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Board of Registration in Pharmacy

Policy 2023-07: Non-Sterile Compounding

The Board of Registration in Pharmacy ("Board") is providing an overview of requirements for non-sterile compounding by Board-licensed pharmacies. This is not intended to be an exhaustive list. Licensees are expected to adhere to the United States Pharmacopeia ("USP"), and any state and federal requirements. Except for complex non-sterile compounding, all pharmacies licensed by the Board are expected to engage in non-sterile compounding in accordance with Board regulations.

I. Definitions

A. **Non-sterile compounding** is defined as the process of combining, admixing, diluting, pooling, reconstituting other than as provided in the manufacturer's labeling, or otherwise altering a drug or bulk drug substance to create a non-sterile preparation (adapted from USP <795>).

B. **Complex non-sterile compounding** is defined as the compounding of drug preparations which require special training, a special environment or special facilities or equipment or the use of compounding techniques and procedures that may present an elevated risk to the compounder or the patient (MGL c.112 § 39D). This type of compounding requires an additional specialty license. See section VII below.

> **Note: The Board considers the compounding of National Institute for Occupational Safety and Health ("NIOSH") drug containing preparations or other hazardous agents to be complex non-sterile compounding.**

II. General

A. Pharmacies must have policies and procedures for non-sterile compounding, including personal protective equipment ("PPE") and training, based on the type of compounding performed.

Note: The requirement of USP <795> for a "designated person" may be fulfilled by the pharmacy's Manager of Record or any licensed pharmacist on-site.

B. Patient-specific prescriptions are required to dispense any compounded preparation into, within, or from Massachusetts.

Note: Flavoring may be added upon request of the patient or their agent for Schedule VI medications even if it has not been requested by the prescriber. The prescription may be updated with this information in accordance with Policy 2018-01: *Permitted Prescription Changes and Additions*.

C. In accordance with MGL c.112 § 39D, copies of commercially available, Food and Drug Administration ("FDA") approved drugs or drug preparations, including those for veterinary use, may not be compounded except to meet the unique medical need of an individual patient by producing a significant difference between the compounded drug preparation and a comparable commercially available drug. This must be justified with a documented medical need as determined by the prescribing practitioner including, but not limited to, the removal of a dye for medical reasons, a change in strength, or a change in dosage, form, or delivery mechanism. Cost is not a suitable justification. Regarding the compounding of a copy of a drug, see Policy 2020-02: *Compounding Copies of Commercially Available Drugs*.

D. In exercising the pharmacist's corresponding responsibility, evaluate each prescription utilizing sound clinical judgement to determine whether a compound, or any active ingredient(s) in the compound, is necessary and appropriate.

E. Pharmacies may provide emergency kits ("e-kits") containing limited quantities of Schedule VI compounded medications to a licensed veterinarian for the purpose of direct administration or dispensing in emergency situations in accordance with Policy 2019-06: *Compounded Emergency Medications for Veterinarian Use*.

F. Pharmacies may participate in research drug studies with compounded medications in accordance with Policy 2018-06: *Retail Pharmacy Participation in Research Drug Studies*.

III. Non-Sterile Compounding Process

A. As outlined in USP <795>, a pharmacy must follow a master formulation record (i.e., formulation sheet) that includes any quality control procedures (e.g., visual inspection, etc.) each time it prepares a compounded non-sterile preparation. The master formulations must be based on USP standards as well as any relevant scientific data and / or direct validation testing, as applicable.

B. Simple reconstitution of FDA approved, conventionally manufactured non-sterile drug products in accordance with manufacturer package insert instructions is not considered compounding.

C. Flavoring agent(s) added to conventionally manufactured non-sterile drug products is considered compounding. In addition to a policy and procedure, a pharmacy must ensure that the addition of the flavoring agent does not affect stability or alter the final concentration beyond the parameters outlined in USP <795>. Available scientific data or studies, whether published or unpublished, may be utilized for this purpose.

D. Breaking or splitting non-hazardous drugs is not considered compounding. However, USP <800> must be followed to perform these activities with hazardous drugs ("HD"). See Advisory: *USP <800> in Community Pharmacies*.

E. Pre-measured compounding kits are still considered compounding and all relevant USP standards must be followed.

F. Active Pharmaceutical Ingredients ("API") must be obtained from a facility that is registered by the FDA.

   Note: Extreme caution must be exercised to assure correct dosages are compounded when using API powders by verifying whether the API is a pure powder or a trituration (dilution).

IV. Facility and Equipment

A. Pharmacies not engaged in complex non-sterile compounding must have a designated compounding area that should have at least 10 square feet of counter space that should not have carpeting. This area must be separated or otherwise protected from water sources (i.e., sink).

   Note: Flavoring agents may be added in a separate designated area (e.g., reconstitution area).

B. Surfaces in compounding areas must be smooth, seamless, impervious, free from cracks and crevices, and non-shedding to facilitate cleaning.

C. The Board does not intend to enforce the cleaning and sanitizing requirements of USP <795> for pharmacies that are not engaged in complex non-sterile compounding, provided the facility, including sinks, utensils, and equipment, is maintained in a clean and sanitary manner. Review the FDA's Insanitary Conditions at Compounding Facilities guidance document.

D. Equipment used for compounding must be in a good state of repair and properly maintained.

E. Scales / balances must be properly maintained and sealed at least once per calendar year. See newsletter article for details.

F. Space, equipment, and materials must be designed, arranged, and used in a way that minimizes errors and cross-contamination.

G. The Board does not intend to enforce the USP <795> temperature monitoring requirements for storage rooms of pharmacies that are not engaged in complex non-sterile compounding, provided that temperatures are maintained within USP standards.

H. Before beginning any renovations, retail pharmacies must apply for approval.

V. Labeling / BUDs

A. Beyond use dates ("BUD") must be assigned in accordance with the most current USP <795>. Assure that BUDs are appropriately assigned and are not defaulted to one year.

B. In addition to standard prescription labeling, a statement that the preparation is a non-sterile compounded drug preparation must also be included (MGL c. 94C § 21). If applicable, a statement that the product was flavored (e.g., auxiliary label, noted on label, etc.) must also be included on the patient's container.

VI. Documentation

A. A reconstitution log (or similar documentation) for the preparation of commercially available products (e.g., antibiotic suspensions, erythromycin-benzoyl peroxide gel, etc.) is recommended.

B. Each compounded non-sterile preparation must be documented on a compounding record (i.e., compounding log).

> **Note:** The compounding record serves as the accountability documentation as required by MGL c.112 § 39D.

C. In the case of **pre-measured compounding kits** and **flavoring agents** added to conventionally manufactured non-sterile drug products, the compounding record may also serve as the master formulation record and may be in the form of a log sheet. The following information must be documented and be readily retrievable:

1. date of preparation;
2. prescription number;
3. name, vendor / manufacturer / NDC, lot number, and expiration date of each component;
4. any relevant calculations and quantities/volumes of additives (e.g., water, flavoring agent(s), etc.);
5. BUD and any special storage requirements (e.g., refrigerate); and
6. identifier (e.g., name, initials, etc.) of individual who prepared the product (e.g., reconstitution, etc.).

D. All pharmacies are required to maintain a defective drug log for any compounded drug preparation that is or may be defective. See Policy 2024-04: *Defective Drug Preparations* for details.

VII. Complex Non-Sterile Compounding

A. An additional pharmacy specialty license is required to prepare and dispense complex non-sterile preparations into, within, or from Massachusetts.

B. The Board considers the following to be examples of complex non-sterile compounding (not all inclusive):

1. compounding of NIOSH drug containing preparations or other hazardous agents;
2. use of complex calculations such as accounting for loss on drying, salt conversions, multiple aliquots, etc.; and

3. preparation of the following dosage forms:
    a. transdermal dosage forms
    b. capsules
    c. suppositories
    d. troches
    e. lollipops
    f. sublingual dosage forms
    g. tablets
    h. tablet triturates
    i. modified-release preparations
    j. other dosage forms intended to deliver systemic effects (inserts, nasal sprays, nasal irrigations, certain gels, etc.)

C. Additional requirements for pharmacies and pharmacists engaged in complex non-sterile compounding:
    1. dedicated compounding room will be required for complex non-sterile compounding, but is currently required for HD compounding (i.e., containment secondary engineering control with containment primary engineering control);
    2. HD and non-HD non-sterile compounding may not occur in the same room or primary engineering control. A separate room with a separate containment hood(s) is required for HD compounding (per USP <800>);
    3. compounding of non-sterile preparations using bulk drug substances must comply with FDA's guidance "Bulk Drug Substances Used in Compounding Under Section 503A of the FD&C Act"; bulk drug substances must be accompanied by a valid certificate of analysis;
    4. retail complex non-sterile compounding pharmacies licensed by the Board are required to report volume and distribution data each calendar year upon renewal; and
    5. pharmacists who oversee or engage in complex non-sterile compounding must obtain 3 continuing education hours in non-sterile compounding each calendar year (see the Board's Continuing Education (CE) Requirements policy for details).

Please direct any questions to: Pharmacy.Admin@mass.gov