Title 20—DEPARTMENT OF INSURANCE, FINANCIAL INSTITUTIONS AND PROFESSIONAL REGISTRATION
Division 2220—State Board of Pharmacy
Chapter 8—Third-Party Logistic Providers and Drug Outsourcer Facilities

EMERGENCY RULE

20 CSR 2220-8.040 Standards of Operation (Drug Outsourcers)

PURPOSE: This rule provides standards of operation for drug outsourcers licensed by the board.

EMERGENCY STATEMENT: The Missouri General Assembly recently enacted HB 1719 which establishes a new license classification for drug outsourcers, effective August 28, 2018. The board has simultaneously filed emergency rules to license drug outsourcers. Drug outsourcers are authorized by federal law to engage in sterile compounding which is the act of compounding a drug that must be sterile and free of harmful microorganisms prior to administration to a patient. Sterile compounding requires the use of aseptic techniques in a properly controlled environment to eliminate the risk of preparation contamination. The United States Food and Drug Administration has indicated: "Although compounded drugs can serve an important need, they pose a higher risk to patients than FDA-approved drugs. Compounded drug products are not FDA-approved which means they have not undergone FDA premarket review for safety, effectiveness, and quality."

In 2012, the FDA reported that a Massachusetts sterile compounding facility shipped contaminated injectable drug products to patients and healthcare practitioners that caused a nationwide fungal meningitis outbreak that resulted in more than sixty (60) deaths and seven hundred fifty (750) cases of infection. Since 2012, the FDA reported it has "investigated numerous outbreaks and other serious adverse events, including deaths, associated with compounded drugs that were contaminated or otherwise compounded improperly" since the fungal meningitis outbreak.

*The board has determined this emergency rule is needed to protect Missouri patients by establishing standards of operations for drug outsourcers to ensure medication dispensed into Missouri is safe, effective and not adulterated, contaminated or otherwise harmful to Missouri citizens. Absent an emergency rule, no state standards of operation would be in effect for drug outsourcers which could endanger the lives of Missouri patients given the complex and specialized nature of sterile compounding. As a result, the Missouri State Board of Pharmacy finds there is an immediate danger to the public health, safety, and/or welfare and a compelling governmental interest that requires this emergency action. The scope of this emergency rule is limited to the circumstances creating the emergency and complies with the protections extended in the **Missouri** and **United States Constitutions**. The Missouri State Board of Pharmacy believes this emergency rule is fair to all interested persons and parties under the circumstances. This emergency rule was filed November 28, 2018, becomes effective December 8, 2018, and expires June 5, 2019.*

(1) Drug outsourcers shall comply with all applicable state and federal laws governing drug outsourcing activities, including, but not limited to, controlled substance laws and the federal Food, Drug and Cosmetics Act, as amended by the Drug Quality and Security Act.

(A) Except as otherwise required by federal law, drug outsourcers must comply with all applicable current good manufacturing practices (cGMPs) required by federal law and the United States Food and Drug Administration.

(B) A separate Missouri drug distributor license is required if a drug outsourcer is engaged in any additional drug distribution activities as defined by Chapter 338, RSMo, other than drug outsourcing. A pharmacy license is required if medication will be dispensed pursuant to a patient-specific prescription.

(2) No drug outsourcer license will be issued unless the facility is under the direct supervision of a pharmacist who has been designated with the board and who will be responsible for facility operations and ensuring compliance with state and federal law. The pharmacist must hold a current and active pharmacist license issued by Missouri or another U.S. state/territory.

(A) Drug outsourcing activities must be conducted at all times under the supervision of the designated pharmacist. The pharmacist must be actively involved in and aware of the daily operations of the outsourcing facility and must ensure that policies and procedures governing drug outsourcing operations are current and accurate.

(B) In the event the pharmacist designated with the board to supervise the facility changes, the drug outsourcer may not continue operations until a new pharmacist is named to supervise the facility. A change of pharmacist application must be submitted to the board with the applicable fee within fifteen (15) calendar days after a new pharmacist is designated to supervise.

(3) Sterile compounding and drug outsourcing activities must be safely and accurately performed at all times to ensure that only drugs of appropriate quality are distributed. No counterfeit, misbranded, expired, or adulterated drug may be compounded, distributed, sold, or brokered by or on behalf of a drug outsourcer.

(A) All individuals employed or engaged in sterile compounding or drug outsourcer activities must have sufficient education, training, or experience to perform the duties assigned. A list must be maintained of all individuals engaged in sterile compounding or in drug outsourcer activities with a description of the individual's duties.

(B) Drug outsourcers located in this state may only purchase or receive legend drugs and/or drug related devices from an entity licensed as a Missouri drug distributor, third-party logistics provider, drug outsourcer, or pharmacy.

(C) Medication held for distribution must be stored in a secure area where only authorized personnel have access to them. A list of all individuals who have independent access to drug storage areas must be maintained. The list must be maintained for three (3) years and must be readily retrievable on request of the board or the board's authorized designee.

(D) The outside shipping container of received medication and product ingredients must be visually examined for identity and for container and content integrity to prevent the acceptance or distribution of any contaminated, adulterated, or otherwise unfit medication. Any prescription drug or drug ingredient whose immediate or sealed outer container or sealed secondary container has been opened, used, or improperly compromised must be quarantined and physically separated from the facility's active inventory.

(E) Medication shipped for distribution or further use must be carefully inspected prior to shipping/distribution for identity and to ensure no contaminated, adulterated, or misbranded drug or compounded preparation is distributed. Licensees shall maintain and follow security procedures for delivering drugs and compounded preparations from the facility to the destination site.

(F) Drug outsourcers must develop and implement written policies and procedures to ensure the safe and appropriate delivery of prescription drugs within the temperature requirements recommended by the manufacturer or the *United States Pharmacopeia* (USP).

(G) For returned medication, licensees must consider the conditions under which the drug has been held, stored, or shipped, the condition of the drug and its container/carton and any other relevant factor that may reflect on the drug's fitness for further use or distribution. If the conditions under which medication has been returned cast doubt on the drug's safety, identity, strength, quality, or purity, then the drug must be destroyed or returned to the supplier, unless

examination, testing, or other investigation proves that the drug meets appropriate standards of safety, identity, strength, quality, and purity.

(H) Drug products must be labeled as required by the manufacturer and state and federal law, including, section 338.059.2, RSMo.

(4) Facility Standards. The following standards are applicable to all drug outsourcing facilities:

(A) Drug outsourcing facilities must be securely maintained at all times to prevent unauthorized access to the facility, drugs, or drug storage areas. Additionally, the facility must be equipped with a security system that will provide suitable protection against theft and diversion, including, electronic theft or diversion. All facilities must be equipped with an alarm system to detect unauthorized entry after hours.

(B) Appropriate sewage disposal and a hot and cold water supply must be available.

(C) Waste and hazardous materials must be handled and disposed of in compliance with applicable state and federal law.

(D) Drug outsourcing facilities must be free from insects, vermin, and animals of any kind, except for service animals as defined by the Americans with Disabilities Act (ADA).

(E) Medication must be properly stored and maintained in a thermostatically controlled area within temperature and humidity requirements as provided in the FDA approved drug product labeling or the *United States Pharmacopeia* (USP).

(F) Temperatures in drug storage areas must be recorded and reviewed at least once each day the facility is in operation. Alternatively, a continuous temperature monitoring system may be used if the system maintains ongoing documentation of temperature recordings that alerts the pharmacist designated with the board for supervising the facility or alerts designated facility staff when temperatures are outside of the required range.

(G) No outdated, misbranded, or adulterated drugs or devices may be dispensed or maintained within the facility's active inventory, including prescription and related nonprescription items. Outdated, misbranded, or adulterated medication must be quarantined in a clearly identified segregated area and maintained separately from drugs intended for distribution or compounding.

(H) Medication may not be stored on the floor. Drug products must be raised above floor level and placed on a pallet or similar device.

(I) Drug outsourcers must report any recall of medication or a sterile preparation that is, or suspected to be, misbranded, adulterated, or non-sterile. Recalls must be reported to the board in writing within seven (7) days of a recall.

(5) Policies and Procedures. Drug outsourcers must maintain and follow current and accurate policies and procedures governing all aspects of the facility's drug outsourcing activities. Policies and procedures may be physically or electronically maintained at the facility, provided the policies/procedures are immediately retrievable at the request of the board or the board's authorized designee.

(6) Record-Keeping. Drug outsourcer records must be accurately maintained in compliance with state and federal law. Additionally, licensees must maintain inventories and records of all transactions regarding the receipt, distribution, compounding, or other disposition of prescription drugs or sterile preparations. Unless otherwise provided by law, records required by Chapter 338 or this rule must be maintained for three (3) years. Records may be manually or electronically maintained, provided the record is readily retrievable and available for inspection, photographing, or duplication at the request of the board or the board authorized designee or at the request of authorized federal, state, or local law enforcement officials. Records maintained offsite and not electronically retrievable at the drug outsourcer facility must be made available for inspection within two (2) working days of a request by the board or an authorized board designee.

AUTHORITY: sections 338.140, 338.150, 338.280, and 338.350, RSMo 2016, and sections 338.315, 338.330, 338.333, 338.337, and 338.340, RSMo Supp. 2018. Emergency rule filed Nov. 28, 2018, effective Dec. 8, 2018, expires June 5, 2019. An emergency rule and a proposed rule covering this same material will be published in the January 2, 2019, issue of the ***Missouri Register****.*