

Prince Edward Island Pharmacy Board
Sterile Compounding Guidelines

Approved by PEIPB
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Introduction

Health care is increasingly moving into the home setting, creating new challenges for pharmacists. The emergence of home care, the trend to earlier hospital discharges, and the existence of new technologies such as PCA (patient-controlled analgesia) pumps has greatly increased the demand for sterile compounding in the community setting. Pharmacists must, therefore, not only be aware of this increased demand, but also prepare themselves accordingly. Pharmacists may be asked to fill prescriptions for intravenous solutions, and prepare such products as ophthalmic and bladder preparations which require sterile compounding.

Sterile compounding refers to the preparation, mixing, assembling, packaging or labeling of a product using aseptic technique – procedures that will minimize, or prevent, the introduction of microorganisms to the prepared product. These products may be administered intravenously, intramuscularly, applied topically to skin, mucous membranes, eyes, or via other routes.

Pharmacists are health practitioners educated and skilled in the science of compounding medications. Furthermore, pharmacists can compound sterile products if they have the skills and facilities necessary to ensure that certain products are prepared in a non-contaminated environment, free of particulate matter. Sterile compounding practices vary between community pharmacies, indicating that there are no clear guidelines for pharmacists to follow. Studies also show a wide variance between hospitals in their sterile compounding practices. The improper compounding of sterile products can lead to serious consequences for patients in community and hospital settings. Pharmacists have a responsibility to provide sterile compounding services to their patients in a manner consistent with expected standards of practice, which are being developed by provincial regulatory bodies to ensure patient safety. Pharmacists should be cognizant of the importance of technique, staff education, appropriate facilities (including a laminar air flow hood), and proper monitoring to maintain the safety of products for patient care.

It is important that the patient record be complete. All therapy needs to be documented in one profile. Pharmacies contracting sterile compounding service must ensure their patient profile is complete. Pharmacies compounding on contract or providing compounds directly to a patient need to ensure the patients regular pharmacy is provided current patient information.

Background

The compounding of sterile products falls under Section C.01.065 of the federal *Food and Drug Regulations*. Although this section applies to commercial manufacturers of sterile products only, the Health Protection Branch does expect appropriate procedures regarding technique, facilities, and equipment for sterile compounding to be followed by hospital and community pharmacists. The Canadian Society of Hospital Pharmacists (CSHP) *Guidelines for Preparation of Sterile Products in Pharmacies*¹ (1996) also is a useful tool in the establishment of sterile compounding facilities and procedures.

¹ Reference sources are listed in Appendix E

Risk levels in sterile compounding

The following table summarizes the level of risk associated with compounding sterile products:

Risk Level	Risks
Low Risk	<ul style="list-style-type: none">- product is compounded with commercially available components- compounding involves few aseptic manipulations- closed system transfers are used
High Risk, Category 1	<ul style="list-style-type: none">- prepared from commercially prepared compounds- closed system pooling of sterile drug products- complex, numerous manipulations over a long period of time- multi-day infusion via a portable pump or reservoir
High Risk, Category 2	<ul style="list-style-type: none">- product prepared from non-sterile drug substance- open system transfers are used

For a comparison of risk levels as defined by USP Section 1206 and ASHP Technical Assistance Bulletin Categories, along with examples, see Appendix A

Requirements:

Pharmacists who are contemplating sterile compounding should:

1. Study, understand (and have on the premises) the key resources on this topic.

References considered to be essential starting points include:

- CSHP: Guidelines for the Preparation of Sterile Products in Pharmacies,
- CSHP/CPhA: Sterile Products Preparation Video and Manual.
- American Society of Health System Pharmacists: Technical Bulletin on Quality Assurance for Pharmacy Prepared Sterile Products.
- The USP, Trissel's and Remington's are also helpful reference tools.

Sources for these publications are listed in Appendix E.

2. Understand the terminology involved in sterile compounding, eg Sterile, aseptic; Aseptic technique; Class 100 environment; quality control

3. Establish an area dedicated to the preparation of sterile products.

The area should have limited access and should be well lit with nonporous washable floors and sterile work surface. A minimum area of 60 ft² is recommended and should be of a size to accommodate the volume of workload being performed. This area shall not be publicly accessible, and traffic within shall be minimized to prevent air turbulence.

A sterile compounding service in a community pharmacy can be established and operated within a reasonably small area if it is well planned and organized. The aseptic preparation area may be a separate room, or located in a low or controlled traffic area with limited access. Ideally, the area should be adjacent to the dispensary, clean and free from excess clutter and debris. The CSHP's standards for an aseptic preparation area should be followed.

A laminar airflow hood is essential for the preparation of sterile products and should be located in the aseptic preparation area. Storage shelves, refrigerators, sinks, etc., should be located in a separate adjacent area to help reduce possible contamination. Inventory in the aseptic area should be kept at minimal levels and no exterior packaging of pharmaceuticals should be present. Materials such as needles, syringes and alcohol swabs can be kept in the preparation area but only at minimal levels. Activities such as gowning/gloving (if needed), hand washing and disinfecting should be done in a separate support area with clear, posted guidelines and procedures.

4. Invest in the necessary equipment (and maintenance of this equipment) and materials for proper sterile compounding, including but not limited to:

- Class 100 laminar airflow hood or a Class II biological safety cabinet, if cytotoxic agents are prepared. These should be certified at least yearly. See Appendix B for a more detailed review of the functioning of laminar airflow devices.
- Sink with hot and cold running water for hand washing and cleanup
- A refrigerator and/or freezer (with thermometer)

- Compounding supplies - needles, syringes, filters, alcohol, chlorhexidine, etc.
- Appropriate disposal containers for syringes, needles, hazardous waste
- Proper garb (caps, gowns, facial covering, gloves)
- Antimicrobial soap/sanitizing solution
- Maintenance includes checking pre-filters every 2-4 months, replacing as necessary, and certification of the hoods every six to twelve months.

5. Ensure all personnel involved with preparing sterile products are properly trained and evaluated in all aspects of aseptic technique and product preparation.

See Appendix C and D for a brief overview of aseptic technique and procedures. The reference sources listed elsewhere provide much more detail about sterile compounding procedures.

Competency in sterile product preparation must be reassessed and documented on an appropriate basis (eg annually); unqualified persons must not prepare sterile products. The CSHP reference text has a useful section on re-certification.

6. Ensure up-to-date policies and procedures are written and available.

This may include policies and procedures such as:

- Specific compounding procedures
- Record keeping and Quality control
- Handling of hazardous waste
- Staff qualifications and duties
- Sterile procedures
- Sterility testing

7. References

There should be current, authoritative references available on admixture compatibility as well as other compounding references. Essential references include Trissel's "Handbook on Injectable Drugs" and King's "Guide to Parenteral Admixtures"

8. Ensure quality control by having random cultures preformed on preparations.

Random testing for contamination serves to ensure quality products, and can also be utilized to assess individual operator technique as well.

9. Understand and ensure the proper storage and handling of products used in the preparation of sterile compounds.

10. Ensure all compounded products are properly labeled, including expiry dates.

All products must bear expiry dates based on appropriate stability information.

11. Maintain proper documentation.

This includes such items as log sheets for compounded products, quality control documentation, inspection reports, logs for daily cleaning, admixture checks for sterility, etc.

12. Ensure patients receiving sterile compounds are properly counseled regarding the appropriate use and storage of these products.

Summary

Pharmacists possess the knowledge and skills to properly prepare sterile compounds. It is crucial that pharmacists understand the risks associated with the preparation of these products and with their limitations in this area. If a pharmacist does not have a good understanding of sterile compounding or if he/she does not possess the appropriate equipment, etc., it is better for the pharmacist to:

- Advise a patient to seek a pharmacy capable of preparing sterile products
- Contact the prescriber and suggest an alternate product
- Contact the local hospital pharmacy to evaluate options

These guidelines for sterile compounding may be adapted in individual pharmacies. Sterile compounding should not be attempted if products cannot be compounded properly, and it should be clear that not all pharmacies may be equipped to fill a prescription for a sterile product.

Pharmacists must review their resources to determine if sterile compounding is a service they wish to offer.

Provided that proper technique is used, policies and procedures followed, and facilities designed correctly, sterile compounding can be done with minimal risk of contamination in the community pharmacy, furthering the pharmacist's ability to meet the specific needs of certain patients.

This document provides guidelines and information for the pharmacist to assess the feasibility of establishing a sterile product compounding service. It is not meant to be all-inclusive, but serve as a starting point for development of a service.

Remember that the onus is ultimately on the pharmacist to ensure the proper preparation of sterile products.

Appendix A Comparison of Risk Categories

USP Section <1206>	ASHP Technical Assistance Bulletin
<p>Low Risk Category Sterile drug products transferred from vials or ampoules into sterile final containers with syringe and needle Sterile drug products transferred into sterile elastomeric infusion containers with aid of mechanical pump and appropriate sterile transfer device, with or without subsequent addition of sterile drug products with sterile syringe and needle Sterile nutritional solutions combining dextrose injection and amino acid injection via gravity transfer into sterile empty containers, with or without addition of sterile drugs to final container with sterile syringe and needle</p>	<p>Risk Level I Single patient admixtures Single patient ophthalmics with preservatives Single patient syringes without preservatives used in 28 hours Batch prefilled syringes with preservatives</p>
<p>High Risk Category I Sterile nutritional solutions compounded with automated compounder, involving repeated attachment of fluid containers to proximal openings of compounder tubing set and of empty final containers to distal opening Additive transfers into filled final container from individual drug products containers or from pooled additive solution Ambulatory pump reservoirs prepared by adding more than one drug product, with evacuation of air from reservoir prior to dispensing Ambulatory pump reservoirs prepared for multiday (ambient temperature) administration</p>	<p>Risk Level 2 TPNs for administration after 7 days Injections for use in portable pump or reservoir Batch reconstituted antibiotics without preservatives Batch prefilled syringes without preservatives</p>
<p>High Risk Category II Injectable morphine solutions prepared from nonsterile morphine substance and suitable vehicles Sterile nutritional solutions prepared from nonsterile ingredients, with initial mixing in non-sealed or nonsterile reservoir</p>	<p>Risk Level 3 Alum bladder irrigations Morphine injections made from powder or tablets eg for PCA TPN solutions made from dry amino acids Autoclaved IV solutions TPNs sterilized by final filtration</p>

Note: USP section 1206 has been revised and is now Section 797

Appendix B Laminar Air Flow Hood

All sterile compounding in a community pharmacy should be performed in a laminar air flow hood. These hoods are designed to reduce the risk of airborne contamination during the preparation of sterile products.

Laminar air flow hoods have two basic functions:

- . To filter bacteria and exogenous materials from the air.
- . To maintain constant air flow out of the hood to prevent contaminated room air from entering the hood.

The hood functions as a high efficiency dual filtering system. Air is taken into the unit and passes through a prefilter, removing gross contaminants such as dust or lint. The prefilter is very similar to those found in household furnaces. It is easily removed and can be cleaned by washing or vacuuming the particles. It should be checked periodically and replaced if needed. After passing through the prefilter, air is channelled through the high efficiency particulate air (HEPA) filter to remove fine bacterial contaminants. This filter is built into the hood and is responsible for the sterile environment in the hood. The HEPA filter is not easily removed and generally requires outside maintenance for cleaning. Air flow velocity determines the filtering capacity of the hood. If air flow is reduced, the filter is presumed to be clogged with contaminants and must be cleaned. Levels of air flow velocity are predetermined and exist for different types of hoods (see Table 1).

Table I

(adapted from *CSHP Guidelines for Preparation of Sterile Products in Pharmacies*, 1996)

Grade	US Federal Standard 209D	Air changes per hour	Maximum permitted # of particles per m ³ equal to or above:		Maximum permitted # of viable microorganisms per m ³
			0.5 microns	5 microns	
A laminar air flow station	100	Flow of 0.3 m/s (vertical) or 0.45 m/s (horizontal)	3,500	0	Less than 1
B	100	5-20	3,500	0	5
C	10,000	5-20	350,000	2,000	100
D	100,000	5-20	3,500,000	20,000	500

There are two types of laminar air flow hoods available for compounding non-toxic sterile products:

- . Horizontal Air Flow. The air flow is directed forward. Work is performed in the hood and the product is protected, however the operator is not protected from particles or fumes originating from the ampoules or vials.
- . Vertical Air Flow. The air flow is directed downward and away from the operator providing a safer working environment. This is the preferred hood for community pharmacies.

When working under a laminar air flow hood, these sample guidelines should be followed to ensure proper use:

- . Ideally, the hood should be operating continually, 24 hours a day. Since this is not feasible in a community setting, the hood should be turned on at least 30 minutes prior to use.
- . The working counter top and sides should be cleaned with a suitable disinfectant prior to, and after each use.
- . Any bottles, vials or containers should be wiped down, or sprayed, with alcohol or disinfectant before being brought into the hood to prevent possible contamination.
- . Objects placed in the hood should be suitably placed to provide good air flow with minimal obstruction. Work should always be at least 15 cm into the hood.
- . The HEPA filter should be checked, cleaned and re-certified once a year.
- . It is recommended that anyone working under a hood wear a gown, hair bonnet, gloves and mask. Facial hair should also be covered.

Appendix C Aseptic Technique

Aseptic technique is defined as procedures that will minimize the chance of contamination with micro-organisms. Contaminants may be brought into the aseptic area by equipment, supplies, or people, so it is important to control these factors during preparation. Sample guidelines to follow are:

- . Anyone using the laminar air flow hood should wash their hands with a suitable antimicrobial detergent at the beginning of their work and when re-entering the aseptic preparation area.
- . Conduct all manipulations inside a properly maintained and certified laminar flow hood (LFH). Allow the LFH to operate for at least 30 minutes before use in order to produce a particle free environment.
- . Be sure there are no objects between the HEPA filter and the sterile surfaces, and that there is adequate space between objects. Place the smaller supplies closer to the HEPA filter and larger supplies further away from the filter.
- . Appropriate dress (ie. gown, gloves or mask if needed) suitable for sterile preparation should be worn.
- . Activities unrelated to product preparation should be kept to a minimum.
- . Eating or drinking, or the storage of food, drinks or personal items should not be allowed in the aseptic area.
- . Only one person should be working in the hood at any given time.
- . All items that will be used during preparation should be checked for defects and expiry dates prior to use.
- . All non-sterile item surfaces should be disinfected with an appropriate disinfectant prior to being placed into the hood. This includes scissors, clamps, pumps, etc.
- . All items necessary for the preparation should be placed into the hood prior to commencing the procedure.
- . Direct contact between a sterile product and any non-sterile product should be avoided.
- . All non-sterile surface areas should be swabbed with alcohol (70% isopropyl) and left for 30 seconds before puncturing. This includes ampoules, vials and intravenous solution portholes.
- . Ampoules and vials should be opened and contents aspirated using appropriate techniques to avoid particulate contamination. This may require the use of filters for glass containers/ampoules.
- . Reconstituted powders should be mixed carefully according to manufacturer's recommendations to ensure complete dissolution of the drug.

- . All finished products should be carefully inspected after preparation for visible precipitation. This should be done outside the laminar air flow hood.
- . Each prepared sterile product should be assigned an expiry date based upon available data. If none is available, a short period should be applied (eg. 24 hours) based upon manufacturer's recommendations, pharmaceutical texts, professional literature, or in-house stability/sterility studies. If aseptic technique

is not followed, the final product may in fact be contaminated. It is important that proper technique be utilized to ensure the integrity of the product.

Appendix D Procedures and General Information on Sterile Compounding and aseptic Technique

Some of the training resources available for training of staff include:

1. “Sterile Product Preparation- A Multimedia Learning Tool” from American Society of HealthSystem Pharmacists
2. “Principles of Sterile Product Preparation” – a reference text from American Society of HealthSystem Pharmacists
3. “Sterile Product Preparation Video and Manual” from Canadian Society of Hospital Pharmacists
4. “Training Manual for Intravenous Admixture Personnel” from Baxter Healthcare

References such as these are necessary for training staff in proper technique, safeguards to follow in preparing sterile products, and quality control issues.

Pharmacists considering sterile compounding must be knowledgeable of the following aspects of compounding:

- Facilities, equipment and sanitation
- Ingredient storage and handling
- Dress requirements
- Aseptic preparation technique, sterilization
- Compatibility, stability and interactions
- Latex allergy
- Quality control standards – inspection, testing, checking
- Validation procedures – product and staff
- Label requirements
- Storage and expiry dates
- Disposal
- Documentation

Appendix E Reference sources

1. American Society of Health-System Pharmacy

7272 Wisconsin Avenue

Bethesda, MD 20814

Phone: 301-657-3000 Website: www.ashp.org

2. Canadian Pharmacists Association

1785 Alta Vista Drive

Ottawa, Ontario

K1G 3Y6

Tel: 1-800-917-9489 or (613) 523-7877 Fax: (613) 523-0445 Website:

www.cdnpharm.ca

3. Canadian Society of Hospital Pharmacists

1145 Hunt Club Road, Suite 350

Ottawa, ON K1V 0Y3

Phone: 613-736-9733 Fax: 613-736-5660 Website: www.cshp.ca

4. U.S. Pharmacopeia

12601 Twinbrook Parkway, Rockville, MD 20852 1790 U.S.A.

Phone: 800-227-8772 or 301-881-0666 Website: www.usp.org

5. Login Brothers

324 Salteaux Crescent

Winnipeg, Manitoba R3J 3T2

Phone: 800-665-1148 Fax: 800-665-0103 Website: www.lb.ca

6. Amazon online

www.amazon.ca

7. King Guide Publications

King Guide Publications, Inc.

PO Box 10317 Napa, CA 94581

Phone: (707) 257-7573 Fax: (707) 257-7566 Website: www.kingguide.com

References:

2. Ontario College of Pharmacists - Sterile Compounding: A guide for Community Pharmacists, 2003
3. The Nova Scotia College of Pharmacists - Council Policy: Sterile Compounding, 1999
4. Prince Edward Island Pharmacy Board Policy Statement - Sterile Compounding, 2001
5. Wyoming Board of Pharmacy regulations Chapter 13, 2003
6. Canadian Society of Hospital Pharmacists Guidelines for Preparation of Sterile Products in Pharmacies@ 1996
7. American Society of Health-System Pharmacists Guideline on Quality Assurance for Pharmacy-Prepared Sterile Products@, 2000
8. California Society of Health-system Pharmacists Guidelines for Sterile Compounding, 2003
9. Colorado State Board of Pharmacy guidelines 2003
10. School of Pharmacy, University of North Carolina "Sterile Compounding Techniques", 2003