.5 Other employees

Employees must follow and comply with specific procedures for sterile-product compounding.

### 5.1.2 Training and assessment

Compounding personnel and cleaning and disinfecting personnel have a major impact on the risks associated with contamination of preparations. Stringent work methods<sup>8,9</sup> are therefore required.

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

Compounding personnel must keep their compounding knowledge up to date.

#### 5.1.2.1 Conditions

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

---

<sup>7</sup> 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](http://napra.ca/Content_Files/Files/Model_Standards_of_Prac_for_Cdn_Pharm_March09_Final_b.pdf)

<sup>8</sup> Thomas M, Sanborn M, Couldry R. IV admixture contamination rates: traditional practice site versus a class 1000 cleanroom. *Am J Health Syst Pharm*. 2005;62(22):2386-92.

<sup>9</sup> Trissel LA, Gentempo JA, Saenz LM, Woodard MY, Angeles CH. Effect of two work practice changes on the microbial contamination rates of pharmacy-compounded sterile preparations. *Am J Health Syst Pharm*. 2007;64(8):837-41.

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

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

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

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

### **5.1.2.2 Initial training and assessment program**

#### **Personnel assigned to the compounding of non-hazardous sterile products**

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

- reading and understanding the policies and procedures related to sterile-product compounding (see Appendix 1);
- theoretical training, with assessment covering various topics, including those listed in Appendix 3;
- individualized practical training and assessment in the workplace clean room (see section 7 and Appendix 3);
- assessment of aseptic techniques, based on gloved fingertip sampling (GFTS) and a media fill test, for the various types of sterile products to be compounded.

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

#### **Cleaning and disinfecting personnel**

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

- theoretical training and assessment covering the issues and particularities of cleaning and disinfecting the premises and equipment (see Appendix 3 for a list of the competencies required for theoretical assessment of cleaning and disinfecting personnel);
- practical training and assessment in the areas reserved for compounding sterile products.

Any cleaning and disinfecting employee who has successfully completed theoretical and practical training in the workplace may perform cleaning duties in the sterile-product compounding facilities, in accordance with established procedures.

The sterile compounding supervisor must ensure appropriate training of all new cleaning

and disinfecting personnel.

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

### **5.1.2.3 Competency assessment program**

#### **Sterile compounding supervisor**

##### Training

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

##### Assessment

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

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

A pharmacist whose activities are limited to supervising a pharmacy technician or TSP during sterile-product compounding

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

#### **Duty pharmacist in a health care facility**

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

## **Frequency of assessment**

### **Compounding personnel**

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

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

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

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

### **Cleaning and disinfecting personnel**

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

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

## **Content of assessment**

### **Compounding personnel**

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

- a theoretical test measuring required knowledge of policies and procedures and the aseptic compounding process (see Appendix 3);
- a practical test in the workplace clean room (including GFTS and a media fill test) to evaluate compliance with operating procedures and knowledge of aseptic compounding processes.

### **Cleaning and disinfecting personnel**

A competency assessment program for cleaning and disinfecting personnel must be implemented in the workplace (see Appendix 3 for more details on the training required).

## **Failures (all personnel)**

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

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

#### 5.1.2.4 Management of the competency assessment program

##### **Sterile compounding supervisor and delegation of employee training**

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

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

**OR**

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

##### **External evaluator**

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

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

## 5.2 Policies and procedures<sup>10, 11, 12</sup>

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

- The sterile compounding supervisor must establish the content of policies and procedures, providing detailed descriptions of all activities in the pharmacy's compounding of non-hazardous sterile products (see Appendix 1). The

---

<sup>10</sup> United States Pharmacopeial Convention (USP). General chapter <1075>: good compounding practices. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008–2009. p. 867.

<sup>11</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 44, 47, 54, 55.

<sup>12</sup> Pharmacy Compounding Accreditation Board (PCAB). Standard 1.40: Standard operating procedures compliance indicators. In: *PCAB accreditation manual*. Washington, DC: PCAB; 2011. p. 7. Available from: <http://www.pcab.org/cms/wp-content/themes/pcab/img/PCAB-Accreditation-Manual.pdf>

supervisor must also ensure application of and compliance with these policies and procedures.

- Procedures must be clear, must follow a standard format and must include an index for easy access to information when it is needed. Appendix 4 may be used as a model for developing these procedures.
- The sterile compounding supervisor must ensure that all established policies and procedures are promptly updated whenever there is a change in practice. In addition, policies and procedures must be reviewed at least every 3 years.
- The drafting and revision dates, the date of each change and the names of authors and reviewers must be included in each policy or procedure.
- Where compounding is undertaken by another pharmacy, as permitted by provincial/territorial legislation, pharmacists who dispense but do not compound medications should include in their general procedures information about procedures for acquiring compounded sterile preparations for their patients (choice of supplier, entry in the file, delivery, etc.).

## **5.3 Facilities and equipment**

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

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

### **5.3.1 Useful references**

#### **5.3.1.1 ISO Standard 14644-1**

The ISO14644-1 classification describes air cleanliness requirements in facilities and clean rooms. This standard specifies the allowable concentration of airborne particles for each class. To achieve and maintain the ISO class for a clean room, all sources that generate particles must be controlled.

**Table 1**

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

$\mu\text{m}$  = micrometre;  $\text{m}^3$  = cubic metre; ISO = International Organization for Standardization

### **5.3.1.2 NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings<sup>13</sup>**

The US Department of Health and Human Services, through its Centers for Disease Control and Prevention and the National Institute for Occupational Safety and Health (NIOSH), publishes and updates a list of hazardous products. This published list can be used by individual pharmacies to develop their own lists of hazardous products that require special handling precautions. The conditions required for the compounding of hazardous sterile products are presented in the companion document, Model Standards for Pharmacy Compounding of Hazardous Sterile Products.

In addition, NIOSH published an alert on preventing occupational exposure to antineoplastic and other hazardous drugs in 2004<sup>14</sup>.

### **5.3.2 Facilities reserved for the compounding of non-hazardous sterile products**

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

<sup>13</sup> 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>

<sup>14</sup> 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>



Pharmacy Compounding of Hazardous Sterile Products, describes the facilities required for the compounding of hazardous products.

### 5.3.2.1 Dimensions

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

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

### 5.3.2.2 Lighting

The lighting must be sufficient and fixtures located so as to

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

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

The air in controlled rooms must be “clean,” and levels of airborne particulates must be controlled. Thus, the facility’s heating, ventilation and air conditioning (HVAC) system must be designed to minimize the risk of airborne contamination in controlled rooms. It must also be designed to achieve and maintain the appropriate ISO class for clean rooms<sup>15</sup> and anterooms (see section 5.3.2.5, Table 2 and Table 3).

The air supplied to areas used for compounding non-hazardous sterile products must pass through a high-efficiency particulate air (HEPA) filter to ensure a very high level of cleanliness. The intake air must come from the ceiling via diffusers, each fitted with a terminal HEPA filter<sup>16</sup>.

All sources that generate particles must be controlled to achieve and maintain the ISO class for clean rooms and anterooms used to compound non-hazardous sterile products<sup>17</sup>.

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

---

<sup>15</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 372-4.

<sup>16</sup> Health Canada, Health Products and Food Branch Inspectorate. *Good manufacturing practices (GMP) guidelines – 2009 edition, Version 2*. GUI-0001. Ottawa, ON: Health Canada; 2009, revised 2011 Mar 4. p. 85. Available from: <http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/docs/gui-0001-eng.php>

<sup>17</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 372-4.

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

The particle count must be performed by trained, qualified personnel at least twice a year as part of an internal quality control program for facilities and the laminar airflow workbench (LAFW) or the compounding aseptic isolator (CAI). The particle count may also be measured by a qualified certifier (see Appendices 5 and 6).

Return air intakes must be installed at the bottom of walls<sup>18</sup>, forcing the particles to flow downward. In older facilities, an airflow analysis must be performed under dynamic operating conditions (using the air speed achieved at the front of the LAFW) to ensure that the location of the return air intakes does not hinder the compounding process.

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

#### **5.3.2.4 Windows and openings**

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

#### **5.3.2.5 Compounding areas**

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

##### **Clean room**

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

The clean room must be isolated from the rest of the pharmacy and from other non-controlled areas, to reduce the risk of introducing viable and non-viable contaminants<sup>19</sup>. It must be physically separated from contiguous areas by walls, doors and pass-throughs.

<sup>18</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 373.

<sup>19</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 372-3.

## Use

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

## Contents

The primary engineering control is installed in the clean room. For non-hazardous compounding, the primary engineering controls may be LAFWs or CAIs<sup>20</sup>.

**Table 2**

<b>Functional parameters of the compounding clean room</b>
<p><b><i>The following functional parameters must be met:</i></b></p> <ul style="list-style-type: none"><li>• The clean room must be kept under positive pressure relative to the anteroom and adjacent areas<sup>21</sup>.</li><li>• The pressure differential must be at least 5.0 Pa<sup>22</sup> (ideally between 5.0 Pa and 12.5 Pa, equivalent to 0.02 to 0.05 inches water column)<sup>23,24</sup> relative to the anteroom<sup>25</sup>. Smaller pressure differentials may be more difficult to measure and maintain.</li><li>• ISO Class 7 air quality must be maintained in the clean room under dynamic operating conditions<sup>26</sup>.</li><li>• There must be at least 30 or more air changes per hour (ACPH)<sup>27</sup>. Depending on the size of the room and the number of people working in it, a greater number of ACPH may be required.</li><li>• The temperature of the clean room must be less than or equal to 20°C, taking into account employees' comfort once all clean room garb (including PPE) has been donned. Medication storage temperatures must not exceed 25°C.</li></ul> <p>Note: There is no requirement for relative humidity; refer to the recommendations of the Canadian Society of Hospital Pharmacists<sup>28</sup>. See also the pressure diagram for the anteroom and clean room (Figure 1, page 23).</p>

<sup>20</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 372-3.

<sup>21</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

<sup>22</sup> Direction de l'expertise et de la normalisation, répertoire des guides de planification immobilière : aires réservées aux préparations stériles – Unité de pharmacie. Québec, QC : Ministère de la santé et des services sociaux, Publications du Québec ; 2013. p. 16.

<sup>23</sup> Health Canada, Health Products and Food Branch Inspectorate. *Good manufacturing practices (GMP) guidelines – 2009 edition, Version 2*. GUI-0001. Ottawa, ON: Health Canada; 2009, revised 2011 Mar 4. p. 74. Available from: <http://www.hc-sc.gc.ca/dhp-mpps/compli-conform/gmp-bpf/docs/gui-0001-eng.php>

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

<sup>25</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 372-3.

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

<sup>27</sup> International Organization for Standardization (ISO). *ISO 14644-4 Cleanrooms and associated controlled environments – Part 4: Design, construction and start-up*. Geneva, Switzerland: ISO; 2001.

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

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

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

### **Anteroom**<sup>29</sup>

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

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

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

- a space or area referred to as “microbiologically dirty,” located at the entrance to the anteroom, in the section adjacent to the pharmacy;
- a space or area referred to as “microbiologically clean,” adjacent to the dirty area on one side and the clean room on the other.

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

The functional parameters of the anteroom for the compounding of non-hazardous sterile products are explained in Table 3.

### **Use**

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

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

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

---

<sup>28</sup> Canadian Society of Hospital Pharmacists (CSHP). Sterile preparation of medicines: guidelines for pharmacists. Ottawa, ON: CSHP; 1996.

<sup>29</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 372-3.

## Contents

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

The anteroom must contain the following items:

- PPE accessories and storage space for hair covers and shoe covers, placed in the correct order to allow users to follow the correct garbing sequence;
- easy-to-clean wall sink, ideally made of stainless steel or other material not harmed by cleaning products and large enough to allow users to wash their hands and forearms without touching the sides of the sink, with minimal splashing;
- soap dispenser (cartridge or disposable, non-refillable unit);
- long-acting alcohol-based hand gel dispenser;
- hand-drying system:
  - lint-free paper towels with a dispenser (preferred)
  - air hand dryer designed specifically for use in a controlled area (i.e., the anteroom)
- mirror or other means to verify garbing;
- waste container;
- eyewash station<sup>30</sup>, if available (if not located in the anteroom, the eyewash station must be installed nearby);
- cart reserved for use in the “clean” area of the anteroom and the clean room.

## Supplies

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

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

Other essential equipment may be stored in the anteroom as long as the anteroom’s ISO air quality classification is maintained.

---

<sup>30</sup> Canadian Centre for Occupational Health and Safety (CCOHS). Emergency showers and eyewash stations. Hamilton, ON; CCOHS; 2010. Available from: [http://www.ccohs.ca/oshanswers/safety\\_haz/emergency\\_showers.html](http://www.ccohs.ca/oshanswers/safety_haz/emergency_showers.html)

**Table 3**

<b>Functional parameters of the anteroom for the compounding of non-hazardous sterile products</b>
<p><b><i>The following functional parameters must be met:</i></b></p> <ul style="list-style-type: none"><li>• The anteroom must be kept under positive pressure relative to the non-controlled room adjacent to the anteroom.</li><li>• The pressure differential must be at least 5.0 Pa<sup>31</sup> (ideally between 5.0 Pa and 12.5 Pa, equivalent to 0.02 to 0.05 inches water column) relative to the non-controlled room adjacent to the anteroom. Smaller pressure differentials may be more difficult to measure and maintain.</li><li>• ISO Class 8 air quality must be maintained in the anteroom under dynamic operating conditions.</li><li>• There must be at least 20 air changes per hour (ACPH)<sup>32</sup>. Depending on the size of the room and the number of people working in it, a greater number of ACPH may be required.</li><li>• The temperature of the anteroom must be less than or equal to 20°C, taking into account employees' comfort once all clean room garb (included PPE) has been donned. Medication storage temperatures must not exceed 25°C.</li></ul> <p>Note: See also the pressure diagram for the anteroom and clean room (Figure 1, page 23).</p>

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

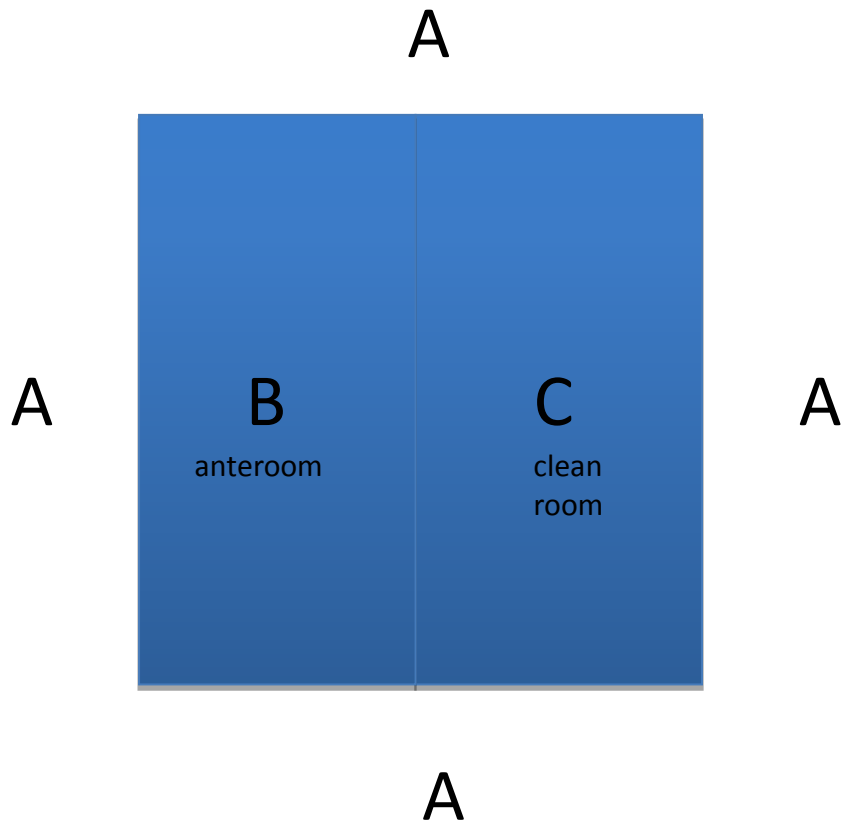
Because horizontal surfaces require daily cleaning, their presence in the anteroom must be kept to a minimum, to avoid unduly increasing the workload for cleaning and disinfecting personnel.

---

<sup>31</sup> Direction de l'expertise et de la normalisation. Répertoire des guides de planification immobilière : aires réservées aux préparations stériles – Unité de pharmacie. Québec, QC: Ministère de la santé et des services sociaux, Publications du Québec ; 2013. p. 16.

<sup>32</sup> International Organization for Standardization (ISO). *ISO 14644-4 Cleanrooms and associated controlled environments – Part 4: Design, construction and start-up*. Geneva, Switzerland: ISO; 2001.

**Figure 1: Pressure diagram**



<b>Pressure differentials:</b>	
Pressure differentials to be maintained at all times:	1) $12.5 \text{ Pa} \geq (P_C - P_B) \geq 5.0$ 2) $12.5 \text{ Pa} \geq (P_B - P_A) \geq 5.0$
<b>Legend:</b>	
A = facilities environment B, C = sterile compounding room P = pressure Pa = pascal (SI unit of measure for pressure)	

### **Area for unpacking supplies**

Space should be provided for unpacking supplies.

To limit the presence of dust and particles, supplies must be removed from cardboard boxes outside the clean room<sup>33</sup> and the anteroom.

### **5.3.2.6 Shared facilities**

#### **Compounding of non-hazardous and hazardous sterile products**

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

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

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

#### **Clean room for the compounding of non-hazardous sterile products**

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

#### **Clean room for the compounding of hazardous sterile products**

The functional parameters of the clean room for this type of facility are the same as those required for the compounding clean room described in the Model Standards for Pharmacy Compounding of Hazardous Sterile Products.

#### **Shared anteroom**

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

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

- a space or area referred to as “dirty,” located adjacent to the pharmacy, at the entrance to the anteroom;

---

<sup>33</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 375.



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

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

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

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

**Table 4**

Functional parameters of a shared anteroom for the compounding of non-hazardous and hazardous sterile products
<p><b><i>The following functional parameters must be met:</i></b></p> <ul style="list-style-type: none"> <li>• The anteroom must be kept under positive pressure relative to the adjacent areas.*</li> <li>• The pressure differential must be at least 5.0 Pa<sup>34</sup> (equivalent to 0.02 inches water column) relative to the adjacent area.</li> <li>• ISO Class 7 air quality must be maintained in the anteroom under dynamic operating conditions<sup>35</sup>.</li> <li>• There must be at least 30 air changes per hour (ACPH)<sup>36</sup>. Depending on the size of the room and the number of people working in it, a greater number of ACPH may be required.</li> <li>• The temperature of the anteroom must be less than or equal to 20°C, taking into account employees’ comfort once all clean room garb (including PPE) has been donned. Medication storage temperature must not exceed 25°C.</li> </ul>
<p>*Excluding the clean room for the compounding of non-hazardous sterile products</p>

<sup>34</sup> Direction de l’expertise et de la normalisation. Répertoire des guides de planification immobilière : aires réservées aux préparations stériles – Unité de pharmacie. Québec, QC: Ministère de la santé et des services sociaux, Publications du Québec ; 2013. pp. 18, 22.

<sup>35</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 368.

<sup>36</sup> International Organization for Standardization (ISO). *ISO 14644-4 Cleanrooms and associated controlled environments – Part 4: Design, construction and start-up*. Geneva, Switzerland: ISO; 2001.

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

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

### 5.3.2.7 All other facilities

The specifications recommended in the previous sections are similar to the recommendations for facilities laid out in chapter <797> of the United States Pharmacopeia – National Formulary (USP–NF)<sup>37</sup> for non-hazardous and hazardous sterile-product compounding rooms. Other approaches could also be suitable. For facilities where the functional parameters must differ in some respect, explanations and justifications must be provided. Other technologies, techniques, materials and procedures require prior approval from the provincial/territorial regulatory authority.

### 5.3.2.8 Materials and finishes

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

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

#### Ceilings

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

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

In the clean room and the anteroom, joints between the ceiling and walls should be free of sharp corners where foreign substances could accumulate<sup>38</sup>. Instead, the corners should be rounded.

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

If a conventional recessed panel ceiling is installed<sup>39</sup>, the panels must be impregnated with polymer to make them impermeable and hydrophobic, and the edges must be

---

<sup>37</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 368, 372, 373. USP, response provided by USP for these facilities, March 21, 2012.

<sup>38</sup> Health Canada, Health Products and Food Branch Inspectorate. *Good manufacturing practices (GMP) guidelines – 2009 edition, Version 2*. GUI-0001. Ottawa, ON: Health Canada; 2009, revised 2011 Mar 4. p. 10. Available from: <http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/docs/gui-0001-eng.php>

<sup>39</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 372-3.

coated with clean room silicone to seal them to the support frame<sup>40</sup>. The tiles on this type of ceiling require periodic preventive sealing because the sealer eventually dries. When facilities undergo certification, this type of ceiling must be tested for tightness. Also, this type of ceiling is not recommended for new facilities.

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

### **Walls**

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

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

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

### **Floors**

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

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

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

There must be no carpets or rugs. Anti-fatigue mats must be avoided because they are typically made of porous materials<sup>41</sup>.

## **5.3.2.9 Accessories**

### **Ceiling fixtures**

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

### **Plumbing**

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

---

<sup>40</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 372-3.

<sup>41</sup> Canadian Centre for Occupational Health and Safety (CCOHS). Anti-fatigue mats. Hamilton, ON: CCOHS; 1997, confirmed current 2006. Available from: <http://www.ccohs.ca/oshanswers/ergonomics/mats.html>

### **Functional parameter control systems**

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

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

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

### **5.3.2.10 Work surfaces and furniture**

#### **Work surfaces**

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

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

#### **Furniture**

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

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

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

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

#### **Pass-through**

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

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

If there is no pass-through, the clean room cart may be used to transport materials from

the “clean” area of the anteroom into the clean room.

### **Interlocking door system**

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

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

#### **5.3.2.11 Signage**

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

#### **5.3.2.12 Facility maintenance**

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

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

### **Filters and pre-filters**

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

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

## **5.3.3 Equipment**

### **5.3.3.1 Laminar airflow workbench and compounding aseptic isolator<sup>42</sup>**

The LAFW or CAI is positioned in the clean room. The equipment’s ventilation system and its HEPA filter serve to filter the air in the compounding environment. The air quality must comply with ISO Class 5.

Before an LAFW or CAI is used,

- personnel must read and understand the user’s manual;
- the LAFW or CAI must be installed according to the manufacturer’s recommendations and certified by a qualified certifier (see Appendix 5);
- cleaning and disinfection must be performed.

---

<sup>42</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 362-4, 372-4.

The sterile compounding supervisor must ensure that the certification is completed according to certification standards currently in force (see Appendix 6).

An LAFW or CAI must operate continuously<sup>43</sup>, 24 hours a day. If the LAFW or CAI has been turned off, it must be allowed to run for at least 30 minutes or as recommended by the manufacturer, before cleaning, disinfection and compounding of sterile products is undertaken<sup>44, 45</sup>.

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

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

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

### **Location of LAFW, CAI and other furniture**

The LAFW, CAI and other pieces of furniture should be positioned to avoid interfering with facility ventilation systems.<sup>46, 47, 48</sup>

To facilitate cleaning and disinfecting activities, such as cleaning the floor and exterior of the LAFW or CAI, and to avoid interfering with the operation of the LAFW or CAI, there must be sufficient clearance around the LAFW or CAI (usually 0.3 m<sup>49</sup>)<sup>50</sup>. Some types of LAFW can be built into the wall and sealed or wall-mounted and sealed, but this is not possible with other types. When positioning an LAFW or CAI, the manufacturer's recommendations must be strictly followed to avoid interfering with normal operation. A smoke test may be used to validate proper operation during certification.

---

<sup>43</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 379-80.

<sup>44</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 379-80.

<sup>45</sup> 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](https://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html)

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

<sup>47</sup> Peters GF, McKeon MR, Weiss WT. Potentials for airborne contamination in turbulent- and unidirectional-airflow compounding aseptic isolators. *Am J Health Syst Pharm* 2007;64(6):622-31.

<sup>48</sup> Controlled Environment Testing Association (CETA). *CETA compounding isolator testing guide: CAG-002-2006*. Raleigh, NC: CETA; 2006, revised 2008 Dec 8. Available from: <http://www.cetainternational.org/reference/CETACompoundingIsolatorTestingGuide2006.pdf>

<sup>49</sup> 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. 7-9. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>

<sup>50</sup> Direction de l'expertise et de la normalisation. Répertoire des guides de planification immobilière : aires réservées aux préparations stériles – Unité de pharmacie. Québec, QC: Ministère de la santé et des services sociaux, Publications du Québec ; 2013. p. 17.

## LAFW<sup>51, 52, 53</sup>

The LAFW must be positioned in an ISO Class 7 clean room that is adjacent to an ISO Class 8 anteroom and must not be placed near doors or other sources of drafts that might adversely affect unidirectional airflow.

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

## CAI<sup>54, 55, 56</sup>

The CAI must be positioned in an ISO Class 7 clean room or better adjacent to an ISO Class 8 anteroom.

However, ISO Class 8 air quality in a clean room and anteroom may be acceptable if all of the following conditions are met:

- 1- The CAI maintains an ISO Class 5 environment (see Table 1) at all times during compounding, including when ingredients, equipment and devices are being transferred into and out of the CAI.
- 2- Particulate sampling from 15 to 30 cm upstream of the critical exposure site within the CAI shows ISO Class 5 air quality during compounding.
- 3- Particulate sampling conducted as close as possible to the doors when materials are being transferred, without obstructing the passageway, shows no more than 3520 particles (0.5 µm diameter or larger) per cubic metre of air (ISO Class 5) in the CAI.

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

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

Compounding personnel working in a CAI must comply with the garbing procedure for the compounding of sterile products.

---

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

<sup>52</sup> Peters GF, McKeon MR, Weiss WT. Potentials for airborne contamination in turbulent- and unidirectional-airflow compounding aseptic isolators. *Am J Health Syst Pharm* 2007;64(6):622-31.

<sup>53</sup> Controlled Environment Testing Association (CETA). *CETA compounding isolator testing guide: CAG-002-2006*. Raleigh, NC: CETA; 2006, revised 2008 Dec 8. Available from: <http://www.cetainternational.org/reference/CETACompoundingIsolatorTestingGuide2006.pdf>

<sup>54</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

<sup>55</sup> Peters GF, McKeon MR, Weiss WT. Potentials for airborne contamination in turbulent- and unidirectional-airflow compounding aseptic isolators. *Am J Health Syst Pharm* 2007;64(6):622-31.

<sup>56</sup> Controlled Environment Testing Association (CETA). *CETA compounding isolator testing guide: CAG-002-2006*. Raleigh, NC: CETA; 2006, revised 2008 Dec 8. Available from: <http://www.cetainternational.org/reference/CETACompoundingIsolatorTestingGuide2006.pdf>



### **Maintenance of LAFW and CAI**

LAFWs and CAIs must be maintained in accordance with the manufacturer's recommendations.

LAFWs and CAIs must be certified<sup>57</sup>

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

If an LAFW or CAI on wheels is moved (e.g., to clean under the wheels), and then moved back to exactly the same place, re-certification is not necessary.

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

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

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

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

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

#### **5.3.3.2 Other devices, instruments or accessories related to the compounding of non-hazardous sterile products**

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

The decision to place equipment, instruments or accessories not directly related to sterile-product compounding (carts, cabinets, computer monitors, etc.) in the clean room depends on whether such placement will have an impact on maintaining environmental conditions in the clean room (air quality control, surface sampling, etc.)<sup>58</sup>.

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

---

<sup>57</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 373.

<sup>58</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 372.



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

### **Automated compounding device and balance**

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

A larger LAFW must be provided for an ACD dedicated to total parenteral nutrition.

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

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

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

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

### **Carts**

If carts are used, one cart must be reserved for the "dirty" area of the anteroom and must remain there<sup>59</sup>.

A second cart, dedicated to the "clean" area of the anteroom, may enter the clean room<sup>60</sup>.

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

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

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

Carts should be cleaned and disinfected on a regular basis.

### **Refrigerator and freezer**

#### **Choice**

---

<sup>59</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 379.

<sup>60</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 379.

The refrigerator and freezer used to store medications must be commercial biomedical grade units<sup>61, 62, 63</sup>. Domestic refrigerators and freezers must not be used.

### Use and placement

Refrigerators and freezers must be used only for storing medications. They must not be used to store food. Ideally, refrigerators and freezers are placed outside controlled areas. Depending on workflow, refrigerators may be placed in anterooms, provided there is control of particulates through the use of air returns and provided the number of air changes per hour is sufficient to maintain the required ISO air quality classification.

### Refrigerators with two doors

Refrigerators with doors on two sides (pass-through refrigerators) may be used to store sterile products, provided they are designed for clean rooms and the refrigeration system is not located on the clean room side. If such a refrigerator is installed, the sterile compounding supervisor is responsible for ensuring that the required characteristics for any compounding rooms affected by its installation are met under operating conditions.

### Temperature and temperature control

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

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

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

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

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

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

### Incubator

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

---

<sup>61</sup> Health Canada, Health Products and Food Branch Inspectorate. *Guidelines for temperature control of drug products during storage and transportation*. GUI-0069. Ottawa, ON: Health Canada; 2011. Available from: <http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/docs/gui-0069-eng.php>

<sup>62</sup> Public Health Agency of Canada (PHAC). *National vaccine storage and handling guidelines for immunization providers*. Ottawa, ON: PHAC; 2007. p. 19. Available from: <http://www.phac-aspc.gc.ca/publicat/2007/nvshglp-ldemv/pdf/nvshglp-ldemv-eng.pdf>

<sup>63</sup> *Drug and Pharmacies Regulation Act*, R.S.O. 1990, c. H.4. Available from: [http://www.e-laws.gov.on.ca/html/statutes/english/elaws\\_statutes\\_90h04\\_e.htm](http://www.e-laws.gov.on.ca/html/statutes/english/elaws_statutes_90h04_e.htm)

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

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

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

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

### **Camera and computer equipment**

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

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

Equipment cables must be covered to facilitate cleaning.

### **Communication system**

A functional communication system (intercom, telephone or other) may be installed to allow verbal communication between the various controlled areas and the pharmacy. These devices should be used in "hands-free" mode, must be easy to clean and must be resistant to damage from cleaning products.

### **Waste containers**

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 containers must be emptied and cleaned at least once a day, outside of compounding hours.

### **5.3.3.3 Personal protective equipment and clothing**

Compounding personnel and anyone else who accesses controlled areas must wear appropriate protective clothing. This PPE is described in Table 5.

**Table 5**

<b>Personal protective equipment (PPE) for the compounding of non-hazardous sterile products</b>
<p>PPE to be worn<sup>64</sup> for the compounding of non-hazardous sterile products and when accessing facilities for the compounding of non-hazardous sterile products includes the following:</p> <ul style="list-style-type: none"><li>• pair of shoe covers</li><li>• hair cover</li><li>• beard cover (if applicable)</li><li>• surgical mask</li><li>• clean, non-shedding protective gown (enclosed at the neck and with sleeves that fit snugly around the wrists)</li><li>• pair of non-powdered sterile gloves (compounders only)*</li></ul>
<p>*Personnel entering the clean room to perform tasks other than compounding, including those who perform verification of final compounded sterile preparations, may wear non-sterile gloves donned after aseptic handwashing. The gloves must be disinfected with sterile 70% isopropyl alcohol before the person enters the clean room.</p>

### **5.3.4 Cleaning and disinfecting in areas reserved for the compounding of non-hazardous sterile products**

#### **5.3.4.1 General**

Cleaning and disinfecting (housekeeping) in areas reserved for the compounding of non-hazardous sterile products must be performed to ensure the cleanliness required for the quality and integrity of final sterile preparations<sup>65</sup>.

Cleaning and disinfecting procedures must be strictly enforced in the clean room and the anteroom.

Policies and procedures for cleaning and disinfecting tasks must be developed, and cleaning and disinfecting personnel must be trained and assessed on correct application of these policies and procedures.

Only trained and qualified cleaning and disinfecting personnel may be allowed to clean areas reserved for sterile compounding<sup>66</sup>.

#### **5.3.4.2 Disinfectant**

---

<sup>64</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 376-7.

<sup>65</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 376.

<sup>66</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 376.

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

The sterile compounding supervisor must

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

Use of an alternative disinfectant in the rotation is unnecessary. However, the daily use of a germicidal disinfectant should be augmented with weekly (or monthly) use of a sporicidal agent<sup>67</sup>.

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

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

#### **5.3.4.3 Equipment used for cleaning and disinfection and its storage**

Equipment used for cleaning and disinfecting must be accessible.

To avoid cross-contamination and to protect cleaning and disinfecting personnel, cleaning equipment (mop heads, towels, etc.) must be reserved exclusively for cleaning compounding areas for non-hazardous sterile products<sup>68</sup>.

Non-shedding (lint-free)<sup>69</sup> equipment (mop heads, towels), preferably made of cellulose or microfibre, must be used for cleaning controlled areas.

This equipment (mop heads, towels, etc.) should preferably be disposable. If reusable accessories are used, they must be reserved for cleaning and disinfecting within the facility, must be washed and dried after each use and must be stored in a clean cabinet dedicated to storing this equipment<sup>70</sup>.

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

Cleaning equipment (mop handle, outside of bucket, etc.) must be disinfected before each entry into a controlled area. A closed, dedicated cabinet located in the anteroom or nearby must be provided for storing equipment (mop handle, etc.), refills (mop heads,

---

<sup>67</sup> United States Pharmacopeial Convention (USP). General chapter <1072>: disinfectants and antisepsis. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008–2009.

<sup>68</sup> Okeke CC, Allen LV Jr. Considerations for implementing United States Pharmacopeia chapter <797> pharmaceutical compounding – sterile preparations. Part 4: Considerations in selection and uses of disinfectants and antiseptics. *Int J Pharm Compound*. 2007;11(6):4929.

<sup>69</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 376.

<sup>70</sup> McAteer F. Points to consider for developing a USP-797 compliant cleaning and sanitization program. *Clean Rooms*. 2007;21(8):44,48. Available from: <http://electroiq.com/issue/?issue=2302>

towels) and cleaning products used for cleaning and disinfecting. Cleaning and disinfecting personnel must have access to a water supply and a place to dispose of waste water in the pharmacy.

#### **5.3.4.4 Garbing of cleaning and disinfecting personnel**

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

#### **5.3.4.5 Cleaning frequency**

The minimum frequency of cleaning and disinfecting in clean rooms and anterooms will be either daily or monthly.<sup>71</sup>

Daily cleaning is required for the following surfaces and areas:

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

Monthly cleaning is required for the following surfaces and areas:

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

Cleaning should be performed from the "cleanest" area to the "dirtiest" area (i.e., from the closed end of the clean room toward the anteroom exit).

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

## **5.4 General maintenance log**

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

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

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

---

<sup>71</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding – sterile preparations. In: *USP pharmacists' pharmacopeia*. 2nd ed., Suppl. 2. Rockville, MD: USP; 2008. p. S2/47.

## 6. PRODUCT AND PREPARATION REQUIREMENTS

### 6.1 Beyond-use date and dating methods

#### 6.1.1 Beyond-use date for preparations

For the purposes of these Model Standards, the BUD is the date and time after which the compounded sterile preparation cannot be used or administered to a patient. It is based on the date and time when the sterile preparation was compounded<sup>72</sup>.

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

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

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

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

- expiration date based on chemical and physical stability<sup>73, 74, 75</sup> according to reference texts;
- storage time related to risk of microbial contamination ("microbiological stability"<sup>76</sup> related to the compounding process).

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

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

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

<sup>72</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

<sup>73</sup> Trissel LA. *Handbook on injectable drugs*. 17th ed. Bethesda, MD: American Society of Health-System Pharmacists; 2013.

<sup>74</sup> King JC. *King guide to parenteral admixtures* [electronic version]. Napa, CA: King Guide Publications Inc.; [updated quarterly].

<sup>75</sup> Trissel LA. *Trissel's 2 clinical pharmaceuticals database* [electronic database]. Cashiers, NC: TriPharma Communications; [updated regularly].

<sup>76</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 365-7, 382-3.

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

The BUDs for commercial products specified in the following three subsections (6.1.2.1, 6.1.2.2 and 6.1.2.3) apply when the products are stored in the original package and container.

#### 6.1.2.1 Preservative-free sterile product, including “bulk” packaging

- BUD: 6 hours (controlled room temperature or refrigerator temperature)<sup>77</sup> (see Table 6).
- The contents of a bulk vial cannot be divided for the sole purpose of extending stability.
- Six hours after initial needle puncture, the sterile product (e.g., vial, minibag) cannot be used to prepare a batch.

**Table 6**

<b>Beyond-use dates (BUDs)* for compounded sterile preparations when a preservative-free vial is used<sup>78</sup></b>			
<b>BUD without any additional sterility testing</b>	<b>BUD for compounded (final) preparation at controlled room temperature</b> (calculated from time of initial needle puncture)	<b>BUD for compounded (final) preparation stored in refrigerator</b> (calculated from time of initial needle puncture)	<b>BUD for compounded (final) preparation stored in freezer</b>
<b>Vial used within 6 hours of initial needle puncture</b>	Low risk = 48 hours Medium risk = 30 hours High risk = 24 hours	Low risk = 14 days Medium risk = 9 days High risk = 3 days	Low, medium and high risk = 45 days

\*See Table 7 in section 6.1.3, below, for information about risk levels.

- Administration of the compounded sterile preparation must start before the BUD has been exceeded.
- To properly manage risk, a label must be affixed to the vial indicating the time of initial needle puncture. The vial must be punctured in an LAFW that maintains ISO Class 5 air quality or a CAI that meets the requirements of these Model Standards. Once the vial is removed from the ISO Class 5 LAFW or CAI, it must be discarded.

<sup>77</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

<sup>78</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.



### 6.1.2.2 Open ampoule

- BUD: immediate use.

### 6.1.2.3 Multiple-dose vial containing a preservative

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

## 6.1.3 Beyond-use date according to risk of microbial contamination

After a stationary phase (phase 1), which varies by species, bacteria replicate within 20 to 30 minutes (phase 2 growth). Once contamination occurs, bacterial growth increases rapidly starting 6 hours after onset of contamination<sup>79</sup> For example, contamination of 10 colony-forming units per millilitre (CFU/mL) at 6 hours will increase to 640 CFU/mL by 9 hours, to 41 000 CFU/mL by 12 hours, and to  $6.9 \times 10^9$  CFU/mL by 24 hours.

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

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

### **Sterile unit**

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

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

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

---

<sup>79</sup> Cundell AM. USP Committee on Analytical Microbiology — stimuli to the revision process. *Pharmaceutical Forum*. 2002;28(6).

**Table 7**

<b>Contamination risk levels<sup>80, 81</sup></b>		
<b>Low</b>	<b>Medium</b>	<b>High</b>
<ul style="list-style-type: none"> <li>Final product compounded using up to 3 “sterile units”</li> <li>No more than 2 septum punctures at the injection site for each sterile unit</li> <li>Simple aseptic transfer technique</li> <li>Drug prepared for one patient (patient-specific dose)</li> </ul>	<ul style="list-style-type: none"> <li>Final product compounded using 4 or more “sterile units”</li> <li>Complex manipulations</li> <li>Prolonged preparation time</li> <li>Batch preparations (for more than one patient)</li> </ul>	<ul style="list-style-type: none"> <li>Non-sterile ingredients or equipment used for preparation</li> <li>Exposure, for more than 1 hour, of sterile material or content of sterile commercial products to an environment with air quality below ISO Class 5 requirements</li> <li>Non-sterile preparations containing water, stored for more than 6 hours before sterilization</li> </ul>

**Table 8**

<b>Beyond-use dates (BUDs) for compounded sterile preparations, according to risk of microbial contamination<sup>82</sup></b>			
	<b>BUD without additional sterility testing</b>		
<b>Risk of contamination</b>	<b>At controlled room temperature</b>	<b>With storage in refrigerator</b>	<b>With storage in freezer</b>
<b>Low</b>	48 hours	14 days	45 days
<b>Medium</b>	30 hours	9 days	45 days
<b>High</b>	24 hours	3 days	45 days

<sup>80</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

<sup>81</sup> American Society of Health-System Pharmacists (ASHP). *The ASHP discussion guide on USP chapter <797> for compounding sterile preparations. Summary of revisions to USP chapter <797>*. Bethesda, MD: ASHP with Baxter Healthcare Corporation; 2008. Available from: [http://www.ashp.org/s\\_ashp/docs/files/discguide797-2008.pdf](http://www.ashp.org/s_ashp/docs/files/discguide797-2008.pdf)

<sup>82</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

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

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

### **Sterility and control test**<sup>83</sup>

A bacterial endotoxin sterility and control test must be performed for high-risk sterile-product preparations (see Table 8) in the following situations:

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

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

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

### **6.1.4.1 Beyond-use dates for immediate-use preparations**

In health care facilities, a pharmacy department providing compounded sterile preparations must ensure that compounded doses are ready to be administered without further handling by another health care professional and must develop its services in accordance with this requirement.

Compounded sterile preparations prepared for immediate use in the patient's room or on patient care units must comply with the following conditions:

- The preparation does not exceed three "sterile units."
- The preparation does not contain any hazardous drugs (e.g., chemotherapeutic agents).
- For each unit used, there are no more than two punctures at the injection site of a preservative-free sterile product.
- Aseptic technique does not require more than 1 hour of continuous preparation.
- Aseptic technique is rigorously applied.
- Compounding is performed in a critical situation where immediate administration to the patient is required.

---

<sup>83</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 361.

The following BUDs apply, with no requirement for additional sterility tests:

- Controlled room temperature: 1 hour
- Refrigerator: 1 hour
- Freezer: does not apply

**Administration of the preparation must begin less than 1 hour after the start of compounding; otherwise, the preparation must be discarded.**

The container must always be correctly identified. In addition to mandatory information on the drug label, the compounding start date and time should be included on the label.

#### 6.1.4.2 Preparations with beyond-use dates of 12 hours or less

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

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

Chapter <797> of the USP–NF states that the microbial contamination risks associated with compounding such products under these conditions remain high, even if only low-risk products are compounded and even if there is full compliance with hygiene, asepsis, garbing and maintenance rules<sup>84</sup>.

Given the associated risks, the compounding of sterile products under these conditions must be only a **temporary** measure, and administration must start within 12 hours after the start of compounding (Table 9); otherwise, the preparation must be discarded.

<sup>84</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 365.

**Table 9**

<b>Summary of beyond-use dates (BUDs) for compounded sterile preparations in short-term critical situations</b>			
	<b>BUDs for compounded sterile preparations in short-term critical situations without additional sterility test</b>		
<b>Type of preparation</b>	<b>At controlled room temperature</b>	<b>With storage in the refrigerator</b>	<b>With storage in the freezer</b>
<b>Immediate-use preparation</b>	1 hour	1 hour	NA
<b>Preparation in LAFW (ISO Class 5 or better) in an environment where conditions do not meet ISO Class 7 standards for LAFWs or ISO Class 8 standards for CAIs</b>	12 hours	12 hours	NA

NA = not applicable.

The container must always be correctly identified. In addition to mandatory information on the drug label, the compounding start date and time and the BUD should be included on the label.

## **6.2 Compounded sterile preparation protocols**

Protocols for compounded sterile preparation must include all information required to prepare the compound:

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

Appendix 7 presents a model for writing compounded sterile preparation protocols for each

drug.

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

### **6.3 Compounded sterile preparation log**

A compounded sterile preparation log must be completed during the compounding process.

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

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

#### **6.3.1 Compounded sterile preparation log for one patient (individual preparations)**

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

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

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

#### **6.3.2 Compounded sterile preparation log for products prepared in batches**

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

- preparation identification (name and concentration)
- compounding procedure
- for each ingredient (including primary and secondary diluents),
  - name
  - quantity/volume measured
  - batch number
  - expiration date
- quantity prepared
- prepared batch number
- compounding date
- preparation BUD
- compounder and verifier at each stage of the process

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

## **6.4 Patient file**

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

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

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

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

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

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

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

### **6.5.1 Conditions that may affect preparation quality**

The sterile compounding supervisor or delegate must assess the possibility of temporarily removing any compounding personnel with a condition that may affect preparation quality<sup>85</sup> including:

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

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

### **6.5.2 Conduct before entering the anteroom**

Before entering the anteroom, compounding personnel must take the following steps<sup>86</sup>:

- remove personal outerwear (e.g., coat, hat, jacket, scarf, sweater, vest, boots and dirty outdoor shoes), which tends to shed particles or squamous cells;
- remove jewelry, studs and other accessories from fingers, wrists, forearms, neck and other body parts if they might interfere with the effectiveness of PPE (e.g., for adjusting gloves and sleeves and for antiseptic washing of hands and forearms);

---

<sup>85</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 376-7.

<sup>86</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 376-7.



- remove all cosmetics (makeup, false eyelashes, perfume and hair products such as hairspray), which can produce particles that are possible sources of contamination;
- tie back long hair;
- remove nail polish<sup>87</sup> or any nail application, extensions or other synthetic nail-lengthening products;
- ensure that nails are short and that skin around the nails is undamaged;
- ensure that skin of hands and forearms is undamaged;
- change into dedicated, low-shedding apparel suitable for the controlled area (e.g., scrubs);
- fully cover legs and feet, and wear closed shoes and socks;
- wash hands.

### 6.5.3 Conduct in controlled areas (clean room and anteroom)

In controlled areas, the following measures should be taken.

- Food items, drinks, chewing gum, candy and smoking are prohibited<sup>88</sup>.
- Food items or drinks must not be stored in refrigerators reserved for storing compounded sterile preparations.
- All access doors to controlled areas must be kept closed.
- Anyone who enters the anteroom or a clean room must be authorized and must follow all hand hygiene and garbing procedures.
- Only essential conversations are allowed to minimize the risk of particulate contamination. Coughing, sneezing and talking in the direction of the LAFW should also be avoided.

## 6.6 Aseptic compounding of non-hazardous sterile products

### 6.6.1 General

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

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

<sup>87</sup> Centers for Disease Control and Prevention. Guideline for hand hygiene in health-care settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. *MMWR Morb Mortal Wkly Rep.* 2002;51(RR-16):1-48.

<sup>88</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 379-80.

- disinfecting and introducing products and equipment into the clean room;
- disinfecting the LAFW or CAI;
- disinfecting and introducing products and equipment into the LAFW or CAI;
- using aseptic techniques to compound sterile products in the LAFW or CAI;
- verifying, labelling and packaging final compounded sterile preparations.

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

The number of people in the clean room and anteroom must be limited to the minimum number required to perform aseptic compounding activities<sup>89</sup>.

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

All stages of compounding non-hazardous sterile products must be performed in an LAFW or CAI that maintains ISO Class 5 air quality requirements.

## **6.6.2 Hand and forearm hygiene and garbing**

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

### **6.6.2.1 Hand and forearm hygiene**

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

- Under running water, use a nail cleaner to remove debris from underneath fingernails.
- Wash hands and forearms to the elbows with soap and water, for a period of 30 to 60 seconds.
- Rinse with water.
- Dry hands and forearms with disposable, lint-free paper towel.
- Dispense alcohol-based hand rub (ABHR) onto one palm.
- Immerse fingertips of the other hand into the ABHR.
- Cover the forearm of the other hand with ABHR until the ABHR evaporates.
- Repeat with other hand and other forearm.
- Don non-shedding gown.
- Enter the clean room.
- Dispense ABHR onto palm of one hand. Rub both hands with ABHR, making sure that all surfaces of the hands are covered. Continue to rub until the ABHR has evaporated.

---

<sup>89</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD:USP; 2013. p. 379-80.

- Allow hands to dry.
- Don sterile gloves.

This handwashing sequence must be documented in the policies and procedures and updated as appropriate.<sup>90</sup>

#### **6.6.2.2 Garbing**

Personnel must wear the PPE required for compounding sterile products, whether compounding is performed in an LAFW or a CAI.

Compounding personnel must don garb in the sequence described in the policies and procedures. The selected sequence must be documented and reviewed regularly<sup>91</sup>.

Shoe covers are required at all times in the clean area of the anteroom and the clean room. All shoes worn must be closed, dry, clean and easy to maintain.

Shoes dedicated to walking in the “clean” area of the anteroom and the clean room may also be used. If so, they must be cleaned and disinfected regularly. If dedicated shoes are worn outside the clean area of the anteroom, they must be disinfected before being used again in the clean area of the anteroom or the clean room; otherwise, shoe covers must be worn.

### **6.6.3 Introducing products and equipment into the clean room**

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

Where packaging allows, compounding equipment and products must be disinfected with sterile 70% isopropyl alcohol just before being introduced into the clean room for the compounding of sterile products<sup>92</sup>.

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

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

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

---

<sup>90</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 376-7.

<sup>91</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 376-7.

<sup>92</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 376-7.

#### **6.6.4 Cleaning and disinfecting the laminar airflow workbench or compounding aseptic isolator**

Only compounding personnel are allowed to clean and disinfect the LAFW or CAI. They must take the following steps:

- Follow hand and forearm hygiene and garbing procedures.
- Disinfect the work surface of the LAFW or CAI according to existing procedures, ensuring the minimum frequency of disinfection outlined in Table 10. If a different frequency is followed, it should be established and justified by the results of environmental control testing.

All specialized devices or instruments used for compounding sterile preparations, including the LAFW, must be cleaned and disinfected before they are introduced into the clean room, in accordance with manufacturer's recommendations.

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

- Disinfect non-powdered sterile gloves with sterile 70% isopropyl alcohol and allow to dry before starting to clean and disinfect the LAFW or CAI.
- Ensure that the head and upper body do not enter the LAFW or CAI.
- Use non-shedding, disposable swabs.
- Avoid contaminating the surface of swabs used for cleaning and disinfecting.
- Change swabs after completing disinfection of each section of the LAFW or CAI.
- Disinfect the LAFW or CAI with clean swabs and germicidal disinfectant detergent, followed by sterile 70% isopropyl alcohol, at the start or end of the day or shift (minimum twice per day).
- Follow the cleaning method described in the pharmacy's procedures (with regard to equipment, sequence, movements).
- Follow the disinfecting method described in the pharmacy's procedures.
- Wait until the disinfectant has dried before compounding the first preparation in the LAFW or CAI<sup>93</sup>.
- Record cleaning and disinfecting activities in the maintenance log.

---

<sup>93</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 391.

**Table 10**

<b>Minimum frequency and areas of the laminar airflow workbench to be cleaned and disinfected by compounding personnel*</b>		
<b>Surface</b>	<b>Frequency</b>	<b>Cleaning products†</b>
All surfaces	<ul style="list-style-type: none"> <li>- At the start of each day</li> <li>- At the end of each workday</li> </ul>	Germicidal disinfecting detergent, followed by sterile 70% isopropyl alcohol (minimum twice daily)
Work surface	<ul style="list-style-type: none"> <li>- Before starting any sterile-product preparation</li> <li>- At each shift change</li> <li>- Where surface contamination is suspected</li> <li>- If there has been non-compliance with aseptic techniques</li> </ul>	Sterile 70% isopropyl alcohol
Work surface and any surface that has been splashed	<ul style="list-style-type: none"> <li>- When there is a spill</li> </ul>	Rinsing with sterile water for injection or irrigation, followed by sterile 70% isopropyl alcohol
All surfaces and subfloor	<ul style="list-style-type: none"> <li>- Weekly (at the end of a work day) or as recommended by the manufacturer</li> </ul>	Cleaning with water and germicidal detergent, followed by rinsing with sterile water for injection and then disinfecting with sterile 70% isopropyl alcohol
*Requirements are similar for compounding aseptic isolator.		
†Other products may be acceptable for cleaning, if approved by the infectious disease department of the health care facility.		

### 6.6.5 Aseptic technique for compounding sterile products

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

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

Gloved hands must be disinfected with sterile 70% isopropyl alcohol before re-introduction into the LAFW or CAI or after gloves have come into contact with a microbiologically

contaminated surface<sup>94</sup>. If gloves are torn, hands must be washed before new gloves are donned. Gloves must be changed regularly. The frequency and circumstances of glove changes must be defined in a procedure.

The external packaging of products and supplies must be intact, dry and unsoiled. Otherwise, the products and supplies must be discarded. Containers (e.g., bags of solution, vials and ampoules) must be examined before use.

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

Ophthalmic solutions prepared from sterile powder products that require dilution must always be filtered with a 5- $\mu$ m filter. Filtration is not necessary when the products used are available as sterile solutions in vials<sup>95</sup>.

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

## 6.6.6 Verification of final compounded sterile preparations

### 6.6.6.1 Role of personnel in verification

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

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

When compounding, compounding personnel must undertake the following activities:

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

### 6.6.6.2 Process for verification

---

<sup>94</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 379-80.

<sup>95</sup> Buchanan EC, Schneider PJ. *Compounding sterile preparations*. 3rd ed. Bethesda, MD: American Society of Health-System Pharmacists; 2009. p. 29.

Verification may be performed in one of three ways:

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

#### **6.6.6.3 Verification by image capture or live camera**

Verification may be conducted by capturing images of the critical site (in the LAFW) with a camera connected to a monitor. Such verification must be performed before the compounded sterile preparation is delivered to the patient. However, in this situation, if the verifying pharmacist notices that one or more procedures have not been followed correctly, all sterile preparations compounded during this period must be destroyed, and the destruction of preparations (because of non-compliance identified during verification) must be entered in the preparations log.

Appendix 8 gives examples of compounded sterile preparations that must be verified at each step of the compounding process.

#### **6.6.6.4 Verification not required**

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

Appendix 9 gives examples of compounded sterile preparations for which verification is not required during the compounding process.

#### **6.6.6.5 Delegation of verification**

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

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

- implementation of policies and procedures;
- implementation of a quality assurance program, including regular evaluations of the TSP involved;

- verification of a percentage of preparations by the supervisor.

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

Each preparation must be inspected by a person other than the individual who performed the aseptic preparation. This person must inspect each unit against a black and white background for evidence of particulates, verify the clarity, colour and volume of the solution, check the container for possible leaks and verify its integrity<sup>96</sup>.

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

## **6.6.7 Labelling of final compounded sterile preparations**

### **6.6.7.1 General**

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

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

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

Each container for a compounded sterile preparation must be labelled.

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

Compounding personnel must label the following items:

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

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

The patient care (dispensing) pharmacist must add a label containing all information

---

<sup>96</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 381.



required by the respective provincial/territorial regulatory authority before administering the compounded sterile preparation received from the compounding pharmacist to the patient; a supplementary document must be prepared, if required. The label affixed by the compounding pharmacist or pharmacy technician must be retained.

#### **6.6.7.2 Label and insert**

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

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

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

- pharmacy identification (name, address and telephone number of the compounder's or dispenser's pharmacy);
- drug identification (active ingredients, concentration, form, route of administration, volume, solute, amount prepared);
- special precautions (e.g., if product is 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 is undertaken by another pharmacy, as permitted by provincial/territorial legislation), provided there is mutual agreement between the compounding pharmacist and the dispensing pharmacist.

## **6.7 Packaging**

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

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

### 6.7.1 Packaging process

During packaging, compounding personnel must

- put all final compounded sterile preparations in packaging that maintains each preparation's stability, integrity and storage conditions;
- place items with an attached needle in a second rigid container;
- 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 transportation precautions (e.g., temperature, fragility, safety) and instructions (name and address of patient) on the outside packaging of each item.

### 6.7.2 Packaging procedure

To maintain the integrity of compounded sterile preparations and the safety of patients and delivery personnel, the sterile compounding supervisor must develop and implement a packaging procedure for final compounded sterile preparations. Appendix 4 presents a model for writing such procedures. The packaging procedure must specify the following details:

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

## 6.8 Storage<sup>97,98</sup>

---

<sup>97</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 384.

The sterile compounding supervisor must develop a storage procedure (see Appendix 4), and this procedure must be followed at all times.

All commercial products used for preparations must be stored immediately upon receipt. In addition, they must be handled and stored so as to prevent cross-contamination and incompatibilities.

Product storage conditions specified by the manufacturer must be strictly observed, regardless of where the products are stored (warehouse, pharmacy, delivery vehicle, loading dock, etc.).

For final compounded sterile preparations or products used for preparations, the storage temperature must be controlled and must remain within the limits specified in Appendix 10, 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 log<sup>99</sup>.

A biomedical refrigerator or freezer must be available for storing products, ingredients and final compounded sterile preparations that need to be refrigerated or frozen (see section 5.3.3.2).

Alternative storage must be provided when conditions are beyond acceptable temperature variations and when refrigerators and freezers are being cleaned.

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

A procedure for verifying the BUDs of stored compounded sterile preparations and the expiration dates of commercial products must be developed and implemented to ensure that unusable products and compounded sterile preparations are quickly discarded.

## 6.9 Transport and delivery of final compounded sterile preparations

Policies and procedures must be developed and implemented for the transport of compounded sterile preparations and their delivery to patient care units, patients and dispensing pharmacists (see Appendix 4). A policy for return of expired or unused compounded sterile preparations from the patient's home or the patient care unit in a health care facility must also be developed.

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

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

---

<sup>98</sup> United States Pharmacopeial Convention (USP). General chapter <1079>: good storage and shipping practices. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008–2009. p. 880.

<sup>99</sup> United States Pharmacopeial Convention (USP). General chapter <1079>: good storage and shipping practices. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008–2009. p. 879.

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

The sterile compounding supervisor must ensure that personnel involved in preparation and delivery of products (pharmacy technician, TSP and driver) receive training on the transport and delivery procedures.

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

In health care facilities, unused preparations returned from the patient care unit to the pharmacy may be reused if it can be shown that they have been properly stored (at the correct temperature, with protection from light, etc.) and there is no evidence of tampering<sup>100</sup>.

When a private carrier is used, the pharmacist must verify the steps taken to ensure maintenance of the cold chain throughout transport and storage of compounded sterile preparations.

When a private carrier is to deliver compounded sterile preparations to a patient, the sterile compounding supervisor must ensure that the transport conditions will comply with the required storage conditions.

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

The dispensing pharmacist must ensure that transport conditions are maintained until the product is delivered to the patient.

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

In community or hospital pharmacies, when information obtained 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 expectations, the pharmacist must be able to

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

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

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

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

---

<sup>100</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 384-5.

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

## 6.11 Incident and accident management

When an incident or accident involving a compounded sterile preparation occurs, the compounding personnel must complete an event report and explanation form (see Appendix 11). In health care facilities, a form developed or selected by the facility may be used.

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

## 6.12 Waste management

In the performance of assigned duties, the pharmacist must<sup>101</sup>

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

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. A list of hazardous products in use must be available in the pharmacy. The list produced by NIOSH, which is part of the US Centers for Disease Control and Prevention,<sup>102</sup> can be used to determine if a particular product is hazardous.

## 7. QUALITY ASSURANCE PROGRAM

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

---

<sup>101</sup> 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](http://napra.ca/Content_Files/Files/Model_Standards_of_Prac_for_Cdn_Pharm_March09_Final_b.pdf)

<sup>102</sup> 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>

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

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

## 7.1 Program content

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

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

Each component of the quality assurance program and its activities must be documented (see Appendix 12).

## 7.2 Results and action levels

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

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

## 7.3. Verification of equipment and facilities

### 7.3.1 Verification of equipment supporting compounding activities

#### 7.3.1.1 Certification

Equipment that supports compounding activities, especially refrigerators, freezers, incubators and air sampling devices, must be certified with respect to its installation and

operation and must be calibrated before being put into service.

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

#### **7.3.1.2 Temperature readings**

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

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

### **7.3.2 Verification of controlled rooms and LAFW or CAI**

#### **7.3.2.1 Certification**

The controlled areas of facilities and the LAFW or CAI must be certified by a recognized organization

- at least every 6 months<sup>103</sup>;
- during installation of new equipment or a new controlled area;
- during maintenance or repair of equipment (repair of LAFW, ventilation system, etc.) or a controlled area (repair of hole in a wall, etc.) that might alter environmental or operational parameters;
- when investigation of a contamination problem or a problem involving non-compliance in the aseptic compounding process requires exclusion of malfunctioning facilities.

The program for monitoring facilities and the LAFW or CAI must include a plan for sampling viable and non-viable particles.

#### **7.3.2.2 Certificate provided by manufacturer (in factory)**

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

#### **7.3.2.3 Environmental verification**

---

<sup>103</sup> 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](https://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html)

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.

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

The sterile compounding supervisor must ensure that personnel on site

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

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

The differential pressure between controlled areas must be kept constant according to the specifications described in section 5.3.2.5 (see Tables 2, 3 and 4; Figure 1). Pressure must be measured continuously, and a security system must be in place to immediately advise personnel of non-compliance with specifications and to direct that action be taken, should it be necessary. A procedure must be developed to outline and explain the actions to be taken should the pressure differential be non-compliant.

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

**Sampling of non-viable, viable and surface particles in controlled areas and the LAFW or CAI**<sup>104</sup>

A sampling plan for controlled areas and the LAFW or CAI must be established.

**Sampling plan**

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

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

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

The sampling plan must allow for three types of samples:

---

<sup>104</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 373-5.



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

#### Sampling specifications

Samples must be obtained at least every 6 months from the air in controlled areas and in the LAFW <sup>105</sup> or CAI *and* every time that the following conditions are present:

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

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

#### Sampling of non-viable particles in air

Non-viable particles in the air in controlled areas and the LAFW must be sampled at least every 6 months<sup>106</sup>, as follows:

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

The sterile compounding supervisor must ensure the competency of the certifier and the personnel chosen to conduct the sampling. Appendix 5 describes certification activities.

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

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

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

Appendices 5 and 6 describe certification activities and the standards used by certifiers.

---

<sup>105</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 373-5.

<sup>106</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 373-5.

## Sampling of viable particles in air and on surfaces

Sampling for viable particles must include

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

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

The sterile compounding supervisor must

- obtain from the manufacturer a calibration certificate for the viable air sampler, to ensure that it is regularly calibrated according to the manufacturer's recommendations and to properly train personnel in its use;
- use the appropriate nutrient medium for plating of samples:
  - tryptic soy agar (low sulphur content) or soybean-casein digest medium for air samples;
  - tryptic soy agar with lecithin and polysorbate for surface samples;
- assure the microbial proliferation capacity of each batch of nutrient medium used (the certificate for this test, provided by the manufacturer, must be retained<sup>107</sup>).

The samples obtained must be either

- sent to a certified external laboratory; or
- incubated in the community or health care facility pharmacy, provided that
  - the incubator used is certified periodically;
  - procedures are in place for use and maintenance of the incubator and for surveillance of temperatures;
  - personnel are properly trained and are competent to read and interpret the results and to take appropriate preventive or corrective actions.

Samples must be incubated, in an inverted position<sup>108</sup>, between 30°C and 35°C, to be read in 48 to 72 hours; alternatively, another equivalent method must be used.

The contamination level at which corrective action is required will vary depending on the desired ISO air classification.<sup>109</sup> The following examples indicate contamination levels that would trigger corrective action with different types of sampling.

---

<sup>107</sup> United States Pharmacopeial Convention (USP). General chapter <51>: antimicrobial effectiveness. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008–2009.p. 706-8.

<sup>108</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 375.

<sup>109</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 375, 379.

Volumetric sampling of facility air:

- Areas requiring ISO Class 5 air quality, threshold contamination > 1 CFU/m<sup>3</sup> of air
- Areas requiring ISO Class 7 air quality, threshold contamination > 10 CFU/m<sup>3</sup> of air
- Areas requiring ISO Class 8 air quality, threshold contamination > 100 CFU/m<sup>3</sup> of air

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

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

GFTS (total for two hands):

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

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

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

## 7.4 Quality assurance of personnel involved in aseptic compounding

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

### 7.4.1 Gloved fingertip sampling<sup>110</sup>

GFTS must include

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

---

<sup>110</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 378.

Using tryptic soy agar contact plates with lecithin and polysorbate<sup>111</sup>, the assessor takes thumbprints and prints of each gloved fingertip from both hands of the assessed employee, asking the employee to gently press each thumb and fingertip on the agar in the contact plate.

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

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

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

## 7.4.2 Media fill test

The media fill test is a compounding simulation test conducted with nutrient media that promote bacterial growth to verify maintenance of the aseptic process for a given employee. For more information on this test, consult chapter <797> in the USP–NF<sup>112</sup>.

For the media fill test, the simulation chosen for assessment of personnel must be representative of activities performed in real compounding conditions in the particular environment and must represent the most complex preparations according to the microbiological risk level of preparations made there<sup>113</sup>.

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

The proliferation capacity of every batch of nutrient medium used must have been tested by the manufacturer, and the certificate for this test result must be retained by the compounding pharmacy<sup>114</sup>.

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

The containers filled with nutrient medium to be used for the media fill test must be incubated between 20°C and 25°C or between 30°C and 35°C for 14 consecutive days<sup>115</sup>.

---

<sup>111</sup> United States Pharmacopeial Convention (USP). General chapter <1116>: microbial evaluation of clean rooms and other controlled environments. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008–2009. pp. 900-8.

<sup>112</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 365-8.

<sup>113</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 365-8.

<sup>114</sup> United States Pharmacopeial Convention (USP). General chapter <51>: antimicrobial effectiveness. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008–2009. pp. 706-8.

<sup>115</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. pp. 365-9.

If two temperatures are used, the containers should be incubated for 7 consecutive days at each of the temperatures, starting with the lower temperature.

## 7.5 Quality assurance of compounded sterile preparations

The 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 compounding protocol for each compounded 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 a patient's compounded sterile preparations log and the batch compounded sterile preparations log, ensuring the performance of all verification steps required during and after compounding.

## 7.6 Documentation of quality control activities

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

The sterile compounding supervisor must

- investigate missing documentation, situations of non-compliance (where action is required) and deviations from protocols;
- identify trends concerning microbial load in controlled areas and types of micro-organisms found;
- consult a microbiology specialist, if necessary;
- take corrective and preventive actions.

For the sampling of viable air and surface particles, the nutrient medium readings should be documented on a separate form for each type of sampling.

All completed documentation concerning components of the environmental verification of controlled areas, the LAFW or CAI and support equipment must be filed and retained with other compounding records in an easily accessible location inside the pharmacy.

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

All completed documentation concerning the quality assurance program for the aseptic

compounding process for personnel (by GFTS and media fill test), including nutrient medium readings, should be retained and made accessible.

## 8.0 SOURCE FOR ADDITIONAL INFORMATION

For more information on sterilization of high-risk compounds, depyrogenation by dry heat, and use of allergen extracts and radiopharmaceuticals as compounded sterile products, please refer to chapter <797> in the most recent edition of USP–NF.

## 9. GLOSSARY

Term	Definition
Accident	Action or situation in which the risk event occurs and has or could have an impact on the health status or well-being of the user (patient), personnel, professional concerned or third party. An accident differs from an incident, which has no effect on the patient.
Anteroom	A room equipped with two doors, with an interlocking system that allows only one door to open at a time, which allows passage or movement of someone or something from one environment to another, while keeping these environments isolated from each other.
Aseptic techniques	Steps in the aseptic process that include all manipulations performed inside the laminar airflow workbench by compounding personnel.
Assessment	Action of assessing and defining an employee's performance and competency. Also the action of determining something's value or importance.
Beyond-use date (BUD)	For the purposes of these Model Standards, the date after which the final compounded sterile preparation can no longer be used or administered. It is determined from the date or time that the preparation is compounded <sup>116</sup> .
Cleaning and disinfecting (housekeeping)	Cleaning activities involving the removal of dirt, dust and other substances that may host microorganisms, guaranteeing access to a clean and healthy environment <sup>117</sup> .
Clean room	A room in which atmospheric properties (temperature, humidity, particle and microorganism content, pressure, airflow, etc.) are controlled. The room's functional parameters are kept at a specific level. The room is designed to minimize introduction, generation and retention of particles.

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

<sup>117</sup> United States Pharmacopeial Convention (USP). General chapter <1072>: disinfectants and antisepsis. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008–2009.

Commercial container	Container holding a commercially manufactured drug or sterile nutrient, the consumption and sale of which are authorized in Canada; if the drug or sterile nutrient is authorized by Health Canada's Special Access Programme, such consumption and sale may be limited.
Competencies	Significant job-related knowledge, skills, abilities, attitudes and judgments required for competent performance of duties by members of a profession.
Compounding	Act of preparing something, through preliminary work, to put it into a usable state. Also refers to the material that has been compounded (e.g., a chemical or pharmaceutical preparation).
Compounding aseptic isolator (CAI)	Isolator specifically used for compounding non-hazardous sterile products. Designed to ensure an aseptic environment during the transfer of material and drugs and during the performance of aseptic technique. It must not allow any exchange of air between the air inside the clean room and the isolator, unless the air is first filtered by a high-efficiency particulate air filter.
Compounding personnel	Pharmacists, pharmacy technicians or technical support personnel assigned to the compounding of sterile products.
Compounding pharmacist or pharmacy technician	Pharmacist or pharmacy technician who compounds or supervises the compounding of sterile products according to prescriptions issued to the pharmacy where the pharmacist or pharmacy technician works or for a dispensing pharmacist who has requested this service (where compounding is undertaken by another pharmacy, as permitted by provincial/territorial legislation).
Compounding procedure	Procedure that describes all steps to be followed in the compounding of sterile products and performed according to a particular packaging method (e.g., syringe filled for intravenous use, elastomeric preparation).
Compounding protocol	Protocol that describes all steps to be followed in the compounding of a specific sterile preparation and with which the compounder must comply. The protocol must include all of the information to be recorded in the preparation log.
Containment system	Arrangement of equipment to contain the particles of hazardous products in the chosen space.
Contiguous	A term describing a location or space that adjoins another. Example: The clean room is contiguous with the anteroom and the surrounding pharmacy areas. Synonyms: adjacent, adjoining, bordering, abutting, surrounding, neighbouring



Controlled area or room	An area or space where the only activities taking place are those related to the compounding of sterile products. In such locations, to obtain the specified ISO class parameters, the concentration of viable and non-viable particles suspended in the air is verified according to a sampling plan. Corrective measures are taken when necessary so that the area remains at the expected ISO class level <sup>118</sup> . The clean room and anteroom are examples of controlled areas. May also be known as a classified area or room.
Critical area	Work area inside a laminar airflow workbench ensuring ISO Class 5 air, in which personnel compound sterile products and where critical sites are exposed to unidirectional airflow from a high-efficiency particulate air filter.
Critical site	Any surface likely to come into contact with a sterile drug or liquid (e.g., vial septa, injection sites) or any exposed opening (open vials, needle hubs) and likely to be in direct contact with the ambient air or air filtered by means of a high-efficiency particulate air filter or humidity (oral secretions or mucous membranes) or likely to be contaminated by touch <sup>119</sup> .
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 <sup>120</sup> .
Disinfection	Treatment that eliminates most of the pathogens present on an object or surface <sup>121</sup> .
Facilities	All devices, rooms and spaces that are organized, arranged and modified to better adapt them to the activities to be conducted therein.  Facilities include the clean room and the anteroom.
Filling a prescription	All activities related to the validation (including therapeutic appropriateness), preparation and packaging of a patient's medication prepared pursuant to a prescription.
Final sterile preparation	A sterile preparation ready to be stored and then administered to a patient, which has been prepared according to a preparation-specific compounding protocol which respects the prescribing physician's prescription.
Gloved fingertip sampling (GFTS)	A process that involves microbiological examination based on imprints from the person being assessed, obtained by having the person press gloved thumbtips and fingertips into the contact plate agar. Both hands are tested in this manner <sup>122</sup> .

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

<sup>119</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

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

<sup>121</sup> United States Pharmacopeial Convention (USP). General chapter <1072>: disinfectants and antisepsis. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008–2009.

<sup>122</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.



Hand hygiene	All methods related to handwashing that is performed using soap and water, followed by a waterless, alcohol-based hand rub containing, for example, chlorhexidine and alcohol.
Hazardous drugs	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 <sup>123</sup> .  Drugs are considered hazardous because they involve risks for the worker, because of their effects <sup>124</sup> .
Hazardous material	A material that, because of its properties, constitutes a danger to an employee's health, safety or physical integrity <sup>125</sup> . Hazardous materials are dangerous products regulated by a workplace hazardous material information system; as such, they are considered "controlled" products under the <i>Controlled Products Regulations</i> . <sup>126</sup>
Hazardous products	Substances that entail risks for the worker because of their effects. For the purposes of these Model Standards, the term "hazardous product" refers to both hazardous drugs and hazardous materials, depending on the situation.
Housekeeping	See Cleaning and disinfecting
Incident	An action or situation that has no impact on the health status or well-being of the user (patient), personnel, professional concerned or third party, but which has 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 <sup>127</sup> .
Incubator	Microbial culture sterilizer, a device used in microbiology to keep cultures at a constant temperature.
Insert	Document or leaflet containing information about a drug additional to that written on the computer-generated label produced by the prescription management software; provides the patient with information as required by regulations.
Label (for identifying a sterile preparation)	Label that identifies the drugs prepared or sold with or without a prescription. It is usually computer-generated and adhesive. It must bear the information required by federal/provincial/territorial regulations.

<sup>123</sup> 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>

<sup>124</sup> 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>

<sup>125</sup> 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>

<sup>126</sup> *Controlled Products Regulations*, SOR/88-66, 1987. Available from: <http://laws-lois.justice.gc.ca/eng/regulations/SOR-88-66/>

<sup>127</sup> Commission de la santé et de la sécurité du travail (CSST). *Material safety data sheet user's guide*. CSST; 2010. Available from: <http://www.reptox.csst.qc.ca/Documents/SIMDUT/GuideAng/Htm/GuideAng.htm>.

Laminar airflow workbench (LAFW)	A device that provides an ISO Class 5 environment for the exposure of critical sites when sterile preparations are being compounded. The airflow is unidirectional (laminar flow), and the first air (air exiting the HEPA filter <sup>128</sup> ) is free from airborne particulates.
Laminar flow hood	See “Laminar airflow workbench”
Log	Book or notebook in which data are recorded or compiled to demonstrate that the quality of the pharmacy aseptic compounding process has been maintained.  A log may be in computerized format.
Maintenance of competency	Continued ability to integrate and apply knowledge, know-how, judgment and personal qualities necessary to practise in a safe and ethical fashion in a designated role and framework <sup>129</sup> .
Maintenance (of facilities and equipment)	Operations for maintaining the proper functioning of facilities or equipment according to established specifications or for re-establishing the satisfactory operational condition of facilities, including the heating, ventilation and air conditioning system and related equipment.
Material safety data sheet (MSDS)	A “document that provides information on a controlled product, namely its toxic effects, the protective measures for avoiding overexposure or chemical hazards, and the procedures to follow in an emergency. The supplier sends the MSDS to the employer when the product is sold. It must be kept on the premises by the employer in a location known by the workers, and be easily and rapidly accessible to those who are likely to come in contact with the product. The employer should have it before a product is used for the first time” <sup>130</sup> .
Media fill test	Test used to qualify aseptic techniques of compounding personnel and the environment’s ability to produce preparations that are “sterile.” For this test, a nutrient medium replaces the actual product when the aseptic technique is performed <sup>131,132</sup> .
Multiple-dose vial	Commercial drug container in multiple-dose format for parenteral administration only. The product usually contains an antimicrobial preservative <sup>133</sup> .

<sup>128</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

<sup>129</sup> Canadian Nurses Association. *Joint position statement: Promoting continuing competence for registered nurses*. Ottawa, ON: The Association; 2004. Available from: [http://www.cna-aicc.ca/~media/cna/page-content/pdf-en/ps77\\_promoting\\_competence\\_e.pdf](http://www.cna-aicc.ca/~media/cna/page-content/pdf-en/ps77_promoting_competence_e.pdf)

<sup>130</sup> Commission de la santé et de la sécurité du travail (CSST). *Material safety data sheet user's guide*. CSST; 2010. Available from: <http://www.reptox.csst.qc.ca/Documents/SIMDUT/GuideAng/Htm/GuideAng.htm>

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

<sup>132</sup> Health Canada, Health Products and Food Branch Inspectorate. *Good manufacturing practices (GMP) guidelines – 2009 edition, Version 2 (GUI-0001)*. Ottawa, ON: Health Canada; 2009, revised 2011 Mar 4. p. 85. Available from: <http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/docs/gui-0001-eng.php>

<sup>133</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

Personal protective equipment (PPE)	All garb and accessories, such as mask, gloves, smock, and safety goggles, that protect the sterile preparation and the worker. It enables compliance with the expected specifications of a controlled environment and protects the worker from exposure to physical or chemical risks <sup>134 135</sup> .
Pharmacy bulk vial	Commercial container for parenteral sterile preparations, intended for packaging containing several individual doses. Such packaging is used only by pharmacies with an intravenous admixture program. During the final packaging, in several doses, the pharmacy bulk vial must be perforated with a transfer device only once, by introducing a needle or transfer “spike.”
Patient care (dispensing) pharmacist	Pharmacist providing care to patients, who delivers or administers a product after verification of its therapeutic appropriateness; the product may be prepared by the patient care (dispensing) pharmacist or by compounding personnel in another pharmacy, where compounding is undertaken by another pharmacy, as permitted by provincial/territorial legislation.
Pharmacist	Registrant in good standing of one of the pharmacy regulatory authorities in Canada
Pharmacy technician	An adult who has earned a college degree or diploma from an accredited pharmacy technician program and has passed the national examination. Such persons are licensed or authorized by a provincial/territorial health professional regulatory authority to practice 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 these principles.
Prescription validation	The pharmacist's decision to declare a prescription valid after verifying its legality, contents and relevance with respect to the patient and the patient's condition.
Primary engineering control (PEC)	Equipment ensuring ISO Class 5 level for the quality of high-efficiency particulate air-filtered air at the critical sites exposed during the aseptic technique.  The primary engineering control for non-hazardous products includes laminar airflow workbenches and compounding aseptic isolators.  The primary engineering controls for compounding hazardous preparations are called biological safety cabinets and compounding aseptic containment isolators <sup>136</sup> .
Procedure	All steps to be taken, the means to be used and the methods to be followed in performing a task.

<sup>134</sup> 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>

<sup>135</sup> 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>

<sup>136</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013. p. 263.

Process for aseptic compounding	All activities leading to completion of a final compounded sterile preparation, especially hand hygiene and garbing, introduction of products and materials into the clean room, disinfection of the primary engineering control, use of aseptic techniques for compounding products in the primary engineering control, and verification and labelling of compounded sterile preparations. Its purpose is to maintain the sterility of a product or drug compounded from sterile components.
Protocol	Document describing in detail all steps to be followed or behaviours to be adopted in specific clinical circumstances.
Repack/repacking	The process of packing again or the action of repacking (“reprocessing”). Examples include making 12-tablet packages from a pack (bottle) of 100 tablets and filling 1-mL syringes from a 10-mL pack (vial).
Single-dose vial	Single-dose commercial container corresponding to a fixed dose of a drug intended for parenteral administration only <sup>137</sup> .
Stability (period of)	Length of time during which a properly compounded sterile preparation maintains, within specified limits and throughout the storage and usage period, the properties and characteristics that it had when it was compounded.
Sterile compounding supervisor	A person assigned by the department head of the health care facility or by the pharmacist-owner of a community pharmacy to supervise and organize all activities related to the compounding of sterile products.
Sterilization by filtration	For situations or products with high risk of microbial contamination, any sterilization procedure using a sterilizing-grade membrane to produce a sterile final solution (where a sterilizing-grade membrane is a membrane approved for filtering 100% of a <i>Brevundimonas (Pseudomonas) diminuta</i> culture to a concentration of 10 <sup>7</sup> colony-forming units/cm <sup>2</sup> of filtering surface and to a minimum pressure of 50 psi; depending on the manufacturer, the nominal size of the membrane pores is 0.22 µm or 0.2 µm <sup>138</sup> ).
Technical support personnel (TSP)	An adult who has earned a vocational school diploma for completing a pharmacy technician assistant course or any adult who has received proper training that is deemed equivalent.
Training	Acquisition of a totality of theoretical, technical and practical knowledge concerning pharmacy preparation.
Unidirectional airflow	Airflow moving in a single direction in a robust and uniform manner and at sufficient speed to reproducibly sweep particles away from the critical site.

<sup>137</sup> United States Pharmacopeial Convention (USP). General chapter <797>: pharmaceutical compounding — sterile preparations. USP 36. Rockville, MD: USP; 2013.

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

## 10. LIST OF TABLES

Table 1	Classes of air cleanliness for airborne particulates in clean rooms and clean areas, according to ISO 14644-1
Table 2	Functional parameters of the compounding clean room
Table 3	Functional parameters of the anteroom for the compounding of non-hazardous sterile products
Table 4	Functional parameters of a shared anteroom for the compounding of non-hazardous and hazardous sterile products
Table 5	Personal protective equipment (PPE) for the compounding of non-hazardous sterile products
Table 6	Beyond-use dates (BUDs) for compounded sterile preparations when a preservative-free vial is used
Table 7	Contamination risk levels
Table 8	Beyond-use dates (BUDs) for compounded sterile preparations, according to risk of microbial contamination
Table 9	Summary of beyond-use dates (BUDs) for compounded sterile preparations in short-term critical situations
Table 10	Minimum frequency and areas of the laminar airflow workbench to be cleaned and disinfected by compounding personnel

## 11. APPENDICES

### APPENDIX 1 POLICIES AND PROCEDURES FOR THE COMPOUNDING OF NON-HAZARDOUS AND HAZARDOUS STERILE PRODUCTS

Part I		<b>NON-HAZARDOUS STERILE PRODUCTS</b>	
Policy #	Topic		✓
<b>A</b>	<b>PERSONNEL AND FACILITIES</b>		
1.	<b>Obligations of personnel</b>		
1.1	Attire and dress code (e.g., personal clothing, jewelry, makeup, hairstyles)		
1.2	Health condition (reasons for temporary withdrawal from compounding activities)		
1.3	Expected behaviour in controlled areas (e.g., no drinking, eating, or other activities not related to compounding; expectation that procedures will be followed; avoidance of unnecessary conversations)		
2.	<b>Training and assessment of personnel</b>		
2.1	Initial training and assessment program		
2.2	Program to assess maintenance of competency		
2.3	Training and assessment of cleaning and disinfecting personnel		
3.	<b>Delegation of activities</b>		
3.1	Delegation of pharmaceutical activities to persons other than pharmacists		
4.	<b>Facilities and equipment</b>		
4.1	Access to controlled areas		
4.2	Necessary facilities and equipment		
4.3	Maintenance of facilities and equipment (e.g., certification of rooms and devices, calibration, maintenance of pre-filters and HEPA filters, verification of pressure)		
4.4	Cleaning and disinfecting activities for facilities and equipment		
<b>B</b>	<b>COMPOUNDED STERILE PREPARATIONS</b>		
1.	Bringing equipment and products into the clean room and laminar airflow workbench		
2.	Determining beyond-use date of products used in a preparation		
3.	Determining beyond-use date of final preparations		
4.	Hand and forearm hygiene		
5.	Garbing in compounding areas and for compounding		
6.	Cleaning and disinfecting the Laminar Airflow Workbench		

	7.	Aseptic techniques (with details for each of the techniques used)	
	8.	Verification of the compounding process (including validation of calculations by a pharmacist) and of final preparations	
	9.	Labelling of final preparations	
	10.	Packaging of final preparations	
	11.	Preparation of injectable products outside regular operating hours of the compounding department of a health care facility	
	12.	Storage of products used and final preparations	
	13.	Transport and delivery of final preparations (to the patient, to patient care units or to the dispensing pharmacist)	
	14.	Recording of preparations in the patient's file	
	15.	Biomedical waste management (e.g., at the pharmacy, returns from patients or patient care units, instructions to patients)	
	16.	Recall of sterile products or compounded sterile preparations	
<b>C</b>		<b>QUALITY ASSURANCE PROGRAM</b>	
	1.	Verification and maintenance of equipment	
	2.	Environmental control of facilities and laminar airflow workbench (e.g., pressure verification, air and surface sampling plan)	
	3.	Quality assurance of aseptic process for personnel (e.g., gloved fingertip sampling, media fill tests)	
	4.	Quality assurance of compounded sterile preparations (e.g., existence of a protocol, compliance with prescription, documentation in logs)	

Part II		<b><u>HAZARDOUS STERILE PRODUCTS</u></b>	
Policy #		Topic	✓
<b>A</b>		<b>PERSONNEL AND FACILITIES</b>	
	<b>1.</b>	<b>Obligations of personnel</b>	
	1.1	Attire and dress code (e.g., personal clothing, jewelry, makeup, hairstyles)	
	1.2	Health condition (reasons for temporary withdrawal from compounding activities)	
	1.3	Expected behaviour in controlled areas (e.g., no drinking, eating, or other activities not related to compounding; expectation that procedures will be followed; avoidance of unnecessary conversations)	
	<b>2.</b>	<b>Training and assessment of personnel</b>	

	2.1	Initial personnel training and competency assessment program, including the details of compounding hazardous drugs	
	2.2	Program to assess maintenance of competency, including the characteristics of compounding hazardous sterile products	
	2.3	Training and assessment of cleaning and disinfecting personnel, including the characteristics of compounding hazardous sterile products	
	<b>3.</b>	<b>Delegation of activities</b>	
	3.1	Delegation of pharmaceutical activities to persons other than pharmacists	
	<b>4.</b>	<b>Facilities and equipment</b>	
	4.1	Access to controlled areas	
	4.2	Facilities and equipment for the compounding of hazardous sterile products	
	4.3	Reservation of facilities and equipment for the compounding of hazardous sterile products	
	4.4	Maintenance of facilities and equipment, including the characteristics of compounding hazardous sterile products (e.g., certification of rooms and devices, calibration, maintenance of pre-filters and HEPA filters, pressure verification)	
	4.5	Cleaning and disinfecting activities for facilities and equipment	
<b>B</b>		<b>COMPOUNDED STERILE PREPARATIONS</b>	
	1.	Receiving and unpacking of hazardous sterile products	
	2.	Storage of hazardous sterile products	
	3.	Determining beyond-use date of products used in a preparation	
	4.	Determining beyond-use date of final preparations	
	5.	Hand and forearm hygiene	
	6.	Garbing in compounding areas and for compounding	
	7.	Bringing equipment and products into the clean room and biological safety cabinet	
	8.	Verification of the compounding process (including validation of calculations by a pharmacist) and of final preparations	
	9.	Cleaning, decontamination, deactivation and disinfection of the biological safety cabinet	
	10.	Aseptic techniques for compounding hazardous sterile products	
	11.	Packaging of hazardous compounded sterile preparations	
	12.	Labelling of hazardous compounded sterile preparations	
	13.	Storage of final hazardous compounded sterile preparations	
	14.	Recording of preparations in the patient's file	
	15.	Transport and delivery of final hazardous compounded sterile preparations (to the patient, patient	



		care units or dispensing pharmacist)	
	16.	Hazardous waste management (e.g., at the pharmacy, returns from patients or patient care units, instructions to patients)	
	17.	Accidental exposure of personnel to hazardous drugs (e.g., eyewash station, log)	
	18.	Spills (e.g., spill management, chemical-cartridge respirator, kit)	
	19.	Recall of hazardous products or final hazardous compounded sterile preparations	
<b>C</b>		<b>QUALITY ASSURANCE PROGRAM</b>	
	1	Verification and maintenance of equipment	
	2	Environmental control of facilities and biological safety cabinet (e.g., pressure verification, air and surface sampling plan)	
	3	Quality assurance of aseptic process for personnel (e.g., gloved fingertip sampling, media fill tests)	
	4	Quality assurance of compounded sterile preparations (e.g., existence of a protocol, compliance with prescription, documentation in logs)	
<b>D</b>		<b>ENVIRONMENTAL MONITORING PROGRAM</b>	
	1	Environmental monitoring of chemical contamination	

## APPENDIX 2 MANDATORY AND SUPPLEMENTAL DOCUMENTATION

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

### A. Mandatory documentation

At a minimum, the sterile compounding supervisor must make a recent edition of the following publications available:

- Standards, guidelines and policies of the relevant pharmacy regulatory authority
- Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS). *Prevention guide — safe handling of hazardous drugs*. Montréal, QC: ASSTSAS; 2008. Available from: <http://www.asstsas.qc.ca/publications/publications-specialisees/guides-de-prevention/prevention-guide-safe-handling-of-hazardous-drugs.html>
- National Institute for Occupational Safety and Health (NIOSH). NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2012. Publ. No. 2012-150. Atlanta (GA): Department of Health and Human Services, Centers for Disease Control and Prevention, NIOSH; June 2012. Available from: <http://www.cdc.gov/niosh/docs/2012-150/pdfs/2012-150.pdf>
- Trissel LA. *Handbook on injectable drugs*. Bethesda, MD: American Society of Health-System Pharmacists.
- United States Pharmacopeial Convention (USP). *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008-2009 (contains all USP chapters useful to pharmacists, including General Chapter <797>: Pharmaceutical Compounding — Sterile Preparations).

### B. Supplemental documentation

#### 1. GENERAL TEXTS ON STERILE PREPARATIONS

##### Volumes

- Buchanan EC, Schneider PJ. *Compounding sterile preparations*. 3rd ed. Bethesda, MD: American Society of Health-System Pharmacists; 2009. 481 pages.

##### Periodicals

- *American Journal of Health System Pharmacists*. Available at: [www.ajhp.org](http://www.ajhp.org)
- *Canadian Journal of Hospital Pharmacy*. Available from: <http://www.cjhp-online.ca/index.php/cjhp>
- *International Journal of Pharmaceutical Compounding*. Available at: [www.ijpc.com](http://www.ijpc.com)

##### Websites: associations and agencies

- ASHP Sterile Compounding Resource Center: [www.ashp.org/compounding](http://www.ashp.org/compounding)
- Pharmacy Compounding Accreditation Board: [www.pcab.info](http://www.pcab.info)

#### 2. REFERENCE TEXTS: PHYSICAL-CHEMICAL STABILITY, COMPATIBILITY AND STABILITY

- *Compendium of pharmaceuticals and specialties*. Ottawa, ON: Canadian Pharmacists Association. Updated yearly.
- King JC. *King guide to parenteral admixtures* [electronic version]. Napa, CA: King Guide Publications Inc. Updated quarterly.
- Trissel LA. *Trissel's 2 clinical pharmaceuticals database* [electronic database]. Cashiers, NC: TriPharma Communications. Updated regularly.

#### 3. REFERENCE TEXT: PHARMACOKINETICS

- DiPiro JT, Spruill WJ, Wade WE, Blouin RA, Pruemmer JM. *Concepts in clinical pharmacokinetics*. Bethesda, MD: American Society of Health-System Pharmacists. About 250 pages.

**APPENDIX 3 TRAINING OF COMPOUNDING PERSONNEL AND CLEANING AND DISINFECTING PERSONNEL**

**A. Training of compounding personnel**

#	COMPETENCIES, KNOWLEDGE OR SKILLS COVERED IN TRAINING			
1.	<b>FOR THE COMPOUNDING OF NON-HAZARDOUS AND HAZARDOUS STERILE PREPARATIONS</b>	<b>PH</b>	<b>PT</b>	<b>TSP</b>
1.1	Know the relevant federal/provincial/territorial legislation and regulations related to pharmacy compounding, as well as other governing standards, guides or guidelines.	X	X	
1.2	Know and apply all policies and procedures related to the pharmacy compounding of sterile products, especially those related to hand hygiene, garbing, aseptic techniques, airflow principle, facilities (ISO Classes 5, 7 and 8), material, equipment, behaviour of personnel in compounding rooms, forms and logs to be completed, labelling, storage, distribution to patients, quality controls (sampling) and maintenance and cleaning of sterile-product compounding areas.	X	X	X
1.3	Know physical and chemical properties such as stability, physical-chemical compatibility and incompatibility, osmolality and osmolarity.	X		
1.4	Know pharmaceutical and medical abbreviations.	X	X	X
1.5	Know and understand the importance of particulate and microbial contamination.	X	X	X
1.6	Perform pharmacy sterile-product compounding tasks meticulously, precisely and competently.	X	X	X
1.7	Know and apply appropriate aseptic techniques in the workplace.	X	X	X
1.8	Know the operation and correct use of equipment, materials and automated devices available for the sterile preparations to be compounded. Know how to calibrate the devices used.	X	X	X
1.9	Be able to recognize errors in the compounding technique of compounding personnel.	X		

1.10	Have a good command of the pharmaceutical calculations required to compound sterile products.	X	X	X
1.11	Understand the importance of and apply accurate measurements.	X	X	X
1.12	Apply disinfection measures for sterile-product compounding rooms, facilities and materials.	X	X	X
1.13	Know the data to be monitored in controlled areas (temperature, pressure, humidity) and document in the appropriate logs. Know and apply the corrective measures to be applied when irregularities are found.	X	X	X
1.14	Know how the laminar airflow workbench and secondary ventilation system (heating, ventilation and air conditioning system) operate. Know, apply or enforce appropriate corrective measures when an irregularity is identified.	X	X	X
1.15	Know and apply quality assurance measures for the various compounded sterile preparations.	X	X	X
1.16	Know and follow the pharmacist's verification process.	X	X	X
1.17	Know and use the incident and accident documentation logs.	X	X	X
1.18	Know drug delivery systems.	X	X	X
1.19	Know and establish levels of risk and beyond-use dates.	X		
1.20	Know and, if applicable, perform additional sterility testing.	X	X	X
<b>2.</b>	<b>FOR THE COMPOUNDING OF HAZARDOUS STERILE PREPARATIONS</b>	<b>PH</b>	<b>PT</b>	<b>TSP</b>
2.1	Have the competency required to compound sterile preparations.	X	X	X
2.2	Identify hazardous drugs in the composition of sterile preparations.	X	X	X
2.3	Know and apply deactivation measures.	X	X	X
2.4	Know and use the protection measures necessary to avoid exposure to hazardous substances.	X	X	X
2.5	Know and use personal protective equipment specifically for handling hazardous products.	X	X	X
2.6	Safely handle hazardous drugs (i.e., receive, unpack, store and deliver hazardous drugs).	X	X	X

2.7	Know and apply the appropriate aseptic technique for hazardous drugs in the workplace.	X	X	X
2.8	Know and use the emergency measures to be applied in the case of accidental exposure, accidents or spills.	X	X	X
2.9	Know how to safely destroy hazardous drugs and the materials used in their preparation.	X	X	X
3.	<b>FOR THE COMPOUNDING OF HIGH-RISK NON-HAZARDOUS AND HAZARDOUS STERILE PREPARATIONS (MADE WITH NON-STERILE PRODUCTS)</b>			
3.1	Have the competency required to compound sterile preparations.	X	X	X
3.2	Know and correctly perform the filter integrity verification.	X	X	X
3.3	Know and correctly perform sterilization by filtration.	X	X	X
3.4	Know and correctly perform the analytical method to test for pyrogens.	X		

#### B. Training of cleaning and disinfecting personnel

#	COMPETENCIES, KNOWLEDGE OR SKILLS COVERED IN TRAINING	PH/PT	TSP	C & D
1.	<b>FOR CLEANING AND DISINFECTING THE GENERAL AREA FOR COMPOUNDING OF NON-HAZARDOUS STERILE PREPARATIONS</b>			
1.1	Know all policies and procedures related to cleaning and disinfecting the equipment, furniture and facilities, notably those related to hygiene and asepsis, personal protective equipment, and cleaning and disinfecting tasks.	X	X	X
1.2	Know and don the correct garb.	X	X	X
1.3	Know and correctly apply hand hygiene.	X	X	X
1.4	Know, correctly perform and document cleaning and disinfecting tasks for the general area for compounding of sterile preparations.	X	X	X
2.	<b>FOR CLEANING AND DISINFECTING THE AREA USED FOR COMPOUNDING HAZARDOUS STERILE PREPARATIONS</b>			

2.1	Know, correctly perform and document cleaning and disinfecting tasks for the general area for compounding of hazardous sterile preparations.	X	X	X
2.2	Know and use personal protective equipment specifically for handling hazardous products.	X	X	X
2.3	Know and use the emergency measures to be applied in case of accidental exposure, accidents or spills.	X	X	X
PH = pharmacist; PT = pharmacy technician; TSP = technical support personnel; C&D = cleaning and disinfecting personnel.				

**APPENDIX 4 PROCEDURE TEMPLATE**

Pharmacy name  Or  Hospital XYZ pharmacy department	<b>Procedure #</b> _____  <b>Revised:</b> <b>Yes</b> <input type="checkbox"/> <b>No</b> <input type="checkbox"/>  <b>Approved by</b> _____ <b>Date</b> _____  <b>Effective date:</b> _____
<b>Procedure title:</b>   	
<b>Aim and objective:</b>  ➤ Describe the objective of the procedure.	
<b>Target personnel:</b> Use this section to describe the expected responsibilities for each group that will be affected by this procedure.  <input type="checkbox"/> Head pharmacist <input type="checkbox"/> Compounding personnel <input type="checkbox"/> Pharmacy technician <input type="checkbox"/> Technical support personnel <input type="checkbox"/> Cleaning and disinfecting personnel <input type="checkbox"/> Other: .....	
<b>Required facilities, equipment and material:</b> 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 decision, other related procedures.

**List of logs and assessment of competencies required for this procedure:**

- 1.
- 2.

**References**

Indicate here the references used to draft the procedure, with relevant publication dates and edition numbers, to facilitate successive updates.

**Procedure history:**                      **Procedure #** \_\_\_\_\_

**Drafted by:** \_\_\_\_\_, pharmacist                      **Date:** \_\_\_\_\_ (dd/mm/yyyy)

**Revised by:** \_\_\_\_\_, pharmacist                      **Date:** \_\_\_\_\_ (dd/mm/yyyy)

**Revision:**    Full     Partial                       **Amended version:**    Yes     No

**Change made:**

**Revised by:** \_\_\_\_\_, pharmacist                      **Date:** \_\_\_\_\_ (dd/mm/yyyy)

**Revision:**    Full     Partial                       **Amended version:**    Yes     No

**Change made:**



**APPENDIX 5 BEST PRACTICE INDICATORS FOR CERTIFICATION OF CONTROLLED ROOMS, LAMINAR AIRFLOW WORKBENCHES AND BIOLOGICAL SAFETY CABINETS**

**Note:** The following appendix lists the responsibilities of the certifier, a person engaged to certify sterile-product compounding rooms, laminar airflow workbenches (LAFWs) and biological safety cabinets (BSCs). This information is provided for the benefit of sterile compounding supervisor pharmacists, to allow them to assess the services provided during the certification of areas and equipment in their respective pharmacies.

<b>I. Before certification</b>	
<ul style="list-style-type: none"> <li>▪ Ideally meets the client (sterile compounding supervisor) to discuss the certification process; during the meeting, the certifier             <ul style="list-style-type: none"> <li>➤ asks whether problems have occurred since the last certification;</li> <li>➤ asks whether there are any concerns about the operation of rooms or devices (LAFW, BSC, CAI, CACI).</li> </ul> </li> <li>▪ Knows the PPE required to enter a controlled room and the garbing sequence.</li> <li>▪ Knows the required procedure for washing and disinfecting hands before putting on gloves and entering a controlled room.</li> </ul>	
<b>II. General precertification requirements</b>	
<ul style="list-style-type: none"> <li>▪ Cleans and disinfects all equipment brought into the controlled rooms;</li> <li>▪ Performs certification of the controlled rooms, LAFWs or BSCs following the steps and methods recommended by the applicable standards;</li> <li>▪ Uses the applicable standards for certification (see Appendix 6);</li> <li>▪ Uses the devices required by the standards (see Appendix 6);</li> <li>▪ Uses calibrated devices that are in good condition;</li> <li>▪ Knows the standards to be used for certification and knows how to apply them;</li> <li>▪ Wears the appropriate PPE to enter and work in the compounding rooms for hazardous and non-hazardous sterile products;</li> <li>▪ Is familiar with the products used, especially if they are hazardous;</li> <li>▪ Does not touch hazardous products; if touching a hazardous product is required, asks qualified personnel to do so;</li> <li>▪ If applicable, sets up a protective wall (plastic or other) before opening the device, to limit contamination of the controlled room by hazardous drugs;</li> <li>▪ Performs the work meticulously and professionally.</li> </ul>	

<b>III. Certification steps</b>	
<b>1. Certification of controlled areas</b>	
<ul style="list-style-type: none"> <li>▪ Begins the certification of a clean room by measuring non-viable particles according to ISO 14644-1 specifications;</li> <li>▪ Uses the criteria of standard IEST-RP-CC-006.3 for the certification of the clean room;</li> <li>▪ Measures the volume of air supply or the velocity for each HEPA filter in the room;</li> <li>▪ Measures the air velocity profile for each terminal or line HEPA filter (as applicable) in the controlled room, if the air volume for the HEPA filter cannot be measured;</li> <li>▪ Calculates the air volume for the HEPA filter, if the velocity profile was measured;</li> <li>▪ Verifies the integrity of the HEPA filter with a photometer;</li> <li>▪ Verifies temperature;</li> <li>▪ Verifies humidity;</li> <li>▪ Verifies sound (noise) level;*</li> <li>▪ Verifies light level;*</li> <li>▪ Verifies the behaviour of the room and its equipment using smoke tests;</li> <li>▪ Ensures that the doors to each room are fully closed when measuring pressure differentials between rooms;</li> <li>▪ Obtains the dimensions of the room and its total volume of air supply, to allow calculation of number of air changes per hour.</li> </ul> <p>* <b>Note:</b> The frequency of certain verifications, such as sound and light levels, may vary depending on needs and agreements.</p>	
<b>2. Certification of BSC</b>	
<ul style="list-style-type: none"> <li>▪ Certifies the BSC according to NSF Standard 49-2012 (Appendix F – Field Tests) and the manufacturer's specifications, which can be found on the BSC information plate or in the report included with the BSC at the time of purchase (when there is no information plate);</li> <li>▪ Takes readings to measure the velocity of the air supply of a BSC according to NSF Standard 49-2012 or the manufacturer's specifications;</li> <li>▪ In accordance with ISO 14644-1, <ul style="list-style-type: none"> <li>➤ Proceeds with the count of non-viable particles;</li> <li>➤ Verifies the count of non-viable particles 0.5 µm in diameter;</li> <li>➤ Verifies the count of non-viable particles in at-rest (optional) and in-operation (dynamic) states, measured at five reading points, with a minimum of two 1-minute and 1 m<sup>3</sup> samples per reading point (the acceptable limit is 3520 particles).</li> </ul> </li> </ul>	

<p><b>3. Certification of LAFW</b></p>	
<ul style="list-style-type: none"> <li>▪ Certifies the LAFW in accordance with IEST-RP-CC-002.3;</li> <li>▪ Measures the velocity of the LAFW's air supply by taking a minimum of eight readings in the centre of every 12 square inches, at a distance 12 inches from the surface of the HEPA filter or protective screen;</li> <li>▪ In accordance with ISO 14644-1, <ul style="list-style-type: none"> <li>➤ Proceeds with the count of non-viable particles;</li> <li>➤ Verifies the count of non-viable particles 0.5 µm in diameter;</li> <li>➤ Verifies the count of non-viable particles in at-rest (optional) and in-operation (dynamic) states, measured at five reading points, with a minimum of two 1-minute and 1 m<sup>3</sup> samples per reading point (the acceptable limit is 3520 particles);</li> </ul> </li> <li>▪ Recommends that LAFW pre-filters be changed, if required.</li> </ul>	
<p><b>4. Certification of CAI and CACI</b></p>	
<ul style="list-style-type: none"> <li>▪ Certifies devices according to the manufacturer's recommendations, referring to CETA CAG-002-2006 (Compounding Isolator Testing Guide);</li> <li>▪ Certifies, using the following tests, at minimum (other tests are indicated in CETA CAG-002-006): <ul style="list-style-type: none"> <li>➤ Airflow test</li> <li>➤ Verification of internal pressure</li> <li>➤ Verification of installation site</li> <li>➤ Verification of HEPA filter</li> <li>➤ Containment integrity and enclosure leak test</li> <li>➤ Recovery time test</li> <li>➤ Smoke test</li> <li>➤ Test of preparation entry and output</li> <li>➤ Count of non-viable particles</li> </ul> </li> </ul>	
<p><b>IV. After certification</b></p>	
<ul style="list-style-type: none"> <li>▪ Answers questions and requests from the sterile compounding supervisor related to the certification and its procedure;</li> <li>▪ Does the required quick cleaning of rooms and devices;</li> <li>▪ Groups all waste contaminated by hazardous products and disposes of it as hazardous waste in the appropriate containers;</li> <li>▪ Verifies that all certification labels are correctly printed and affixed;</li> <li>▪ Provides the sterile compounding supervisor with a preliminary report (recommended but not mandatory) in writing or, at a minimum, verbally;</li> <li>▪ Submits a final certification report that includes all information required by pharmacy regulatory authorities to confirm certification;</li> <li>▪ Submits recent calibration certificates for the devices used in the certification, attached to the final certification report.</li> </ul>	

CAI = compounding aseptic isolator; CACI = compounding aseptic containment isolator; CETA = Controlled Environment Testing Association; HEPA = high-efficiency particulate air; NSF = NSF International (public health and safety organization); PPE = personal protective equipment.

**APPENDIX 6 CERTIFICATION OF CONTROLLED ROOMS, LAMINAR AIRFLOW WORKBENCHES AND BIOLOGICAL SAFETY CABINETS**

TARGET	CERTIFICATION STANDARDS	CERTIFICATIONS
<p><b>Laminar airflow workbench</b>  (vertical or horizontal laminar flow hoods)</p>	<ul style="list-style-type: none"> <li>• IEST-RP-CC-002.3: Unidirectional-Flow, Clean-Air Devices</li> <li>• ISO 14644-1</li> </ul>	<p><u>LAFW certification includes steps carried out:</u></p> <ol style="list-style-type: none"> <li>1. <u>In accordance with IEST-RP-CC-002.3:</u> <ul style="list-style-type: none"> <li>• Measurement of air supply profile</li> <li>• HEPA filter integrity test</li> </ul> </li> <li>2. <u>In accordance with ISO 14644-1:</u> <ul style="list-style-type: none"> <li>• Count of non-viable particles (0.5 µm diameter) in operational (dynamic) state; at-rest state is optional</li> <li>• Measurement of air intake velocity</li> <li>• Smoke test</li> </ul> </li> </ol> <p><u>Equipment used:</u></p> <ul style="list-style-type: none"> <li>• Particle counter</li> <li>• Thermal anemometer</li> <li>• Smoke machine</li> <li>• Photometer</li> </ul>

<p><b>Biological safety cabinet, Class II, type B2</b></p> <p><b>(For certification of other types of BSC, please refer to the standards.)</b></p>	<ul style="list-style-type: none"> <li>• NSF Standard 49-2012: Biological Safety Cabinetry: Design, Construction, Performance and Field Certification</li> <li>• ISO 14644-1</li> </ul>	<p><u>Class II, type B2 BSC certification includes steps carried out:</u></p> <ol style="list-style-type: none"> <li>1. <u>In accordance with NSF Standard 49-2012:</u> <ul style="list-style-type: none"> <li>• Measurement of air supply profile</li> <li>• Measurement of air intake velocity</li> <li>• Smoke test</li> <li>• HEPA filter integrity test</li> <li>• Verification that interlock system (between discharge probe and air supply motor) is working properly (for Class II, type B2 BSC)</li> <li>• Verification of device calibration (less than 20% air loss in 15 seconds) (for Class II, Type B2 BSC)</li> </ul> </li> <li>2. <u>In accordance with ISO 14644-1:</u> <ul style="list-style-type: none"> <li>• Count of non-viable particles (0.5 µm) in operational (dynamic) state; at-rest state is optional</li> <li>• Measurement of air intake velocity</li> </ul> </li> </ol> <p><u>Equipment used:</u></p> <ul style="list-style-type: none"> <li>• Particle counter</li> <li>• Thermal anemometer</li> <li>• Smoke machine and aerosol generator</li> <li>• Photometer</li> <li>• Direct volume measurement device</li> </ul>
<p><b>Compounding aseptic isolator</b></p>	<ul style="list-style-type: none"> <li>• Primarily manufacturer's recommendations</li> <li>• CETA CAG-002-2006: Compounding Isolator Testing Guide</li> </ul>	<p><u>Isolator certification includes steps carried out according to manufacturer's recommendations, with reference to CETA/CAG-002-2006.</u></p> <p><u>Specific tests used:</u></p> <ul style="list-style-type: none"> <li>• Airflow test</li> <li>• Verification of internal pressure</li> <li>• Verification of installation site</li> <li>• Verification of HEPA filter</li> <li>• Containment integrity and enclosure leak test</li> <li>• Recovery time test</li> <li>• Smoke test</li> <li>• Test of preparation entry and output</li> </ul>

<b>Compounding aseptic containment isolator</b>	<ul style="list-style-type: none"> <li>• Primarily manufacturer's recommendations</li> <li>• CETA CAG-002-2006: Compounding Isolator Testing Guide</li> </ul>	<ul style="list-style-type: none"> <li>• Count of non-viable particles</li> </ul> <u>Equipment used:</u> <ul style="list-style-type: none"> <li>• Thermal anemometer</li> <li>• Pressure measurement device (in inches of water or pascals)</li> <li>• Tools for adjusting alarms</li> <li>• Smoke machine</li> <li>• Photometer</li> <li>• Particle counter (small)</li> <li>• Aerosol generator</li> <li>• Chronometer</li> </ul>
---	---	---

<p><b>Clean room for the compounding of sterile products and controlled areas</b></p>	<ul style="list-style-type: none"> <li>• NEBB Procedural Standards for Certified Testing of Clean rooms</li> <li>• IEST-RP-CC-006.3: Testing Clean Rooms</li> <li>• CETA CAG-003: Certification Guide for Sterile Compounding Facilities</li> <li>• ISO 14644-1 (section on number of particles, particle counters, and sampling plan and methods).</li> </ul>	<p><u>Certification of controlled areas and rooms includes the following steps:</u></p> <ul style="list-style-type: none"> <li>• Count of non-viable particles in operational (dynamic) state (ISO 14644-1)</li> <li>• Certification of HEPA filter (IEST-RP-CC-006.3)</li> <li>• Verification of terminal or line HEPA filter</li> <li>• Measurement of pressure differential between controlled rooms</li> <li>• Verification of air changes per hour (by measuring volumes of air or room velocity)</li> <li>• Verification of behaviour of rooms and equipment using smoke tests</li> <li>• Temperature verification</li> <li>• Relative humidity verification</li> <li>• Measurement of luminosity</li> <li>• Measurement of noise level (sound)</li> </ul> <p><u>Equipment used:</u></p> <ul style="list-style-type: none"> <li>• Particle counter</li> <li>• Tripod for the room</li> <li>• Tripod for the LAFW or BSC</li> <li>• 0.3-µm filter (for cleaning)</li> <li>• "Tent" to capture air volume</li> <li>• Thermal anemometer</li> <li>• Smoke machine</li> <li>• Photometer</li> <li>• Pressure measurement device (in inches of water or pascals)</li> <li>• Thermometer</li> <li>• Hygrometer</li> <li>• Light meter</li> <li>• Sound level meter</li> </ul>
---	--	---

ANSI = American National Standard Institute; CETA = Controlled Environment Testing Association; IEST = Institute of Environmental Sciences and Technology; NEBB = National Environmental Balancing Bureau

**Note:** Some certifying technicians have credentials from certain US agencies (e.g., NSF International, NEBB, CETA). These credentials, obtained from the agencies in question after appropriate training, indicate that the holder has sound knowledge of the standard and how it must be applied and verified.

Information on certifiers can be found on the following websites: <http://www.nsf.org> (select the following options: regulatory resources / NSF certification / search certified products and systems / Class II Biosafety Cabinet Field Certifiers / search by country) and <http://www.nebb.org> (Certified firms/Directory of firms/NEBB certified firm/Search by country/Canada).

**APPENDIX 7 TEMPLATE FOR THE DRAFTING OF COMPOUNDING PROTOCOLS TO BE COMPLETED FOR EACH DRUG**

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



---

---

**Additional information about the ingredients:**

Include any additional pertinent information about the ingredients required for compounding.

Indicate any specific precautions to be taken when handling the ingredients.

---

---

**Notes on calculations and measurements:**

Indicate any characteristics of the calculations, measurements or ingredient preparation that must be done before the specific procedure is carried out.

Indicate any requirement for verification by the pharmacist.

Examples:

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

**Required devices, instruments and materials**

Indicate all materials and equipment that will be required to compound the sterile products.

---

---

**Compounding method**

Describe all steps of the sterile-product compounding process.

---

---

**Quality controls**

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

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

Specify all quality controls are to be carried out by the pharmacist on the final compounded sterile preparation. Indicate the expected specifications.

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

**Packaging**

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

**Stability and storage**

Specify the preservation requirements of the compounded sterile preparation.

Specify the shelf life of the compounded sterile preparation (beyond-use date).

Indicate the references used to determine shelf life.

<p><b>Labelling</b></p> <p>Indicate mandatory information that must be on the label of the compounded sterile preparation.</p> <hr/> <p>A) When kept at the pharmacy or sent to another pharmacy</p> <hr/> <p>B) When dispensed to a patient</p>	<p><b>Sample label</b></p> <hr/> <p><b>Name of preparation:</b></p> <p><b>Date when preparation was made:</b></p> <p><b>Lot:</b></p> <p><b>Quantity prepared:</b></p> <p><b>Beyond-use date:</b></p> <p><b>Shelf life:</b></p> <p><b>Verified by:</b></p> <hr/> <p><b>Customer label</b></p> <p>In addition to the legally mandated information, add:</p> <ul style="list-style-type: none"> <li>- lot number of compounded sterile preparation</li> <li>- beyond-use date</li> <li>- precautions and pharmacovigilance</li> </ul>
<p><b>Training</b></p> <p>Indicate the training that personnel must undergo before the specific sterile compounding procedure is implemented.</p>	

<b>References consulted:</b>	
Indicate the source of the specific sterile compounding procedure. Indicate any documentation supporting the stability of the final compounded sterile preparation.	
<b>Preparation data sheet history No.:</b>	
<b>Date drafted:</b> (dd/mm/yyyy)	<b>Drafted by:</b>
<b>Revised:</b> (dd/mm/yyyy)	<b>Revised by:</b>
<b>Change made:</b>	<b>Version number changed:</b> <input type="checkbox"/> YES <input type="checkbox"/> NO
<b>Revised:</b> (dd/mm/yyyy)	<b>Revised by:</b>
<b>Change made:</b>	<b>Version number changed:</b> <input type="checkbox"/> YES <input type="checkbox"/> NO

## APPENDIX 8 EXAMPLES OF STERILE PREPARATIONS THAT MUST BE VERIFIED AT EACH STAGE OF COMPOUNDING

Packaging or system used	Examples
Contents of vial or ampoule to be injected into a bag, minibag, Intermate or other container, when the entire contents of the vial (powder) will not be used or when a liquid product is packaged in a vial or ampoule	<p>1 g cefazolin IV every 8 hours</p> <p>Dose prepared using a 10-g vial of powder diluted in 50 mL of 0.9% NaCl. The diluent and product taken from the vial must be checked for each dose before injection into the bags.</p>
Ophthalmic drops	<p>50 mg/mL vancomycin ophthalmic solution prepared from a 500-mg vial. The vehicle used and product taken from the vial must be checked before insertion into the dispenser bottle.</p>
Diluted cassette	<p>50 mg/mL Morphine-HP® in a 10-mL vial diluted to a final concentration of 10 mg/mL for subcutaneous infusion. The volume of morphine and the volume of diluent must be checked before they are put into the cassette.</p>
Preparation made using a volumetric pump (e.g., Baxa-Repeater®, PharmAssist)	<p>Verification of the pump setting each time the volume is changed, and more frequently if necessary (e.g., if a large number of units is prepared).</p>

**APPENDIX 9 EXAMPLES OF STERILE PREPARATIONS THAT DO NOT REQUIRE VERIFICATION DURING THE COMPOUNDING PROCESS**

Packaging or system used	Examples
Syringe filled with a single product	Syringe of 300 µg filgrastim for subcutaneous administration three times per week, prepared from a 300 µg/mL vial of filgrastim
ADD-Vantage™ or Mini-Bag Plus type system	500 mg Primaxin® IV every 6 hours, prepared using the ADD-Vantage™ system ( <a href="http://www.hospira.com/Products/addvantagesystem.aspx">http://www.hospira.com/Products/addvantagesystem.aspx</a> ) or vial compatible with a Mini-Bag Plus
Contents of vial (powder) to be injected into a bag, minibag, Intermate or other container, when the entire contents of the vial will be used	1 g cefazolin IV every 8 hours Dose prepared using a 1-g vial of powder diluted in 50 mL of 0.9% NaCl
Morphine or hydromorphone cassette, when starting with the product at the same concentration (at this point, it is the concentration per millilitre that is important, so the number of empty vials must be counted)	Cassette of morphine at a concentration of 5 mg/mL for subcutaneous administration, prepared from 30-mL vials of 5 mg/mL morphine (undiluted)

## APPENDIX 10 TEMPERATURES FOR DIFFERENT TYPES OF STORAGE

	Temperature range
Freezing	-25°C to -10°C*
Refrigeration (cold)	2°C to 8°C*
Temperature (cool)	8°C to 15°C*
Controlled room temperature	15°C to 20°C†
Drug conservation temperature	15°C to 30°C

\*United States Pharmacopeial Convention (USP). General notices and requirements. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008. p. 29.

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

## APPENDIX 11 INCIDENT/ACCIDENT REPORTING AND FOLLOW-UP FORM

Note: This form is intended for pharmacists who do not use a health care facility's suggested form.

Incident/accident* reporting and follow-up	
Reporting an incident <input type="checkbox"/> accident <input type="checkbox"/>	
<b>General information</b>	
Date and time of incident/accident:	Reported by:
Name of patient affected, if applicable:	Full address:  Phone number:
Pharmacy personnel involved:	
<b>Information about incident/accident</b>	
(Summary of the situation and consequences)	
Disclosed to the patient concerned: <input type="checkbox"/>	
Name of pharmacist responsible for follow-up:	
<b>Analysis of causes</b>	

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)	
<b>Action plan</b>			
<b>Actions</b> (Describe the actions to be taken and the	<b>Responsible</b>	<b>Deadline</b>	✓



steps required to correct the situation, with a specific timeline. Determine who will be responsible for implementation.)			
<b>Monitoring</b>			
Verifications (Verifications to ensure that the corrections and changes are effective and fully implemented.)	Responsible		✓
<b>Closing of the file</b>			
Pharmacist responsible for follow-up: (signature)		Date file closed:	

\*An accident is an action or situation in which the risk event occurs and has or could have an impact on the health status or well-being of the user (patient), personnel, professional concerned or third party. An incident is an action or situation that has no impact on the health status or well-being of the user (patient), personnel, professional concerned or third party, but which has an unusual result that could, on other occasions, lead to consequences.

**APPENDIX 12 COMPONENTS OF A QUALITY ASSURANCE PROGRAM**

COMPONENT	CONTROLS	FREQUENCY
<b>FACILITIES</b>	Certification of clean rooms and anteroom	<ul style="list-style-type: none"> <li>• Every 6 months</li> <li>• When the controlled area is installed</li> <li>• When new equipment is installed</li> <li>• When rooms or equipment are maintained or repaired</li> <li>• When a contamination problem is identified</li> <li>• When investigation of a contamination problem or non-compliance in the aseptic preparation process requires exclusion of malfunctioning facilities</li> </ul>
	Sampling of controlled areas under operational (dynamic) conditions: <ul style="list-style-type: none"> <li>- Viable and non-viable particles, air and surfaces</li> <li>- According to a sampling plan</li> </ul>	<ul style="list-style-type: none"> <li>• Every 6 months (more frequently at the start of the quality assurance program)</li> <li>• When the controlled area is installed</li> <li>• When new equipment is installed</li> <li>• When the controlled area or equipment is repaired or maintained (e.g., high-efficiency particulate-air filter changed)</li> <li>• When a contamination problem is identified</li> <li>• When investigation of a contamination problem or non-compliance in the aseptic preparation process requires exclusion of malfunctioning facilities</li> <li>• According to an internal verification program</li> </ul>

	Verification of temperature and humidity in controlled areas	<ul style="list-style-type: none"> <li>Once a day</li> </ul>
	Pressure differential between controlled areas	<ul style="list-style-type: none"> <li>Continuous reading and notification system to prevent non-compliance</li> <li>Periodic verification (once a week) by the sterile compounding supervisor</li> <li>Notification system (if reading is not continuous, assign personnel to verify and record the differential twice a day)</li> </ul>
<b>EQUIPMENT</b>	Certification of LAFWs and equipment	<ul style="list-style-type: none"> <li>Before first use</li> <li>Every 6 months</li> <li>When new equipment is installed</li> <li>When equipment is repaired or maintained</li> <li>When a contamination problem is identified</li> <li>When investigation of a contamination problem or non-compliance in the aseptic preparation process requires exclusion of malfunctioning facilities</li> </ul>
	Temperature verification (e.g., refrigerator, freezer, incubator)	<ul style="list-style-type: none"> <li>Once a day (if unit has a built-in reading device)</li> <li>Twice a day (if unit has no built-in reading device)</li> </ul>
	Operational indicators of LAFWs and other devices used (e.g., automated compounding device)	<ul style="list-style-type: none"> <li>Verified daily before use</li> <li>Verified continuously by personnel</li> </ul>
	Sampling of LAFWs under operational (dynamic) conditions: <ul style="list-style-type: none"> <li>Viable and non-viable particles, air and surfaces</li> <li>According to a sampling plan</li> </ul>	<ul style="list-style-type: none"> <li>Every 6 months (more frequently at the start of the quality assurance program)</li> <li>When a new LAFW is installed</li> <li>When the LAFW is maintained or repaired</li> <li>When a contamination problem is identified</li> <li>When investigation of a contamination problem or non-compliance in the aseptic preparation process requires exclusion of malfunctioning facilities</li> <li>According to an internal verification program</li> </ul>

<b>PERSONNEL</b>	Competency assessment	<ul style="list-style-type: none"> <li>• At initial qualification: theoretical and practical aspects</li> <li>• At periodic qualifications: theoretical and practical aspects</li> <li>• When assessing incidents and accidents</li> <li>• When a contamination problem is identified</li> </ul>
	Gloved fingertip sampling	<ul style="list-style-type: none"> <li>• At initial qualification: theoretical and practical aspects</li> <li>• At periodic qualifications: theoretical and practical aspects</li> <li>• When assessing incidents and accidents</li> <li>• When a contamination problem is identified</li> </ul>
	Media fill tests	<ul style="list-style-type: none"> <li>• At initial qualification: theoretical and practical aspects</li> <li>• At periodic qualifications: theoretical and practical aspects</li> <li>• When assessing incidents and accidents</li> <li>• When a contamination problem is identified</li> </ul>
<b>FINAL COMPOUNDED STERILE PREPARATION</b>	Verification of compounding protocols (usage and maintenance)	<ul style="list-style-type: none"> <li>• In accordance with the quality assurance program</li> </ul>
	Verification that preparation matches prescription	<ul style="list-style-type: none"> <li>• In accordance with the quality assurance program</li> </ul>
	Verification of label compliance	<ul style="list-style-type: none"> <li>• In accordance with the quality assurance program</li> </ul>
	Entry in logs	<ul style="list-style-type: none"> <li>• In accordance with the quality assurance program</li> </ul>
LAFW = laminar airflow workbench.		

## 12. BIBLIOGRAPHY

*Note to readers:* The references cited in these Model Standards reflect the references appearing in the source document, “Préparation de produits stériles non dangereux en pharmacie – Norme 2014.01,” published by the Ordre des pharmaciens du Québec, 2014. Where possible, certain details have been verified against the source documents. URLs for online documents are current as of July 2014.

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

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>

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

Bussièrès JF, Prot S. Perspectives sur les préparations magistrales en pharmacie au Québec. *Pharmactuel*. 2004;37(3):File 1.

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

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

Canadian Nurses Association (CNA). *Joint position statement: Promoting continuing competence for registered nurses*. Ottawa, ON: CNA; 2004. Available from: [http://www.cna-aiic.ca/~media/cna/page-content/pdf-en/ps77\\_promoting\\_competence\\_e.pdf](http://www.cna-aiic.ca/~media/cna/page-content/pdf-en/ps77_promoting_competence_e.pdf)

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

Centers for Disease Control and Prevention. Guideline for hand hygiene in health-care settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. *MMWR Morb Mortal Wkly Rep*. 2002;51(RR-16):1-48.

Commission de la santé et de la sécurité du travail (CSST). *Material safety data sheet user's guide*. CSST; 2010. Available from: <http://www.reptox.csst.qc.ca/Documents/SIMDUT/GuideAng/Htm/GuideAng.htm>

Controlled Environment Testing Association (CETA). *CETA compounding isolator testing guide: CAG-002-2006*. Raleigh, NC: CETA; 2006, revised 2008 Dec 8. Available from: <http://www.cetainternational.org/reference/CETACompoundingIsolatorTestingGuide2006.pdf>

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

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

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

*Drug and Pharmacies Regulation Act*, R.S.O. 1990, c. H.4. Available from: [http://www.e-laws.gov.on.ca/html/statutes/english/elaws\\_statutes\\_90h04\\_e.htm](http://www.e-laws.gov.on.ca/html/statutes/english/elaws_statutes_90h04_e.htm)

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

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

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](http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/docs/pol_0051-eng.php)

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

Kastango ES. The cost of quality in pharmacy. *Int J Pharm Compound*. 2002;6(6):404.7.

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

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

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](http://napra.ca/Content_Files/Files/Model_Standards_of_Prac_for_Cdn_Pharm_March09_Final_b.pdf)

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>

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>

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](https://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html)

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

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

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

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

Public Health Agency of Canada (PHAC). *National vaccine storage and handling guidelines for immunization providers*. Ottawa, ON: PHAC; 2007. 114 pp. Available from: <http://www.phac-aspc.gc.ca/publicat/2007/nvshglp-ldemv/pdf/nvshglp-ldemv-eng.pdf>

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

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

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

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

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

United States Pharmacopeial Convention (USP). General notices and requirements. In: *USP pharmacists' pharmacopeia*. Rockville, MD: USP; 2008-2009.

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

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

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

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

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