

# Emergency Rules

## Title 20—DEPARTMENT OF INSURANCE, FINANCIAL INSTITUTIONS AND PROFESSIONAL REGISTRATION

### Division 2220—State Board of Pharmacy Chapter 2—General Rules

#### EMERGENCY AMENDMENT

**20 CSR 2220-2.200 Sterile Compounding.** The board is amending sections (9) and (20) of the rule.

*PURPOSE:* This board is amending sections (9) and (20) of this rule to clarify the requirements for in-use times/beyond-use dating and remedial investigations as the result of environmental monitoring.

*EMERGENCY STATEMENT:* This emergency amendment is being promulgated to protect the lives of Missouri citizens by ensuring the continued availability and supply of radiopharmaceuticals and sterile compounding services in this state. Specifically, the rule currently requires sterile compounding pharmacies to immediately terminate sterile compounding if an environmental monitoring sample/test demonstrates results that exceed the United States Pharmacopeia's Chapter 797 action levels, or if a highly pathogenic microorganism is detected in designated ISO classified areas. Sterile compounding 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 technique in a properly controlled aseptic environment to eliminate the risk of preparation contamination.

In May 2018, the board received correspondence from Truman Medical Center, St. Luke's Medical Center, Kansas University Medical Center, and other sterile compounding pharmacies indicating the board's rule was detrimentally and significantly impacting patient care by forcing pharmacies to immediately terminate sterile compounding activities in the event of an identified testing result. Licensees contended the requirement unnecessarily impedes patient care by forcing the complete shutdown of compounding activities even if test results are minor, show no risk of patient harm, or can be easily remedied. In some instances, patients were reportedly denied treatment pending receipt of testing results which could take multiple days. Other sterile compounding pharmacies indicated being forced to suspend needed compounding services to Missouri hospitals, health care facilities, and other medical providers with little or no notice. Significantly, some of these compounded medications may be needed for emergency patient care and/or may not be available from another pharmacy equipped to provide specialized sterile compounding services within a medically appropriate timeframe.

In February 2018, the board was also petitioned by Missouri nuclear pharmacies to amend the rule to prevent interruptions of nuclear pharmacy services. Nuclear pharmacy routinely involves the preparation of radiopharmaceutical kits which generally include a vial containing non-radionuclide components of a radiopharmaceutical preparation "to which the appropriate radionuclide is added or in which the appropriate radionuclide is diluted before medical use." In many instances, the kit contains a multi-dose vial of an ingredient(s) that is used to compound multiple preparations during a work shift that are normally intended for patient use within a short timeframe (e.g., 12 hours after preparation).

In 2016, the board amended its rule to provide single dose and pharmacy bulk ingredient vials/containers may not be used beyond the assigned in-use time which is limited to six (6) hours, unless authorized by the manufacturer. During board inspections in the fall of 2017 and early 2018, the board discovered several nuclear pharmacies were non-compliant with the six (6) hour requirement after misconstruing the requirement to be inapplicable to nuclear practice. In February 2018, board inspectors communicated the board's deter-

mination that compliance with the six- (6-) hour time limitation was applicable to all pharmacies and would be enforced. Multiple Missouri nuclear pharmacies subsequently petitioned the board to amend the rule to protect patients and ensure availability of nuclear medications throughout the state.

Specifically, licensees reported most nuclear kits/ingredients are continuously used during the day to ensure sufficient supplies are available for shipment throughout the state when a product is needed or requested. Licensees reported the rule would require them to limit production of nuclear products to comply with the six- (6-) hour requirement which would detrimentally and significantly impact patient health and safety by reducing the available supply of nuclear medication for Missouri patients. This reduction is particularly significant given the specialized nature of these products and the limited number of pharmacies qualified/equipped to compound radiopharmaceuticals in the state. Patients in rural areas would be disproportionately impacted given many of these communities do not have a nuclear pharmacy within close proximity. In some instances, these products may be needed for use in urgent/emergency care. Significantly, licensees suggested the six- (6-) hour in-use time was unnecessary for nuclear medications due to the short beyond-use date assigned to these products because of their quick radioactive decay.

The board subsequently convened a Sterile Compounding Subcommittee in April 2018 to prepare draft language. The board also met with the Board's Nuclear Pharmacy Working Group from February to June 2018 to develop language to accommodate all practice settings and to review data regarding the stability of radiopharmaceutical products in the event of an extended in-use time.

Based on the comments and board research, the board determined an emergency rule amendment was needed to protect the lives of Missouri citizens by ensuring the continued availability of nuclear pharmacy and compounding services for Missouri's patients, hospitals, healthcare facilities, and other healthcare providers. Absent an emergency amendment, the Missouri drug supply would be significantly and detrimentally impacted, including, the availability of medication for emergency use. 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 amendment 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 amendment is fair to all interested persons and parties under the circumstances. This emergency amendment was filed August 20, 2018, becomes effective August 30, 2018, and expires February 28, 2019.

(9) Aseptic Technique and Preparation. Appropriate quality control methods shall be maintained over compounding methods at all times to ensure proper aseptic technique.

(D) Single-dose vials/containers and pharmacy bulk vial/containers exposed to ISO Class 5 or cleaner air may be used in compounding until the assigned in-use time which shall not exceed six (6) hours after initial needle puncture, unless otherwise specified by the manufacturer. Opened single-dose ampules shall not be stored for any time period. The in-use time must be placed on the vial/container. **For multiple-dose vials/containers with no antimicrobial preservative used in the preparation of radiopharmaceuticals whose beyond-use dates are twenty-four (24) hours or less, the in-use time shall not exceed twenty-four (24) hours.**

*[(20) Remedial Investigations: A remedial investigation shall be required if: 1) any sampling or testing required by this rule demonstrates a colony forming unit (CFU) count that exceeds USP Chapter 797 recommended action levels for the type of sampling/testing and/or 2) if a highly pathogenic microorganism is detected in any preparation or ISO classified area (e.g.,*

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# Emergency Rules

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*Gram-negative rods, coagulase positive staphylococcus, molds, fungus, or yeasts).*

(A) CSPs and any ingredients used within the compounding process that are part of the remedial investigation shall be quarantined until the results of the investigation are known. All affected areas shall be resampled to ensure a suitable state of microbial control as part of the remedial investigation. If a highly pathogenic microorganism is detected, or if the CFU count exceeds USP 797 action levels in any ISO-5 or ISO-7 classified area, no further compounding shall be performed until resampling shows a suitable state of microbial control. The pharmacy shall ensure that no misbranded, contaminated, or adulterated CSP is administered or dispensed for patient use.

(B) The pharmacy shall notify the board in writing within seven (7) days if any preparation or environmental monitoring/testing detects a highly pathogenic microorganism, regardless of CFU count.]

(20) Remedial Investigations. A remedial investigation shall be required if any environmental monitoring sample demonstrates a colony forming unit (CFU) count that exceeds USP Chapter 797 recommended action levels for the type of sampling. A remedial investigation shall include resampling of all affected areas to ensure a suitable state of microbial control. CSPs and any ingredients used within the compounding process that are part of the remedial investigation shall be quarantined until the results of the investigation are known. The pharmacy shall ensure that no misbranded, contaminated, or adulterated CSP is administered or dispensed for patient use.

(A) If an environmental monitoring sample taken from an ISO-5 classified area exceeds USP 797 action levels, the pharmacy must cease compounding in the affected ISO classified area until resampling shows a suitable state of microbial control has been achieved in the affected area. However, a pharmacy may continue to compound during the remedial investigation if—

1. The affected ISO classified area is cleaned and disinfected by using a germicidal cleaning agent and a sporicidal agent followed by sterile alcohol;

2. The beyond-use date assigned to all preparations is no greater than twelve (12) hours; and

3. The affected ISO classified area is resampled under dynamic conditions. If the resampling exceeds USP Chapter 797 action levels, compounding must cease until resampling shows a suitable state of microbial control has been achieved in the affected area, unless otherwise authorized by the board or board's authorized designee to continue compounding upon a showing the facility can be operated in a manner not to endanger the public safety.

(B) If an environmental monitoring sample taken from an ISO-7 classified buffer area exceeds USP 797 action levels, the pharmacy must cease compounding in the affected ISO classified buffer area until resampling shows a suitable state of microbial control has been achieved in the affected area. However, a pharmacy may continue to compound during the remedial investigation if—

1. The affected ISO classified area is cleaned and disinfected by using a germicidal cleaning agent and a sporicidal agent;

2. The beyond-use date assigned to Risk Level 1 preparations is not greater than twenty-four (24) hours or, for Risk level 2 and 3 preparations, no greater than twelve (12) hours; and

3. The affected ISO classified area is resampled under dynamic conditions. If two (2) consecutive resamplings exceed USP 797 action levels, compounding must cease until resampling shows a suitable state of microbial control has been achieved in the affected area, unless otherwise authorized by the board or board's authorized designee to continue compounding upon a

showing the facility can be operated in a manner not to endanger the public health or safety.

(C) The pharmacy shall notify the board in writing within three (3) days of any environmental monitoring sample collected as part of a remedial investigation that exceeds USP 797 action levels.

*AUTHORITY: sections 338.010, 338.140, 338.240, and 338.280, RSMo [Supp.] 2016. This rule originally filed as 4 CSR 220-2.200. Original rule filed May 4, 1992, effective Feb. 26, 1993. For intervening history, please consult the Code of State Regulations. Emergency amendment filed Aug. 20, 2018, effective Aug. 30, 2018, expires Feb. 28, 2019. An emergency amendment and a proposed amendment covering this same material will be published in the October 1, 2018, issue of the Missouri Register.*