Chapter 19 Sterile [Pharmaceutical] Compounding *Preparations and Sterile Drug Products*

Authority: Health Occupations Article, §§12-205, 12-503, [and] 12-505*, and 12-4A - 01 – 12-4A-11*, Annotated Code of Maryland

(Please note that this draft does not include new regulations for the new Sterile Compounding Permit and other revisions to the chapter consistent with that new permit - to be released separately)

.01 Scope.

This chapter applies to a licensed pharmacy **[**in**]*, sterile compounding facility, or other person dispensing or distributing sterile compounding preparations or sterile drug products into, out of, or within*** Maryland engaging in:

A. Compounding or mixing sterile prescription solutions or suspensions to be administered parenterally or by irrigation, inhalation, or intraocular routes; and

B. Compounding of radiopharmaceuticals, except where U.S. Pharmacopeia (USP) General Chapter 797 Pharmaceutical Compounding—Sterile Preparations addresses radiopharmaceuticals, U.S. Pharmacopeia (USP) Chapter 821 Radioactivity, and U.S. Pharmacopeia (USP) Chapter 823 Radiopharmaceuticals for Positron Emission Tomography—Compounding would apply**[.]***; and*

.03 Definitions.

A. In this chapter, the following terms have the meanings indicated.

B. Terms Defined.

(1) "Adverse events" means:

(a) Any adverse patient outcome related to the compounding process; or

(b) Evidence of environmental contamination, including microbial contamination above the threshold set forth in USP 797 Standards.

[(1)**]** ***(1-1)*** "Antineoplastic" means an agent that prevents the development, growth, or proliferation of malignant cells.

(2) "Anteroom" means the area, room, or rooms where personnel perform hand hygiene and garbing immediately adjacent to the designated clean room where the compounding of sterile preparations is performed.

(3) Batch.

(a) "Batch" means a preparation compounded in advance of receipt of a prescription, or a preparation compounded in a supply that will be used on more than one dispensing to a patient or patients or any preparation compounded in excess of the filling of an individual prescription.

(b) "Batch" includes a limited quantity of identical preparations compounded in a single, discrete process, by the same individuals, carried out during one limited time period.

(4) "Biological safety cabinet" means a containment unit:

(a) Suitable for work involving agents that pose higher risk of exposure to operators during compounding; and

(b) Used when there is a need for protection of the preparation, personnel, and environment.

(5) "Clean room" means an International Standards Organization (ISO) Class 7 environment that meets USP 797 Standards, inside which compounding occurs within an ISO Class 5 engineering control device such as a laminar airflow workstation or a biological safety cabinet.

(5-1) "Closed system vial transfer device (CSTD)" means a closed system drug transfer device that mechanically, not by means of vents or filters, prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug aerosols or vapors into the environment.

(5-2) "Compounding" means the preparation, mixing, assembling, packaging, or labeling of a drug only:

(a) As the result of a practitioner's prescription drug order or initiative based on the practitioner/patient relationship in the course of professional practice; or

(b) For the purpose of, or incidental to, research, teaching, or chemical analysis and not for the sale or dispensing of the drug or device; or

(c) In anticipation of a prescription drug order based on routine, regularly observed prescribing patterns.

(6) "Compounded sterile preparation" means sterile medication preparations, such as intravenous, epidural, and intraocular medications, compounded in the **[**pharmacy**]** ***sterile compounding facility*** using currently accepted aseptic compounding techniques under acceptable compounding conditions.

(7) "Compounding aseptic isolator" means an enclosed positive or negative pressure environment especially designed for sterile preparation compounding that maintains a physical barrier between the workspace and the operator.

(8) "Controlled environment" means a designated area for compounding sterile preparations that consists of a clean room and an anteroom.

(9) "Cytotoxic" means drug entities that are damaging or debilitating to cells, tissues, or organs.

(9-1) "Designee" means a public agency or private entity approved by the Board to conduct inspections of sterile compounding facilities or entities that prepare sterile drug products.

(9-2) "Health Care Practitioner" means a licensed dentist, pharmacist, physician, podiatrist, or veterinarian who is authorized to perform sterile compounding for dispensing or administering directly to their patients.

(9-3) "High risk" means a compounding process as defined in U.S. Pharmacopeia (USP) General Chapter 797 Pharmaceutical Compounding – Sterile Preparations (USP 797 Standards).

(10) "Laminar air flow workstation" means an ISO Class 5 ("Class 100") laminar airflow hood inside which sterile compounding occurs.

(10-1) "Low risk" means a compounding process as defined in U.S. Pharmacopeia (USP) General Chapter 797 Pharmaceutical Compounding – Sterile Preparations (USP 797 Standards).

(11) "Media fill verification" means a process of practical examination to verify the aseptic technique of personnel or an aseptic process by manual manipulation of microbiological growth media which simulates compounding processes and techniques used in actual compounding procedures.

(11-1) "Medium risk" means a compounding process as defined in U.S. Pharmacopeia (USP) General Chapter 797 Pharmaceutical Compounding – Sterile Preparations (USP 797 Standards).

(12) "Parenteral" means routes of drug administration or fluid administration other than via the gastrointestinal tract.

(13) "Pharmacist" means an individual who is licensed to practice pharmacy regardless of the location where the activities of practice are performed.

(14) "Pharmacy" means an establishment in which prescription or nonprescription drugs or devices are compounded, dispensed, or distributed.

(15) "Pyrogen testing" means an analysis of sterile preparations for the presence of cell material from microbiological organisms in sufficient quantity to elicit a febrile reaction.

(15-1) "Risk level" means a risk level of low, medium or high as defined in USP 797 Standards.

(16) "Sterile" means free from living microorganisms or any other contaminants.

(16-1)) "Sterile compounding" means compounding of biologics, diagnostics, drugs, nutrients, and radiopharmaceuticals that, under USP 797 Standards, are prepared using aseptic techniques.

(16-2) "Sterile compounding facility" means a pharmacy, a health care practitioner's office, or any other setting in which sterile compounding is performed.

(16-3) "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.

(17) "Total parenteral nutrition" means providing caloric needs by the parenteral route for a patient who is unable to ingest sufficient calories.

(18) "USP 795 Standards" means standards set forth in the US Pharmacopeia (USP) General Chapter 795 Pharmaceutical Compounding—Non-Sterile Preparations.

(19) "USP 797 Standards" means standards set forth in the U.S. Pharmacopeia (USP) General Chapter 797 Pharmaceutical Compounding—Sterile Preparations.

ALL NEW *(actual numbering of the regulations TBD)*

.17 Sterile Drug Products.

A. A person that prepares and distributes sterile drug products into, out of, or within the State shall:

(1) Hold a manufacturer's permit or other permit designated by the U.S. Food and Drug Administration to ensure the safety of sterile drug products; and

(2) Hold a wholesale distributor's permit issued by the Board under Health Occupations Article, Title 12, Subtitle 6C, Annotated Code of Maryland.

B. A person that prepares and distributes sterile drug products into, out of, or within the State may not be required to hold a sterile compounding permit under Health Occupations Article, 12-4A-02, Annotated Code of Maryland.

.18 Sterile Drug Product Waiver.

A. The Board may issue a waiver of the requirements in Regulation .17A(1) of this chapter 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

(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; and

(2) For which there is a clinical need as determined by the Board with input from health care providers in the State under the following criteria:

(a) The licensed health care providers may be from:

(i) The Maryland Hospital Association;

(ii)The Maryland Society of Health-Systems Pharmacists;

(iii) The Maryland State Medical Society; or

(iv) Other relevant professionals as determined by the Board; and

(b) The criteria may not be based on financial or business concerns;

(3) 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) 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:

(1) Any other State licensing entity; or

(2) The licensing entity in the state in which the applicant is located; and

(i) Submits any other documentation as required by the Board; and

(4) The Board shall, in its discretion, determine whether to issue a waiver based upon the Board's review of the information submitted in accordance with §A(1) – (3) of this regulation.

B. A person that prepares and distributes sterile drug products into, out of, or within the State under a Board approved waiver shall submit to the Board within 5 calendar days reports of adverse events and corrective actions taken or proposed.

C. A person that prepares and distributes sterile drug products into, out of, or within the State under a Board approved waiver shall notify the Board in writing within 30 days of any change in the information given on the initial or renewal application.

D. A person that prepares and distributes sterile drug products into, out of, or within the State under a Board approved waiver shall submit reports of an inspection conducted:

(1) Within 1 year of the Board's approval of the waiver that demonstrates compliance with USP 797 Standards; and

(2) By:

(a) The Board or its designee; or

(b) The U.S. Food and Drug Administration;

E. An applicant outside the State is responsible for obtaining an inspection from a designee of the Board to demonstrate compliance with USP 797 Standards;

F. Renewal.

(1) Any waiver issued by the Board may:

(a) Not exceed a duration determined by the Board based on exigent circumstances and clinical need;

(b) Not exceed 2 years; and

(c) Be renewed if the renewal applicant submits:

(i) An application form approved by the Board;

(ii) A fee as set forth in COMAR 10.34.09; and

(iii) Meets the requirements for a waiver under §A(1) – (3) of this regulation.

G. Documentation of Administration of Sterile Drug Products.

The holder of a sterile drug product waiver shall ensure that the recipient of the sterile drug products maintain readily retrievable records of the administration and/or dispensing of the sterile drug products to patients, to include:

(1) Documentation of the lot number or other mechanism for identifying the sterile drug product for the purpose of tracing the sterile drug product back to the sterile compounding facility or other person that prepared it; or

(2) If documentation of the lot number or other identification mechanism is not feasible, documentation of the source of the sterile drug product for the purpose of tracking the sterile drug product back to the sterile compounding facility or other person that prepared it.

H. Amendments to the Waiver.

(1) The holder of a sterile drug product waiver shall submit amendments to the waiver in advance to the Board for approval, including the addition of a specified sterile drug product.

(2) The Board may approve amendments to the waiver if:

(a) The requirements of this chapter and Health Occupations Article, Title 12, Subtitle 4A, Annotated Code of Maryland are met;

(b) The applicant submits any additional information requested by the Board; and

(c) Pays to the Board an amendment fee as set forth in 10.34.09.