

FREQUENTLY ASKED QUESTIONS

STERILE COMPOUNDING PREPARATIONS AND STERILE DRUG PRODUCTS

The Notice of Final Action for the regulations - COMAR 10.34.19 Sterile Compounding Preparations and Sterile Drug Products - was published in the Maryland Register on June 27, 2014 with an Effective Date of January 1, 2015. These regulations implement HB 986, State Board of Pharmacy - Sterile Compounding - Permits, 2013.

Beginning January 1, 2015, any sterile compounding facility that performs sterile compounding for patient-specific dispensing into, out of, or within Maryland will be required to apply for a Maryland Sterile Compounding Permit. An entity that performs compounding of sterile drug products for office use, or other distribution in Maryland, will be required to obtain a Maryland wholesale distributor's permit and a FDA registration or permit.

- To prepare for January 1, 2015, the Board has posted the Sterile Compounding Permit Application on its website for download
- Beginning January 1, 2015, the Board will accept applications for sterile compounding permits.
- **Please be advised that the Board will not accept any applications or fees until January 1, 2015. Any applications or fees received before January 1, 2015 will be returned to the sender.**
- Sterile compounding facilities with completed applications on file with the Board by **February 18, 2015** will not be subject to Board action for sterile compounding without a permit, until such time that the Board makes a final determination on the application.

I. DEFINITIONS.

1. What is a “sterile compounded preparation?”

"Sterile Compounding" means compounding of biologics, diagnostics, drugs, nutrients, and radiopharmaceuticals that, under USP 797, must be prepared using aseptic techniques.

2. What is the “immediate use” exemption?

“Three or fewer sterile products may be prepared in worse than ISO Class 5 air when there is no direct contact contamination, and administration begins within 1 hour and is completed within 12 hours of preparation.”

<http://www.usp797.org/usp797%20Latest%20News.htm>

3. What is a “sterile drug product?”

“Sterile Drug Product” means a drug product that: (a) is prepared using aseptic techniques; and (b) is not required to be prepared in response to a patient specific prescription.

4. What is an FDA Outsourcing Facility?

Federal “law defines an “outsourcing facility” as a facility at one geographic location or address that is engaged in the compounding of sterile drugs; has elected to register as an outsourcing facility; and complies with all of the requirements of Section 503B (of the DQSA).

An outsourcing facility can qualify for exemptions from the FDA approval requirements and the requirement to label products with adequate directions for use, but not the exemption from current good manufacturing practice (CGMP) requirements.

Outsourcing facilities:

- must comply with CGMP requirements;
- will be inspected by FDA according to a risk-based schedule; and
- must meet certain other conditions, such as reporting adverse events and providing FDA with certain information about the products they compound.”

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm393571.htm>

II. ENTITIES REQUIRED TO COMPLY WITH LAW AND REGULATIONS.

1. Who is required to have a sterile compounding permit in Maryland?

Any pharmacy, health care practitioner’s office, or any other setting in which sterile compounding is performed pursuant to a patient specific prescription is required to obtain a sterile compounding permit in Maryland.

2. Would a decentralized hospital pharmacy performing sterile compounding be required to obtain a unique sterile compounding permit for that location?

Any setting, including a decentralized hospital pharmacy, in which sterile compounding is performed pursuant to a patient specific prescription is required to obtain its own sterile compounding permit.

3. How do the recent Sterile Compounding Licensing Requirements apply to Ambulatory Surgery Centers that reside and practice in Maryland?

The law and regulations apply to an ambulatory surgery center if it performs sterile compounding. "Sterile Compounding" means compounding of biologics, diagnostics, drugs, nutrients, and radiopharmaceuticals that, under USP 797, must be prepared using aseptic techniques.

III. APPLICATION REQUIREMENTS.

1. Are any sterile compounding facilities that perform sterile compounding for patient-specific dispensing in Maryland exempt from obtaining a sterile compounding permit?

Yes. Oncologists, hematologists, rheumatologists are exempt from the sterile compounding permit.

A. Oncology, hematology, and rheumatology practices

SB 1108 Sterile Compounding Permits – Definition of “Compounding” established a specific exemption from obtaining a sterile compounding permit for oncology, hematology, and rheumatology practices.

2. Will dentists be required to obtain a sterile compounding permit?

For most dental products USP 797 does not address, or apply to, those products used in activating, bonding or taking impressions during dental procedures.

USP 797 and MD sterile compounding requirements do apply to IV sedation medications and IV general anesthesia medications. If the products are compounded and used within an hour, however; those products would fall under the “Immediate Use” exemption as defined in USP 797.

For preparation of any IV products that do not fall under the “Immediate Use” exemption, the Sterile Compounding Committee recommends that a dental practice review its sterile compounding needs in terms of volume, cost and practicality. Following are options that would comply with federal and state law, and USP 797: (1) using a compounding aseptic isolator (also known as a “glove box”), as set forth in USP 797; (2) contracting with a pharmacy to compound the product pursuant to a patient-specific prescription; or (3) contracting with an FDA-registered outsourcing facility to provide the IV products for office use inventory.

3. What requirements must be met in order to obtain a sterile compounding permit?

An application form must be completed and submitted to the Maryland Board of Pharmacy that includes the applicant’s name, address and contact information, practitioner license number, and the highest USP 797 risk level of compounding engaged in by the applicant and the required fee.

An applicant is subject to an inspection conducted by the Maryland Board of Pharmacy (Board), a designee of the Board; or the U.S. Food and Drug Administration that indicates compliance with USP 797 Standards. If an applicant is outside the State, an inspection must be obtained from a designee of the Board to demonstrate compliance with USP 797 Standards.

The application must include a statement of current compliance with USP 797 Standards. Reports and corrective actions taken or proposed in response to adverse events identified 12 months before submission of the application must also be included.

The applicant must also submit evidence that the sterile compounding facility employs at least one licensed health care practitioner who has training in compounding sterile preparations, clean room technology, laminar flow technology, quality assurance techniques, and clinical application of intravenous drug therapy; and evidence of good standing with any other State licensing entity; or licensing entity in the state in which the applicant is located.

The Board may require any other documentation to support its evaluation of the application. Please refer to COMAR 10.34.19 when the regulations become effective on January 1, 2015.

4. Can one application be used for all of an applicant's sterile compounding facilities?

No. A separate sterile compounding permit is required for each sterile compounding facility at which sterile compounding is performed.

5. Are sterile compounding permits transferrable?

No. A sterile compounding permit is not transferable.

6. If an entity would like to compound for office use, what kind of license is required?

The entity would have to obtain a Maryland wholesale distributor permit and either register with the FDA as an Outsourcing Facility or obtain an FDA manufacturer's permit, as appropriate.

7. What will the permits cost?

E. Sterile Compounding Permit Fees.

- (1) Sterile compounding permit initial fee — \$700;
- (2) Sterile compounding permit renewal fee — \$600; and
- (3) Sterile compounding reinstatement fee (payable if renewal fee is received after January 31) — \$600.

F. Sterile Drug Product Waiver Fees.

- (1) Sterile drug product waiver application fee — \$1,750;
- (2) Sterile drug product waiver application fee for an additional sterile drug product for a person with an existing sterile drug product waiver — \$700; and
- (3) Sterile drug product waiver amendment fee — \$700.

8. How do I renew my sterile compounding permit?

See COMAR 10.34.19.17H:

(1) A sterile compounding permit expires on May 31 of the next even-numbered year after its effective date, unless the sterile compounding permit is renewed for a 2-year term as provided in this regulation.

(2) Before a sterile compounding permit expires, the sterile compounding permit may be renewed for an additional 2-year term if the applicant:

- (a) Otherwise is entitled to the permit;
- (b) Pays a renewal fee as set forth in COMAR 10.34.09; and
- (c) Submits to the Board a renewal application on the form the Board requires.

9. How do I register as an FDA Outsourcing Facility?

Please go to this website for information:

<http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/pharmacycompounding/ucm378645.htm>

IV. REPORTING REQUIREMENTS.

1. Do I need to notify the Board of any changes in information I provide on a sterile compounding application?

The applicant shall notify the Board in writing within 30 days of any change in the information given on the initial or renewal application. See COMAR 10.34.19.17E

Additionally, you would have to notify the Board if there is a change in the controlling ownership of the pharmacy or wholesale distributor. See COMAR 10.34.30 Change to Permit – Pharmacy or Wholesale Distributor Permit Holder.

2. Does Maryland have reporting requirements for pharmacies that perform sterile compounding?

See COMAR 10.34.19.19 Reporting Requirements for Sterile Compounding Permit Holders:

A sterile compounding permit holder shall:

- A. Document and perform routine testing as required by USP 797 Standards for the appropriate risk levels of sterile compounded preparations; and
- B. Report to the Board within 5 calendar days:
 - (1) Adverse events including corrective actions taken or proposed;
 - (2) Deficiencies related to the sterile compounding process;
 - (3) Disciplinary actions in other states or by other state agencies;
 - (4) Changes in accreditation status;
 - (5) Disciplinary actions taken against a health care practitioner who is an owner, operator, or employee of the sterile compounding permit holder; and
 - (6) Disciplinary actions taken against any other known permit, or any other authorization, held by the sterile compounding permit holder.

V. SPECIAL CIRCUMSTANCES.

1. Would a pharmacy be in compliance if it uses a glove box within the specifications and requirements of USP 797?

Each isolator has manufacturer recommendations that you should take into consideration when utilizing this equipment. USP 797 allows isolators to be utilized in conformance with the manufacturer's written documentation based on validated environmental testing. However, please be advised that the use of an isolator does not exempt the permit holder from quality assurance requirements such as media fill testing.

2. If I prepare sterile compounded preparations for “immediate use,” does this mean I do not have to obtain a sterile compounding permit from the Board of Pharmacy?

Yes.

3. If a commercially available FDA product is available, what would the Board of Pharmacy’s position be on compounding the same material using USP 797 conditions instead of buying the commercially available agent?

Please be advised that you may not compound a prescription for a medication that is readily and commercially available. The Food and Drug Administration Modernization Act of 1997 (FDAMA) prohibits pharmacists from compounding “copies” of commercially available drug products. See 21 USCS § 353a.(b)(1)(D).

After January 1, 2015, when the sterile compounding permit is anticipated to be available, you may apply for a waiver to the sterile compounding permit if certain criteria are met.

4. May a compounding pharmacy and a doctor conduct clinical research on the efficacy of a product? The doctor wants a pharmacy to supply the product as an equivalent of a placebo for free, but not pursuant to a prescription. The bottle will not have patient information such as name, product info etc. but may only have an anonymous number that is associated with each specific patient.

Compounding is allowed in Maryland pursuant to a patient specific prescription. The compounding prescription is patient specific if it has an anonymous number.

Please also follow COMAR 10.34.04.08C Transfer and Outsourcing of Prescriptions and Prescription Orders - Preparation of Stock and Investigational Medications.

C. A pharmacist may prepare, package, and label investigational drugs not destined for a specific individual at the time of preparation, packaging, and labeling if:

(1) The study for which medications are prepared, packaged, and labeled is approved by an institutional review board as defined in federal law; and

(2) The pharmacy permit holder ensures that records disclosing the identity of the subject who eventually receives the medication are:

(a) Received by a pharmacist on duty at the pharmacy within 30 days after being provided to a patient; and

(b) Maintained in the pharmacy.

5. May a pharmacy provide samples of compounded medications to physicians and provide compounded medications of non-commercial products for use by physician in office.

Compounding is only allowed pursuant to a patient specific prescription.

See Health Occupations Article, 12-101, Annotated Code of Maryland and Health Occupations Article, 12-4A-01, Annotated Code of Maryland

If you would like to perform office use compounding, you should be registered with the FDA as an **Outsourcing Facility**

6. What if I do not have a patient specific prescription?

You may compound without a patient specific prescription, if you are registered with the FDA as an Outsourcing Facility. You would also be required to obtain a Maryland wholesale distributor's permit if you are distributing more than 5% of your gross annual sales.

VI. EXCEPTIONS, EXCLUSIONS AND WAIVERS.

1. Are any sterile compounding facilities excluded from compliance with the new law and regulations?

A. Oncology, hematology, and rheumatology practices

SB 1108 Sterile Compounding Permits – Definition of “Compounding” established a specific exemption from obtaining a sterile compounding permit for oncology, hematology, and rheumatology practices.

B. Ophthalmologists

HB 1088 Health Occupations – Compound Drugs – Provision to Ophthalmologists for Office Use, allows a sterile compounding facility to provide an ophthalmologist for office use, without a patient-specific prescription: (1) compound antibiotics for the emergency treatment of bacterial endophthalmitis or viral retinitis; and (2) compound antivascular endothelial growth factor agents for the emergency treatment of neovascular glaucoma, wet macular degeneration, or macular edema.

The sterile compounding facility should register as an FDA Outsourcing Facility and is required to obtain a Maryland wholesale distributor permit.

C. Allergen Extract Compounding

Allergen extract compounding is a special exemption in USP 797 and is, therefore, not subject to the provisions of a sterile compounding permit under Maryland law provided that the 11 enumerated conditions, as specified by USP 797, are met:

1. The compounding process involves simple transfer via sterile needles and syringes of commercial sterile allergen products and appropriate sterile added substances (e.g., glycerin, phenol in sodium chloride injection).
2. All allergen extracts as CSPs shall contain appropriate substances in effective concentrations to prevent the growth of microorganisms. Nonpreserved allergen extracts shall comply with the appropriate CSP risk level requirements in the chapter.
3. Before beginning compounding activities, personnel perform a thorough hand-cleansing procedure by removing debris from under fingernails using a nail cleaner under running warm water followed by vigorous hand arm washing to the elbows for at least 30 seconds with either nonantimicrobial or antimicrobial soap and water.
4. Compounding personnel don hair covers, facial hair covers, gowns, and face masks.
5. Compounding personnel perform antiseptic hand cleansing with an alcohol-based surgical hand scrub with persistent activity.
6. Compounding personnel don powder-free sterile gloves that are compatible with sterile 70% isopropyl alcohol (IPA) before beginning compounding manipulations.
7. Compounding personnel disinfect their gloves intermittently with sterile 70% IPA when preparing multiple allergen extracts as CSPs.
8. Ampul necks and vial stoppers on packages of manufactured sterile ingredients are disinfected by careful wiping with sterile 70% IPA swabs to ensure that the critical sites are wet for at least 10 seconds and allowed to dry before they are used to compound allergen extracts as CSPs.
9. The aseptic compounding manipulations minimize direct contact contamination (e.g. from glove fingertips, blood, nasal and oral secretions, shed skin and cosmetic, other nonsterile materials) of critical sites (e.g., needles, opened ampuls, vial stoppers).
10. The label of each multiple-dose vial (MDV) of allergen extracts as CSPs lists the name of one specific patient and a BUD and storage temperature range that is assigned based on manufacturer's recommendations or peer-reviewed publications.
11. Single-dose allergen extracts as CSPs shall not be stored for subsequent additional use.

2. Who would qualify for a waiver?

A. The Board may issue a waiver to a person that prepares and distributes sterile drug products into, out of, or within the State only:

(1) For a specified sterile drug product where exigent circumstances exist under the following criteria:

- (a) The specified sterile drug product in the size and strength needed is:
 - (i) Listed on the current drug shortages index by the U.S. Food and Drug Administration or other nationally recognized index; or
 - (ii) Only prepared and distributed by the person applying for the waiver; and
- (b) The absence of the specified sterile drug product would result in a patient care or a patient safety risk;

(2) For which there is a clinical need as determined by the Board with input from relevant professionals as determined by the Board;

- (3) If the request for the waiver is not based on financial or business concerns; and
- (4) If the applicant meets the following requirements:
 - (a) Submits an application form approved by the Board;
 - (b) Identifies in the application the highest USP 797 risk levels of compounding engaged in by the applicant;
 - (c) Pays a fee as set forth in COMAR 10.34.09;
 - (d) Submits reports of inspections conducted within a year of the application by:
 - (i) The Board or its designee; or
 - (ii) The U.S. Food and Drug Administration;
 - (e) Submits a statement of compliance with USP 797 Standards;
 - (f) Submits reports and corrective actions taken or proposed in response to adverse events identified 12 months before submission of an application for a waiver;
 - (g) If a pharmacy or a wholesale distributor shall employ at least one licensed pharmacist who has training in compounding sterile preparations, clean room technology, laminar flow technology, quality assurance techniques, and clinical application of intravenous drug therapy;
 - (h) Submits evidence of good standing with:
 - (i) Any other State licensing entity; or
 - (ii) The licensing entity in the state in which the applicant is located; and
 - (i) Submits any other documentation as required by the Board.