MISSOURI BOARD OF PHARMACY ADVISORY:

IMPORTANT INFORMATION FOR MISSOURI LICENSED PHARMACIES

The mission of the Missouri Board of Pharmacy is to protect the public through the regulation of pharmacy practice. Missouri pharmacists play a crucial role in ensuring quality patient care. Pharmacy compounding, including sterile compounding, is one of the many valued functions provided by Missouri's trained and licensed pharmacists.

In light of the recent national attention to sterile compounding, the Board is issuing this Board Advisory to remind licensees and sterile compounding pharmacies of the following Missouri requirements:

Note: This Advisory is provided for informational purposes only and does not constitute a comprehensive review of all governing law or sterile compounding requirements. To ensure compliance, licensees should thoroughly review Chapter 338, RSMo, 20 CSR 2220 and all applicable state and federal law(s). This Advisory does not constitute a rule statement of general applicability or binding law. In the event of a conflict or inconsistency, duly promulgated or enacted state or federal law shall control. The Board expressly reserves the right to revise the contents of this Advisory as deemed appropriate or necessary.

GOVERNING LAW

Sterile compounding pharmacies are required to comply with all applicable provisions of Chapter 338, RSMo, and the rules of the Board, including, 20 CSR 2220-2.400 (Compounding Standards of Practice) and 20 CSR 2220-2.200 (Sterile Pharmaceuticals). Compliance is mandatory for all pharmacies holding a Class H (Sterile Compounding) pharmacy permit even if the pharmacy is not currently providing sterile compounding services. To remove Class H from your permit, a Change of Classification form must be submitted to the Board.

The Board anticipates reviewing its sterile compounding rules in 2013 and will also consider proposals to adopt USP 797. Interested parties should monitor the Board's website for future meeting dates and agenda topics.

PRESCRIPTION REQUIREMENTS

Pursuant to rule 20 CSR 2220-2.400, pharmacies may only dispense compounded products pursuant to a patient specific prescription. Drugs may be compounded in "limited quantities" prior to receiving a valid prescription if there is a history of receiving/filling valid prescriptions pursuant to an established relationship between the pharmacist, patient and prescriber. [20 CSR 2220-2.400(7)(C)]. While advance preparation is allowed, **a prescription is required prior to dispensing**.

For purposes of 20 CSR 2220-2.400, a "limited quantity" is defined as a three (3) month supply of a batched product or a one (1) year supply for compounded products intended for external use (i.e.- creams, ointments, lotions or liniments).

COMPOUNDING FOR OFFICE USE

Compounded products may not be sold or dispensed to practitioners or other prescribers for office use. [20 CSR 2220-2.400(1), (12)]. This includes hospitals, surgery centers, etc. Once again, a patient specific prescription is required prior to dispensing. **Compounding for office use without a patient specific prescription constitutes grounds for discipline which may include REVOCATION or SUSPENSION of your**

pharmacy license. *Note: Compounding for office use may also constitute manufacturing under federal law and require a Missouri drug distributor license.*

COMMERCIALLY AVAILABLE PRODUCTS

Generally, Missouri law prohibits licensees from compounding products that are commercially available or that are essentially copies of commercially available products. "Essentially copies" includes different dosage forms (i.e.- suspension vs. solution, tablet vs. capsule).

Licensees may only compound a commercially available product:

- If the product is temporarily unavailable due to problems other than safety or effectiveness (i.e.- on back order). Unavailability must be documented in the pharmacy's records. [20 CSR 2220-2.400(9)]. *Note: Once the commercially available product is available, the pharmacy must stop compounding it;*
- If a "specific medical need" for the prescription exists. [20 CSR 2220-2.400(9)]. The "specific medical need" is deemed to be the ***medical reason*** why the commercially available product can not be used. The nature of the "specific medical need" must be documented on the prescription or otherwise documented in the pharmacy's prescription records. [20 CSR 2220-2.400(9)]. Cost or convenience are generally insufficient to establish a "specific medical need".

Once again, **compounding commercially available products in violation of Missouri law may result in disciplinary action by the Board.**

RECEIPT OF DRUGS

Licensees are reminded that legend drugs may only be received/purchased from entities licensed or registered with the Board. Specifically, § 338.315.1, RSMo, provides:

> *Except as otherwise provided by the board by rule, it shall be unlawful for any pharmacist, pharmacy owner or person employed by a pharmacy to knowingly purchase or receive any legend drugs under 21 U.S.C. Section 353 from other than* ***a licensed or registered drug distributor or licensed pharmacy****. Any person who violates the provisions of this section shall, upon conviction, be adjudged guilty of a* ***class A misdemeanor****. Any subsequent conviction shall constitute a* ***class D felony****.*

See also 20 CSR 2220-2.400(6)(D). Significantly, this prohibition applies to drugs received from pharmacies, hospitals or distributors located in other states that are not licensed in Missouri.

Receiving or purchasing drugs from unlicensed entities threatens the integrity of Missouri's drug supply and places the public at risk. License status may be checked on the Board's website at https://renew.pr.mo.gov/licensee-search.asp.

POLICIES & PROCEDURES

Pursuant to 20 CSR 2220-2.200(2), Class H sterile compounding pharmacies must maintain a policy and procedure manual that addresses all aspects of sterile compounding performed by the pharmacy.

Given the recent news, permit holders should take this opportunity to review their policies and procedures for adequacy.

Board inspectors continue to observe instances of incomplete or outdated manuals. Policy & procedure manuals should be regularly reviewed and updated to ensure appropriate practices. At a minimum, manuals must be reviewed annually. [20 CSR 2220-2.200(2)]. **Policy and procedure manuals and documentation of the annual review will be required during inspection**.

Board inspectors have also observed instances where pharmacy staff are unaware of recent policy/procedure changes. Manuals should be accessible to and reviewed by all pharmacy staff, including, new hires. Staff review is also recommended after any substantive change or modification to sterile compounding procedures or a breach in aseptic technique.

TRAINING

Due to the specialized nature of sterile compounding, training of pharmacy personnel is essential to ensuring patient safety. Rule 20 CSR 2220-2.200 contains detailed sterile compounding training and assessment requirements. Licensees should review the rule to ensure pharmacy staff are **trained and assessed at regular intervals**.

At a minimum, staff engaged in preparing sterile products must receive suitable didactic and experiential training in sterile compounding procedures. [20 CSR 2220-2.200(3)]. Staff engaged in preparing Risk Level 3 products must also have specific education and training in Risk Level 3 products/procedures. Additionally, a competency assessment must be conducted for all staff preparing Risk Level 2 or Risk Level 3 products via process simulation. The assessment must evaluate competence in all Risk Level 2 procedures and, if applicable, Risk Level 3 procedures. [20 CSR 2220-2.200(3)(B), (C)].

In addition to the required training and competence assessment, pharmacy staff must pass a process validation of aseptic techniques before compounding sterile products. The validations must include manipulations in all risk levels performed by the individual being assessed. **Process validations must be completed annually** and whenever:

- The pharmacy's quality assurance program yields an unacceptable result, or;
- Microbial growth is detected.

If microbial growth is detected after process validation, **the entire sterile process must be evaluated, corrective action taken and the process simulation test performed again**.

Inspectors continue to observe instances where training is not properly documented and/or the required annual process validation was either untimely or not conducted. Licensees should establish procedures for annually tracking process validation dates. Documentation of the required training and competency assessment must be maintained in the pharmacy's records for two (2) years and readily retrievable during inspection.

FACILITIES & EQUIPMENT

As highlighted in recent news, proper facility and equipment maintenance is vital to ensuring patient safety. Regular cleaning and disinfection must be conducted to prevent contamination and ensure sterility.

Licensees should review 20 CSR 2220-2.200(5) for specific facilities and equipment requirements. Licensees are reminded of the following rule requirements:

- Eating, drinking and smoking are prohibited in the controlled area.
- Ingredients and containers must be inspected for defects, expiration and integrity before use.
- Workbenches/hoods must be recertified every six (6) months and when moved. *Note: This is a common inspection violation.* Recertification documentation must be maintained in the pharmacy's records.
- Risk Level 2: The controlled area must meet Class 10,000 clean room standards. Floors must be disinfected daily, equipment surfaces weekly and wall monthly.
- Risk Level 3: Sterile products must be prepared in a Class 100 workbench, a Class 10,000 clean room, a Class 100 clean room or within a positive pressure barrier isolator. Floors must be disinfected daily. Equipment surfaces, walls and ceilings must be disinfected weekly.
- Access to Risk Level 3 clean rooms must be limited to individuals preparing sterile products. [20 CSR 2220-2.200(5)(C)].
- Daily refrigerator and temperature logs/recordings must be completed and maintained. [20 CSR 2220-2.200(9)].
- Non-sterile equipment that will come in contact with the sterilized final product must be sterilized before introduction in the clean room. [Risk Level 3]
- Proper garb/apparel must be used in the controlled area for Risk Level 2 & 3 products as provided in 20 CSR 2220-2.200(6).

- *Note: Inspectors have encountered licensees improperly assigning sterile product risk levels. Licensees should review Missouri's rules to ensure compliance. When in doubt, the Board recommends assigning and utilizing procedures for the higher risk level.*

END PRODUCT TESTING

End product testing is key to verifying and ensuring consistent sterility. 20 CSR 2220-2.200(12) contains mandatory end product testing requirements for all risk levels. Licensees should review the rule and the pharmacy's policies/procedures to ensure compliance.

Licensees are reminded of the following:

- A **pharmacist** must verify that each sterile product was accurately compounded prior to release. Final products must also be inspected for container leaks, integrity, solution cloudiness, phase separation, particulates, appropriate solution color and solution volume. [20 CSR 2220-2.200(12)(A)]. Final verification may not be delegated to pharmacy technicians or non-pharmacists.
- Risk Level 3: All risk level 3 products must be tested for sterility, pyrogens, and endotoxins. End product sterility testing must be conducted for a statistically valid sample of each sterile compounding product batch. USP chapter 71 offers guidance on proper sample size. Parenteral sterile products must also be tested for pyrogens and endotoxins according to recommended USP methods. Products with beyond-use dates greater than 30 days must be tested for potency. [20 CSR 2220-2.200(12)(C)].
- Risk Level 3 sterile products compounded from nonsterile components **must be quarantined** pending end-product testing results in accordance with USP. [20 CSR 2220-2.200(12)(C)]. USP Chapter 71 requires sterility tests to be incubated for 14 days. Risk Level 3 products compounded from nonsterile components must be quarantined for the full 14 days. [20 CSR 2220-2.200(12)(C)].

20 CSR 2220-2.200(12)(D) authorizes emergency dispensing of Risk level 3 products pending test results if the product is needed for immediate administration and no alternative product is available. The release of Risk Level 3 products prior to the USP required 14-day incubation period for sterility testing is considered emergency dispensing and requires prescriber notification/approval. **The prescriber must be notified of the early release and approve the emergency dispensing**. [20 CSR 2220-2.200(1)(O)]. Prescriber approval and the need for emergency dispensing must be documented in the pharmacy's records. Separate prescriber authorization is required for each emergency dispensing. [20 CSR 2220-2.200(1)(O)].

SUMMARY

The Board cautions licensees and pharmacies engaged in sterile compounding to continuously review their policies and procedures to ensure safe and sterile practices.

Links to the Board's statutes and rules are available on the Board's website at http://pr.mo.gov/pharmacists-rules-statutes.asp. For additional questions, please contact your assigned inspector. Inspector contact information and e-mail addresses are available online at http://pr.mo.gov/boards/pharmacy/Inspectors.pdf.

In response to the national issues raised, the Board has been made aware that other state boards of pharmacy will be conducting compliance inspections in the state of Missouri for those pharmacies that hold a nonresident pharmacy permit/license from the applicable state. These inspections are not being conducted by or on behalf of the Missouri Board of Pharmacy. Questions regarding inspections that are not conducted by the Board should be addressed to the applicable licensing state.