

## **Meeting Notice**

**Missouri Board of Pharmacy  
Conference Call  
May 20, 2016 1:00 p.m.  
Professional Registration  
3605 Missouri Blvd  
Jefferson City, MO 65109**

Notification of special needs as addressed by the Americans with Disabilities Act should be forwarded to the Missouri Board of Pharmacy, P O Box 625, 3605 Missouri Blvd., Jefferson City, Missouri 65102, or by calling (573) 751-0091 to ensure available accommodations. The text telephone for the hearing impaired is (800) 735-2966.

Except to the extent disclosure is otherwise required by law, the Missouri Board of Pharmacy is authorized to go into closed session and that all votes, to the extent permitted by law, pertaining to and/or resulting from this closed meeting will be closed under Section 610.021(1), (5), (7), and (14), and under Section 324.001.8, RSMo.

The Board may go into closed session at any time during the meeting pursuant to § 610.021(1) for purposes of legal advice. If the meeting is closed the appropriate section will be announced to the public with the motion and vote recorded in open session minutes.

If any member of the public wishes to attend the open portion of the telephone conference call, s/he should be present at the Missouri Board of Pharmacy, 3605 Missouri Blvd., Jefferson City, Missouri, at 1:00 p.m. on May 20, 2016.

Please see attached tentative agenda for this meeting.

**TENTATIVE AGENDA  
May 20, 2016 1:00 p.m.**

**Missouri Board of Pharmacy  
Professional Registration  
3605 Missouri Blvd  
Jefferson City, MO 65109  
Conference Call**

**OPEN SESSION**

- 1 Call to Order
- 2 Roll Call
- 3 Review of Sterile Compounding Rule/Draft Revisions to 20 CSR 2220-2.200
- 4 The Board may go into closed session at any point during the meeting and all votes, to the extent permitted by law, pertaining to and/or resulting from this closed meeting will be closed under Section 610.021(1), (5), (7), and (14) and under Section 324.001.8, RSMo. The Board will return to open session at the conclusion of discussion of closed session items.
- 5 Adjournment

1 Title 20—DEPARTMENT OF  
2 INSURANCE, FINANCIAL  
3 INSTITUTIONS AND  
4 PROFESSIONAL REGISTRATION  
5 Division 2220—State Board of Pharmacy  
6 Chapter 2—General Rules  
7

8  
9 PROPOSED AMENDMENT

10 20 CSR 2220-2.200 Sterile Pharmaceuticals. The Board is amending all sections of this rule.  
11 Additionally, the Board is deleting sections (5), (6), (8), (15) and (16) of the current rule and  
12 adding new sections (5), (6), (7), (8), (10), (17), (20) and (21).  
13

14  
15 *PURPOSE: This Board is amending all sections of this rule to update, clarify and*  
16 *delineate requirements for sterile compounding pharmacies.*  
17

18 20 CSR 2220-2.200 Sterile ~~Pharmaceuticals~~ Compounding

19 *PURPOSE: This rule establishes standards for the ~~preparation~~, labeling, ~~and~~ distribution and*  
20 *dispensing of sterile pharmaceuticals compounded sterile preparations by licensed pharmacies,*  
21 *pursuant to a physician's order or prescription.*

22 (1) Definitions.

23 (A) Aseptic processing: The technique involving procedures designed to preclude  
24 contamination of drugs, packaging, equipment, or supplies by microorganisms during  
25 processing.

26 (B) Batch: Compounding of multiple sterile ~~product~~ preparation units in a single discrete  
27 process, by the same individuals, carried out during one (1) limited time period.

28 (C) Beyond-Use date: A date after which a compounded preparation should not be used and is  
29 determined from the date the preparation is compounded. Because compounded preparations are  
30 intended for administration immediately or following short-term storage, their beyond-use dates  
31 must be assigned based on criteria different from those applied to assigning expiration dates to  
32 manufactured drug products.

33 (D) Biological safety cabinet: Containment unit suitable for the preparation of low to moderate  
34 risk agents where there is a need for protection of the ~~product~~ preparation, personnel and  
35 environment, according to National Sanitation Foundation (NSF) International standards.

36 ~~.(E) Class 100 environment: An atmospheric environment which contains less than one~~  
37 ~~hundred (100) particles 0.5 microns in diameter per cubic foot of air, according to federal~~  
38 ~~standards.~~

39 ~~(F) Class 10,000 environment: An atmospheric environment which contains less than ten~~  
40 ~~thousand (10,000) particles 0.5 microns in diameter per cubic foot of air, according to federal~~  
41 ~~standards.~~

42 ~~.(G) Clean room: A room —~~

- 43 ~~1. In which the concentration of airborne particles is controlled;~~
- 44 ~~2. That is constructed and used in a manner to minimize the introduction, generation, and~~  
45 ~~retention of particles inside the room; and~~
- 46 ~~3. In which other relevant variables (e.g., temperature, humidity, and pressure) are controlled~~  
47 ~~as necessary.~~

48 ~~(H) Clean zone: Dedicated space —~~

- 49 ~~1. In which the concentration of airborne particles is controlled;~~
- 50 ~~2. That is constructed and used in a manner that minimizes the introduction, generation, and~~  
51 ~~retention of particles inside the zone; and~~
- 52 ~~3. In which other relevant variables (e.g., temperature, humidity, and pressure) are controlled~~  
53 ~~as necessary.~~

54 ~~This zone may be open or enclosed and may or may not be located within a clean room.~~

55 (E) Buffer Area: An ISO Class 7 or better area where the primary engineering control is  
56 physically located that is constructed and used in a manner to minimize the introduction,  
57 generation, and retention of particles inside the room and in which other relevant variables (e.g.,  
58 temperature, humidity, and pressure) are controlled as necessary.

59 ~~(F) Compounding: For the purposes of this regulation, compounding is defined as in 20 CSR~~  
60 ~~2220-2.400(1). Compounded sterile medications may include, but are not limited to, ~~injectables,~~~~  
61 ~~parenteral nutrition solutions, irrigation solutions, inhalation solutions, intravenous solutions and~~  
62 ~~ophthalmic preparations.:~~

- 63 1. Compounded biologics, diagnostics, drugs, nutrients, and radiopharmaceuticals that  
64 must or are required to be sterile when they are administered to patients, including, but not  
65 limited to the following dosage forms: bronchial and inhaled nasal preparations intended for  
66 deposition in the lung, baths and soaks for live organs and tissues, epidural and intrathecal

67 solutions, bladder/wound solutions, injectables, implantable devices and dosage forms,  
68 inhalation solutions, intravenous solutions, irrigation solutions, ophthalmic preparations,  
69 parenteral nutrition solutions, and repackaged sterile preparations. Nasal sprays and irrigations  
70 intended for deposit in the nasal passages may be prepared as nonsterile compounds;

71 2. An FDA approved manufactured sterile product that is either prepared according to  
72 the manufacturers' approved labeling/recommendations or prepared differently than published in  
73 such labeling; and

74 3. Assembling point-of-care assembled systems.

75 (G) Compounding Aseptic Containment Isolator (CACI): A RABS that is designed for  
76 compounding sterile hazardous drugs and designed to provide worker protection from exposure  
77 to undesirable levels of airborne drugs throughout the compounding and material transfer  
78 processes and to provide an aseptic environment for CSPs.

79 (H) Compounding Aseptic Isolator (CAI): A RABS specifically designed for compounding  
80 sterile non-hazardous pharmaceutical ingredients or CSPs and designed to maintain an aseptic  
81 compounding environment within the isolator throughout the compounding and material transfer  
82 processes.

83 ~~(I)~~(I) Controlled area: For purposes of these regulations, a controlled area is ~~the area a~~  
84 separate room designated for preparing sterile ~~products~~preparations or an area designated for  
85 preparing sterile preparations that is separated from other activities/operations by a line of  
86 demarcation that clearly separates the area from other operations. ~~This is referred to as the buffer~~  
87 ~~zone (i.e., the clean room in which the laminar airflow workbench is located) by the United~~  
88 ~~States Pharmacopoeia (USP).~~

89 ~~(K)~~(J) Critical area: Any area in the controlled area where ~~products~~ preparations or containers  
90 are exposed to the environment.

91 ~~(L)~~(K) Critical site: ~~An opening providing a direct pathway between a sterile product and the~~  
92 ~~environment or any surface coming into contact with the product or environment.~~ Any surface,  
93 pathway or opening (e.g., vial septa, injection ports, beakers, needle hubs) that provides a direct  
94 pathway between a compounded sterile preparation or other ingredient used to compound a  
95 sterile preparation and the air, environment or moisture or that poses a risk of touch  
96 contamination.

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97 ~~(M) Critical surface: Any surface that comes into contact with previously sterilized products or~~  
98 ~~containers.~~

99 (L) CSP: Compounded sterile preparation.

100 ~~(N)(M)~~ Cytotoxic drugs: A pharmaceutical product that has the capability of direct toxic action  
101 on living tissue that can result in severe leukopenia and thrombocytopenia, depression of the  
102 immune system and the alteration of a host's inflammatory response system.

103 ~~(O)(N)~~ Emergency dispensing: Is a situation where a Risk Level 3 ~~product~~preparation is  
104 necessary for immediate administration of the ~~product~~preparation -and no alternative product is  
105 available and the prescriber is informed that the ~~product~~preparation is being dispensed prior to  
106 appropriate testing. Documentation of the dispensing of the ~~product~~preparation, the prescriber's  
107 approval for dispensing prior to the receipt of test results and the need for the emergency must  
108 appear within the prescription record. A separate authorization from the prescriber is required  
109 for each emergency dispensing.

110 ~~(P)(O)~~ High-Efficiency Particulate Air (HEPA) filter: A filter composed of pleats of filter  
111 medium separated by rigid sheets of corrugated paper or aluminum foil that direct the flow of air  
112 forced through the filter in a uniform parallel flow. HEPA filters remove ninety-nine point  
113 ninety-seven percent (99.97%) of all particles three-tenths (0.3) microns or larger. When HEPA  
114 filters are used as a component of a horizontal- or vertical-laminar-airflow workbench, an  
115 environment can be created consistent with standards for ~~a Class 100 clean room~~an ISO 5  
116 environment.

117 (P) In-Use Time/Date: The time/date before which a conventionally manufactured product or  
118 a CSP must be used after it has been opened or needle-punctured.

119 (Q) ISO Class 5: An area with less than 3,520 particles (0.5 µm and larger in size) per cubic  
120 meter.

121 (R) ISO Class 7: An area with less than 352,000 particles (0.5 µm and larger in size) per cubic  
122 meter.

123 ~~(Q) Isolator (or barrier isolator): A closed system made up of four (4) solid walls, an air-~~  
124 ~~handling system, and transfer and interaction devices. The walls are constructed so as to provide~~  
125 ~~surfaces that are cleanable with coving between wall junctures. The air handling system provides~~  
126 ~~HEPA filtration of inlet air. Transfer of materials is accomplished through air locks, glove rings,~~

127 ~~or ports. Transfers are designed to minimize the entry of contamination. Manipulations can take~~  
128 ~~place through either glove ports or half suits.~~

129 (S) Multiple-Dose Container: A multiple unit container for articles or compounded sterile  
130 preparations that contains more than one dose of medication and usually contains an  
131 antimicrobial preservative.

132 ~~(R)~~(T) Parenteral: A sterile preparation of drugs for injection through one (1) or more layers of  
133 skin.

134 (U) Primary Engineering Control (PEC): A system that provides an ISO 5 environment for  
135 the exposure of critical sites when compounding sterile preparations. PECs include, but may not  
136 be limited to, horizontal/vertical laminar airflow hoods, biological safety cabinets, RABS such as  
137 compounding aseptic isolators (CAIs) or compounding aseptic containment isolators (CACIs).

138 (V) Point of Care Assembled System: A closed system device that creates a physical barrier  
139 between diluents, fluids or other drug components and is designed to be activated by the end user  
140 by allowing the components to mix prior to administration.

141 ~~(S)~~(W) Process validation or simulation: Microbiological simulation of an aseptic process with  
142 growth medium processed in a manner similar to the processing of the ~~product~~preparation and  
143 with the same container or closure system.

144 ~~(P)~~(X) Quality assurance: For purposes of these regulations, quality assurance is the set of  
145 activities used to ensure that the processes used in the preparation of sterile drug  
146 ~~products~~preparations lead to ~~products~~preparations that meet predetermined standards of quality.

147 ~~(U)~~(Y) Quality control: For the purposes of these regulations, quality control is the set of  
148 testing activities used to determine —that the ingredients, components and final sterile  
149 ~~products~~preparations prepared meet predetermined requirements with respect to identity, purity,  
150 nonpyrogenicity and sterility.

151 (Z) RABS: Restricted access barrier system (RABS): A primary engineering control that is  
152 comprised of a closed system made up of four (4) solid walls, an air-handling system, and  
153 transfer and interaction devices. The walls are constructed so as to provide surfaces that are  
154 cleanable with coving between wall junctures. The air-handling system provides HEPA filtration  
155 of inlet air. Transfer of materials is accomplished through air locks, glove rings, or ports.  
156 Transfers are designed to minimize the entry of contamination. Manipulations can take place

157 [through either glove ports or half suits. Examples of a RABS may include, but is not limited to, a](#)  
158 [CAI or CACI.](#)

159 ~~(V)~~(AA) Repackaging: The subdivision or transfer of a compounded ~~product~~[preparation](#) from  
160 one container or device to a different container or device.

161 [\(BB\) Single-Dose/Single-Unit Container/Vial: A container/vial of medication intended for](#)  
162 [administration that is meant for use in a single patient for a single case, procedure or injection.](#)

163 ~~(W) Sterile pharmaceutical: A dosage form free from living microorganisms.~~

164 ~~(X)~~(CC) Sterilization: A validated process used to render a ~~product~~[preparation](#) free of viable  
165 organisms.

166 ~~(Y)~~(DD) Temperatures:

167 1. Frozen means temperatures between twenty-[five degrees](#) below zero and ten degrees  
168 [below zero](#) Celsius ~~(-20 and 10°C) (four below zero and fourteen degrees Fahrenheit (-4 and~~  
169 ~~14°F))~~. [\(-25° and -10°C\) \(thirteen degrees below zero and fourteen degrees Fahrenheit \(-13° and](#)  
170 [14°F\)\)](#).

171 2. Refrigerated means temperatures between two and eight degrees Celsius (2 and 8°C)  
172 (thirty-six and forty-six degrees Fahrenheit (36 and 46°F)).

173 3. [Controlled R](#)room temperatures ~~means room temperatures between fifteen and thirty~~  
174 ~~degrees Celsius (15 and 30°C) (fifty nine and eighty six degrees Fahrenheit (59 and 86°F))~~. [a](#)  
175 [temperature maintained thermostatically that encompasses the usual and customary working](#)  
176 [environment of 20° to 25° Celsius \(68° to 78° F\). Excursions between 15° and 30° Celsius](#)  
177 [\(59° to 86° F\) as commonly experienced in pharmacies and other facilities shall be deemed](#)  
178 [compliant. Transient spikes up to 40° Celsius are permitted as long as they do not exceed 24](#)  
179 [hours. Spikes above 40° Celsius are permitted if allowed by the manufacturer.](#)

180 [\(EE\) USP: The United States Pharmacopeia and the National Formulary \(USP-NF\) as](#)  
181 [adopted and published by the United States Pharmacopeial Convention, effective May 2013.](#)  
182 [Copies of the USP-NF are published by, and available from, USP, 12601 Twinbrook Parkway,](#)  
183 [Rockville, MD 20852-1790 or online at <http://www.usp.org/>. The USP-NF is incorporated](#)  
184 [herein by reference. This rule does not include any later amendments or additions to the USP-](#)  
185 [NF.](#)

186 ~~(Z)~~(FF) Validation: Documented evidence providing a high degree of assurance that specific  
187 processes will consistently produce a productpreparation meeting predetermined specifications  
188 and quality attributes.

189 ~~(AA)~~(GG) Definitions of sterile compounded productpreparations by risk level:

190 1. Risk Level 1: Applies to compounded sterile productpreparations that exhibit  
191 characteristics A., B., ~~and~~or C., stated below. All Risk Level 1 productpreparations shall be  
192 prepared with sterile equipment; ~~and~~ sterile ingredients and solutions ~~and sterile contact surfaces~~  
193 ~~for the final product~~in an ISO Class 5 environment. Risk Level 1 includes the following:

194 A. ProductPreparations:

195 (I) Stored at controlled room temperature and ~~completely administered within~~ assigned a  
196 beyond-use date of forty-eight (48) hours ~~after preparation or less~~; or

197 (II) Stored under refrigeration ~~for~~ and assigned a beyond-use date of seven (7) days or  
198 less ~~before complete administration to a patient over a period not to exceed forty eight (48)~~  
199 ~~hours~~; or

200 (III) ~~Stored Frozen for~~ and assigned a beyond-use date of thirty (30) days or less ~~before~~  
201 ~~complete administration to a patient over a period not to exceed forty eight (48) hours~~.

202 B. Unpreserved sterile productpreparations prepared for administration to one (1) patient or  
203 batch-prepared productpreparations containing suitable preservatives prepared for administration  
204 to more than one (1) patient with an assigned beyond-use date that does not exceed the beyond-  
205 use date allowed for under section (1)(GG)1.A. of this rule.

206 C. ProductPreparations prepared by closed-system aseptic transfer of sterile, nonpyrogenic,  
207 finished pharmaceuticals (e.g., from vials or ampules) obtained from licensed manufacturers into  
208 sterile final containers obtained from licensed manufacturers with an assigned beyond-use date  
209 that does not exceed the beyond-use date allowed under section (1)(GG)1.A. of this rule.

210 2. Risk Level 2: Sterile productpreparations exhibit characteristic A., B., or C., stated below.  
211 All Risk Level 2 productpreparations shall be prepared with sterile equipment; ~~and~~ sterile  
212 ingredients and solutions ~~and sterile contact surfaces for the final product~~in an ISO Class 5  
213 environment and with closed-system transfer methods. Risk Level 2 includes the following:

214 A. ~~Products stored beyond seven (7) days under refrigeration, stored beyond thirty (30)~~  
215 ~~days frozen or administered beyond forty eight (48) hours after preparation and storage at room~~  
216 ~~temperature~~. Preparations stored under refrigeration and assigned a beyond-use date greater than

217 seven (7) days or preparations stored frozen and assigned a beyond-use date greater than thirty  
218 (30) days or preparations stored at controlled room temperature and assigned a beyond-use date  
219 greater than forty-eight hours.

220 B. Batch-prepared ~~product~~preparations without preservatives that are intended for use by  
221 more than one (1) patient.

222 C. ~~Product~~Preparations compounded by complex or numerous manipulations of sterile  
223 ingredients obtained from licensed manufacturers in a sterile container or reservoir obtained from  
224 a licensed manufacturer by using closed-system aseptic transfer (e.g., automated compounder).

225 3. Risk Level 3: Sterile ~~products~~preparations exhibit either characteristic A. or B.:

226 A. ~~Products~~Preparations compounded from nonsterile ingredients or compounded with  
227 nonsterile components, containers or equipment before terminal sterilization.

228 B. ~~Products~~Preparations prepared by combining multiple ingredients (sterile or nonsterile)  
229 by using an open-system transfer or open reservoir before terminal sterilization.

230 (2) Policy and Procedure Manual/Reference Manuals.

231 (A) A manual, outlining policies and procedures encompassing all aspects of Risk Level 1, 2  
232 and 3 ~~products~~ compounding, shall be available for inspection at the pharmacy. The manual shall  
233 be reviewed on an annual basis. The pharmacy shall have current reference materials related to  
234 sterile ~~products~~ preparations.

235 (3) Personnel Education, Training and Evaluation.

236 (A) Risk Level 1: All pharmacy personnel preparing sterile ~~products~~preparations must receive  
237 suitable didactic and experiential training in aseptic technique and procedures and shall be  
238 skilled and trained to accurately and competently perform the duties assigned. Additional  
239 training must be provided if the risk level of sterile activity conducted by the individual changes  
240 or if there is a change in compounding methods performed. To ensure competency, individuals  
241 preparing sterile preparations must successfully pass an Aseptic Technique Skill Assessment that  
242 complies with section (10) of this rule. The pharmacy shall establish policies and procedures for  
243 staff training and assessment.

244 (B) Risk Level 2: In addition to Risk Level 1 requirements, personnel training must includes  
245 assessment of competency in all Risk Level 2 procedures via process simulation.

246 (C) Risk Level 3: In addition to Risk Level 1 and 2 requirements, operators have specific  
247 education, training and experience to prepare Risk Level 3 ~~products~~ preparations. The pharmacist  
248 knows principles of good compounding practice for risk level ~~products~~preparations, including—

- 249 1. Aseptic processing;
- 250 2. Quality assurance of environmental, component, and end-~~product~~preparation testing;
- 251 3. Sterilization; and
- 252 4. Selection and use of containers, equipment, and closures.

253 (4) Storage and Handling in the Pharmacy.

254 (A) Risk Level 1 and 2: Solutions, drugs, supplies and compounding equipment must be stored  
255 ~~according to manufacturer or USP requirements~~ and maintained in a manner that will maintain  
256 the chemical and microbiological stability of CSPs. Refrigeration ~~and~~, freezer and, if applicable,  
257 incubator temperatures shall be documented daily. Other storage areas shall be inspected  
258 regularly to ensure that temperature and lighting meet requirements. Drugs and supplies shall be  
259 shelved above the floor. Removal of ~~products~~drugs and supplies from boxes shall be done  
260 outside controlled areas. Removal of used supplies from the controlled area shall be done at least  
261 daily. ProductPreparation recall procedures must comply with section (21) of this rule and must  
262 permit retrieving affected ~~product~~preparations from specific involved patients.

263 (B) Risk Level 3: In addition to Risk Level 1 and 2 requirements, the pharmacy must establish  
264 procedures ~~include for~~ procurement, identification, storage, handling, testing, and recall of  
265 components and finished ~~products~~ preparations. Finished ~~but untested~~ Risk Level 3 ~~products~~  
266 preparations awaiting test results must be quarantined under minimal risk for contamination in a  
267 manner that will maintain chemical and microbiological stability.

268 ~~(5) Facilities and Equipment.~~

269 ~~(A) Risk Level 1: The controlled area shall be separated from other operations. The controlled~~  
270 ~~area must be clean and well lit. A sink with hot and cold water must be near, but not in, the~~  
271 ~~controlled area. The controlled area and inside equipment must be cleaned and disinfected~~  
272 ~~regularly. Sterile products must be prepared in at least a Class 100 environment (the critical~~  
273 ~~area). Computer entry, order processing, label generation, and record keeping shall be performed~~  
274 ~~outside the critical area. The critical area must be disinfected prior to use. A workbench shall be~~  
275 ~~recertified every six (6) months and when it is moved; prefilters must be visually inspected on a~~

276 ~~regularly scheduled basis and replaced according to manufacturer's specifications. Pumps~~  
277 ~~utilized in the compounding process shall be recalibrated and documented according to~~  
278 ~~manufacturer procedures.~~

279 ~~(B) Risk Level 2: In addition to all Risk Level 1 requirements, the controlled area must meet~~  
280 ~~Class 10,000 clean room standards; cleaning supplies should be selected to meet clean room~~  
281 ~~standards; critical area work surface must be cleaned between batches; floors should be~~  
282 ~~disinfected daily; equipment surfaces weekly; and walls monthly; with applicable environmental~~  
283 ~~monitoring of air and surfaces. Automated compounding devices must be calibrated and verified~~  
284 ~~as to accuracy, according to manufacturer procedures. Clean rooms not utilized on a daily basis~~  
285 ~~must be cleaned prior to use as stated above.~~

286 ~~(C) Risk Level 3: In addition to Risk Level 1 and 2 requirements, products must be prepared in~~  
287 ~~a Class 100 workbench in a Class 10,000 clean room, in a Class 100 clean room or within a~~  
288 ~~positive pressure barrier isolator. Access to the clean room must be limited to those preparing the~~  
289 ~~products and who are in appropriate garb. Equipment must be cleaned, prepared, sterilized,~~  
290 ~~calibrated, and documented according to manufacturer's standards. Walls and ceilings must be~~  
291 ~~disinfected weekly. All non-sterile equipment that is to come in contact with the sterilized final~~  
292 ~~product must be sterilized before introduction in the clean room. Appropriate cleaning and~~  
293 ~~disinfection of the environment and equipment are required.~~

294 (5) Facilities and Equipment. The pharmacy shall establish and follow proper controls to  
295 ensure environmental quality, prevent environmental contamination and maintain air quality in  
296 all ISO classified areas.

297 (A) Risk Level 1: Risk Level 1 preparations must be prepared in a PEC located in a controlled  
298 area that meets the requirements of this rule. A sink with hot and cold water must be near, but  
299 not in, the controlled area. The controlled area and inside equipment must be cleaned and  
300 disinfected as provided in section (17) of this rule. Activities within the critical area shall be  
301 kept to a minimum to maintain the ISO classified environment. Primary engineering controls  
302 shall meet the requirements of section (6) of this rule; prefilters must be visually inspected on a  
303 regularly scheduled basis and replaced according to manufacturer's specifications. Pumps  
304 utilized in the compounding process shall be recalibrated and documented according to  
305 manufacturer procedures.

306 (B) Risk Level 2: In addition to all Risk Level 1 requirements, Risk Level 2 preparations must  
307 be prepared in a PEC located in a buffer area or prepared in a RABS located within a controlled  
308 area. Risk Level 2 preparations shall at a minimum remain a Risk Level 2 for the life of the  
309 preparation.

310 (C) Risk Level 3: In addition to Risk Level 1 and 2 requirements, Risk Level 3 preparations  
311 must be prepared in a PEC located in a buffer area or prepared in a RABS located within a  
312 controlled area. All non-sterile equipment that is to come in contact with the sterilized final  
313 preparation must be sterilized before introduction in the buffer area or into the RABS. Once  
314 compounded, Risk Level 3 preparations shall at a minimum remain Risk Level 3 for the life of  
315 the preparation.

316 (D) Automated compounding devices shall be tested for content, volume and weight accuracy  
317 prior to both initial and daily use according to manufacturer procedures. Test results shall be  
318 reviewed by a pharmacist to ensure compliance. The identity of the reviewing pharmacist and  
319 the review date shall be documented in the pharmacy's records.

320 (E) All PECs and ISO classified areas shall be certified to ensure compliance with  
321 requirements of this rule prior to beginning sterile compounding activities and every six (6)  
322 months thereafter. Certification shall be conducted by competent staff/vendors using recognized  
323 and appropriate certification and testing equipment. Certification results shall be reviewed by a  
324 pharmacist once received. Deficiencies or failures shall be investigated and corrected prior to  
325 further compounding which may include recertification of the PEC/ISO classified area.

326 1. The PEC and ISO classified areas must be recertified when: (1) any changes or major  
327 service occurs that may affect airflow or environmental conditions or (2) the PEC or room is  
328 relocated or the physical structure of the ISO classified area has been altered.

329 2. Corrections may include, but are not limited to, changes in the use of the affected PEC  
330 or ISO classified area or initiating a recall. The identity of the pharmacist conducting the  
331 required review and the review date shall be documented in the pharmacy's records.

332 (F) Pressure Differential: If the controlled area is equipped with a device to monitor pressure  
333 differential, pressure differential results must be recorded and documented each day that the  
334 pharmacy is open for pharmacy activities. Alternatively, a continuous monitoring system may  
335 be used to record pressure differential results if the system maintains ongoing documentation of  
336 pressure recordings or maintains pressure alerts that are reviewed daily.

337  
338 (6) Primary Engineering Controls (PECs):  
339 (A) PECs must be properly used, operated and maintained and must be located out of traffic  
340 patterns and away from conditions that could adversely affect their operation or disrupt intended  
341 airflow patterns (e.g., ventilation systems or cross-drafts).  
342 (B) PECs shall maintain ISO Class 5 or better conditions during dynamic operating conditions  
343 and while compounding sterile preparations, including, when transferring ingredients into and  
344 out of the PEC and during exposure of critical sites;  
345 (C) PECs shall provide unidirectional (laminar flow) HEPA air at a velocity sufficient to  
346 prevent airborne particles from contacting critical sites.  
347 (D) The recovery time to achieve ISO Class 5 air quality in any PEC shall be identified in the  
348 pharmacy's policies and procedures. Procedures must be developed to ensure adequate recovery  
349 time is allowed before or during compounding operations and after material transfer.  
350  
351 (7) Controlled Areas. The controlled area shall be designed, maintained and controlled to allow  
352 effective cleaning and disinfection and to minimize the risk of contamination and the  
353 introduction, generation and retention of particles inside the PEC.  
354 (A) Controlled areas must be clean and well-lit and shall be free of infestation by insects,  
355 rodents and other vermin. Trash shall be disposed of in a timely and sanitary manner and at least  
356 daily. Tacky mats or similar articles shall be prohibited in the controlled area or any ISO  
357 classified environment.  
358 (B) Traffic flow in or around the controlled area shall be minimized and controlled. Food  
359 items, chewing gum, eating, drinking and smoking are prohibited in the area;  
360 (C) Nonessential objects that shed particles shall not be brought into the controlled area,  
361 including, but not limited to, pencils, cardboard cartons, paper towels, and cotton items (e.g.,  
362 gauze pads). Furniture, carts, supplies and equipment shall be removed from shipping  
363 cartons/containers and properly cleaned and disinfected with sterile alcohol before entering any  
364 ISO classified area. No shipping or other external cartons may be taken into the controlled area  
365 or an ISO classified area.  
366 (D) Only supplies essential for compounding shall be stored in the controlled area. Supplies or  
367 other non-essential equipment shall not be stored in or on the PEC.

368 ~~(6) Apparel.~~  
369 ~~(A) Risk Level 2: In the controlled area, personnel wear low particulate, clean clothing covers.~~  
370 ~~Head and facial hair is covered. Gloves, gowns, and masks are required. During sterile~~  
371 ~~preparation gloves shall be rinsed frequently with a suitable agent and changed when integrity is~~  
372 ~~compromised.~~

373 ~~(B) Risk Level 3: In addition to Risk Level 2 requirements, clean room apparel must be worn~~  
374 ~~inside the controlled area at all times during the preparation of Risk Level 3 sterile products~~  
375 ~~except when positive pressure barrier isolation is utilized. Attire shall consist of a low shedding~~  
376 ~~coverall, head cover, face mask, and shoe covers.~~

377 (8) Garbing and Hand Hygiene. Individuals engaged in, or assisting with, CSPs shall be  
378 trained and demonstrate competence in proper personal garbing, gloving and hand hygiene.  
379 Competence must be documented and assessed through direct visual observation as part of the  
380 aseptic technique skill assessment required by this rule.

381 (A) Risk Level 1: Low-particulate and non-shedding gowns, hair covers, gloves, face masks  
382 and beard covers must be worn during compounding and cleaning. All head and facial hair must  
383 be covered. During sterile preparation, gloves shall be disinfected before use and frequently  
384 thereafter with a suitable agent and changed when integrity is compromised. All personnel in the  
385 controlled area must be appropriately garbed as required by this section.

386 (B) Risk Level 2 and Risk Level 3: In addition to Risk Level 1 requirements, shoe covers and  
387 sterile gloves must be worn while compounding and cleaning, including, over RABS gloves. All  
388 personnel in the controlled or buffer area must garb as required by this section.

390 ~~(7)~~(9) Aseptic Technique and Product Preparation. Appropriate quality control methods shall  
391 be maintained over compounding methods at all times to ensure proper aseptic technique.

392 (A) Risk Level 1: Sterile ~~products~~preparations must be prepared in ~~a Class 100~~ an ISO Class 5  
393 environment. Personnel shall scrub their hands and forearms for ~~an appropriate period at the~~  
394 ~~beginning of each aseptic compounding process~~ a minimum of thirty (30) seconds and remove  
395 debris from underneath fingernails under warm running water before donning the required  
396 gloves. Eating, drinking and smoking are prohibited in the controlled area. Talking shall be  
397 minimized to reduce airborne particles. Ingredients shall be determined to be stable, compatible,

398 | and appropriate for the ~~productpreparation~~ to be prepared, according to manufacturer, USP, or  
399 | scientific references. Ingredients and containers shall be inspected for defects, expiration and  
400 | integrity before use. Only materials essential for aseptic compounding shall be placed in the  
401 | ~~workbenchPEC. Surfaces of ampules and vials shall be disinfected before placement in the~~  
402 | ~~workbench.~~ Supplies, equipment and the surfaces of ampules and vials shall be disinfected  
403 | before entering the PEC by wiping the outer surface with sterile alcohol or an equivalently  
404 | effective non-residue generating disinfectant. Sterile components shall be arranged in the  
405 | ~~workbenchPEC~~ to allow clear, uninterrupted laminar airflow path of HEPA-filtered air over  
406 | critical ~~surfaces of needles, vials, ampules, etc.~~sites. Automated devices and equipment shall be  
407 | cleaned, disinfected and placed in the ~~workbenchPEC~~ to enable laminar airflow. Aseptic  
408 | technique shall be used to avoid touch contamination of critical sites of containers and  
409 | ingredients. Particles shall be filtered from solutions if applicable. Needle cores shall be avoided.  
410 | The pharmacist shall check before, during, and after preparation to verify the identity and  
411 | amount of ingredients before release.

412 | (B) Risk Level 2: In addition to Risk Level 1 requirements, a file containing the formula,  
413 | components, procedures, sample label, and final evaluation shall be made for each  
414 | ~~productpreparation~~batch. A separate work sheet and lot number for each batch shall be  
415 | completed. When combining multiple sterile ~~products~~ preparations, a second verification of  
416 | calculations shall take place. The pharmacist shall verify data entered into any automatic  
417 | compounder before processing and check the end ~~productpreparation~~ for accuracy.

418 | (C) Risk Level 3: In addition to Risk Level 1 and 2 requirements, nonsterile components must  
419 | meet compendial standards ~~if available, as or must be~~ verified by a pharmacist and a certificate  
420 | of analysis. Batch preparation files shall also include comparisons of actual with anticipated  
421 | yields, sterilization methods, and quarantine specifications. Presterilized containers shall be used  
422 | when feasible. Final containers must be sterile and capable of maintaining ~~productpreparation~~  
423 | integrity throughout the shelf life. Sterilization methods must be based on properties of the  
424 | ~~productpreparation and must be conducted in a method recognized for the preparation by USP.~~

425 | (D) Single-dose vials/containers and pharmacy bulk vial/containers exposed to ISO Class 5 or  
426 | cleaner air may be used in compounding until the assigned in-use time which shall not exceed six  
427 | (6) hours after initial needle puncture, unless otherwise specified by the manufacturer. Opened

428 single-dose ampules shall not be stored for any time period. The in-use time must be placed on  
429 the vial/container.

430 (E) Unless otherwise specified by the manufacturer, multiple-dose vials/containers with an  
431 antimicrobial preservative may be used in compounding until the assigned in-use date which  
432 shall not exceed twenty-eight (28) days after initially entering or opening the vial/container (e.g.,  
433 needle-puncture). The in-use date must be placed on the vial/container.

434 ~~(8) Process Validation.~~

435 ~~(A) Risk Level 1: All pharmacy personnel who prepare sterile products shall pass a process~~  
436 ~~validation of aseptic technique before compounding sterile products. Pharmacy personnel~~  
437 ~~competency must be reevaluated by process validation at least annually, whenever the quality~~  
438 ~~assurance program yields an unacceptable result, or whenever unacceptable techniques are~~  
439 ~~observed. If microbial growth is detected, the entire sterile process must be evaluated, corrective~~  
440 ~~action taken, and the process simulation test performed again.~~

441 ~~(B) Risk Level 2: In addition to Risk Level 1 requirements, process simulation procedures shall~~  
442 ~~cover all types of manipulations, products and batch sizes.~~

443 ~~(C) Risk Level 3: In addition to all Risk Level 1 and 2 requirements, written policies shall be~~  
444 ~~maintained to validate all processes, procedures, components, equipment and techniques.~~

445  
446 (10) Aseptic Technique Skill Assessment. Individuals engaged in sterile compounding must  
447 take and successfully pass an aseptic technique skill assessment to verify aseptic competency.  
448 The assessment must include a direct visual observation of the individual's aseptic competency  
449 during a process simulation that represents the most challenging or stressful conditions  
450 encountered or performed by the person being evaluated. The assessment must include media  
451 fill testing for all risk levels.

452 (A) The required visual observation shall assess:

453 1. Proper aseptic technique, manipulations and work practices, including, but not  
454 limited to, avoiding touch contamination, proper use of first air and if  
455 applicable, sterilizing high risk CSPs;

456 2. Cleaning and disinfection;

457 3. Hand hygiene, gloving and garbing;

458 4. Identifying, weighing, and measuring of ingredients;

459 5. Maintaining sterility in ISO Class 5 areas;  
460 6. Labeling and inspecting CSPs for quality.  
461 (B) Media-Fill Testing. Pharmacies shall establish and follow policies and procedures for  
462 media-fill testing. Media-fill testing shall comply with USP Chapter 797's recommended  
463 procedures and methods and must be conducted using the most challenging or stressful  
464 conditions/compounding actually encountered or performed by the person being evaluated using  
465 the same container or closure. A minimum of three media-fill tests must be completed during  
466 initial media-fill testing and one media-fill test completed for ongoing testing.  
467 (C) Frequency: The required Aseptic Technique Skill Assessment must be conducted  
468 prior to initial compounding and every twelve (12) months thereafter for Risk Levels 1 and 2  
469 compounding and every (6) months thereafter for Risk Level 3 compounding. Additionally, an  
470 Aseptic Technique Skill Assessment must be conducted whenever the quality assurance program  
471 yields an unacceptable result, whenever unacceptable techniques are observed, if the risk level of  
472 sterile activity conducted by the individual changes or if there is a change in compounding  
473 methods performed.  
474 (E) Individuals who fail written tests; visual observation of hand hygiene, garbing, and  
475 aseptic technique; or media-fill tests must undergo immediate requalification through additional  
476 training by competent compounding personnel. Individuals who fail visual observation of hand  
477 hygiene, garbing, and aseptic technique; or media-fill tests must pass three successive  
478 reevaluations in the deficient area before they can resume compounding of sterile preparations.  
479 ~~(9)~~(11) Record Keeping.  
480 (A) Risk Level 1: The following must be documented:  
481 1. Training and competency evaluation of pharmacy personnel involved in sterile ~~product~~  
482 ~~preparation~~compounding, including, the dates and results of the required aseptic technique  
483 training, aseptic technique skill assessment and media-fill testing;  
484 2. Refrigerator, ~~and~~ freezer and, if applicable, incubator temperature logs;  
485 3. Certification ~~of workbenches~~ dates and results for any PEC or ISO classified area;  
486 4. ~~Copies of any m~~Manufacturer ~~standards~~manuals that are relied upon to maintain  
487 compliance with this rule; ~~and~~  
488 5. Other facility quality control logs as appropriate including all maintenance, cleaning, and  
489 calibration records; and

490 6. If applicable, pressure recordings including documentation of the review of continuous  
491 monitoring system results as required by section (5)(F).

492 (B) Risk Level 2: In addition to Risk Level 1 requirements, records of any end-  
493 ~~product~~preparation testing and batch preparation records must be maintained.

494 (C) Risk Level 3: In addition to Risk Level 1 and 2 requirements, record requirements for Risk  
495 Level 3 ~~products~~ preparations must include:

- 496 1. Preparation work sheet;
- 497 2. Sterilization records;
- 498 3. Quarantine records, if applicable;
- 499 4. End-~~product~~preparation evaluation and testing records as required in section ~~(12)~~(14); and
- 500 5. Ingredient validation records as required in section ~~(12)~~(14).

501 (D) All records and reports shall be maintained either electronically or physically for two (2)  
502 years and shall be readily retrievable; and subject to inspections by the board of pharmacy or its  
503 agents. At a minimum, records shall be physically or electronically produced immediately or  
504 within two (2) hours of a request from the Board or the Board's authorized designee.

505 ~~(10)~~(12) Labeling.

506 ~~(A)~~ Risk Level 1: Sterile ~~products dispensed to patients~~ preparations shall be labeled in  
507 accordance with section 338.059, RSMo and with the following supplemental information  
508 ~~affixed to a permanent label:~~

- 509 1. Beyond-use date;
- 510 2. Storage requirements if stored at other than controlled room temperature;
- 511 3. Any device specific instructions; ~~and~~
- 512 4. Auxiliary labels, when applicable; and

513 5. If applicable, a designation indicating the preparation is hazardous.

514 ~~(B) Risk Level 2: All requirements for Risk Level 1 must be met.~~

515 ~~(C) Risk Level 3: All requirements for Risk Level 1 must be met.~~

516 ~~(11)~~(13) Beyond-Use Dating.

517 (A) Risk Level 1 and Risk Level 2: All sterile ~~products~~preparations must bear a beyond-use  
518 date. Beyond-use dates ~~are~~must be assigned based on current drug and microbiological stability  
519 information and sterility considerations.

520 (B) ~~Risk Level 2: All requirements for Risk Level 1 must be met.~~

521 ~~(C)~~ Risk Level 3: In addition to all Risk Level 1 requirements, there must be a reliable method  
522 for establishing all ~~expiration~~beyond-use dates, including laboratory testing of product stability,  
523 pyrogenicity, particulate contamination and potency. ~~Expiration dating not specifically~~  
524 ~~referenced in the product's approved labeling or not established by product specific instrumental~~  
525 ~~analysis, shall be limited to thirty (30) days.~~ Beyond-use dating not specifically referenced in the  
526 products approved labeling or not established by product specific instrumental analysis shall be  
527 limited to thirty (30) days. There must be a reliable method for establishing all beyond-use  
528 dating. ~~Products maintaining beyond-use dating~~Preparations assigned a beyond-use date of  
529 greater than thirty (30) days shall have lab testing of ~~product~~preparation stability and potency.

530 ~~(12)~~(14) End-~~Product~~Preparation Evaluation.

531 (A) Risk Level 1: The final ~~product~~preparation must be inspected for clarity, container leaks,  
532 integrity, and appropriate solution cloudiness or phase separation, ~~particulates in solution,~~  
533 ~~appropriate~~ solution color, and solution volume. The pharmacist must verify that the  
534 ~~product~~preparation was compounded accurately as to the ingredients, quantities, containers, and  
535 reservoirs. Background light or other means for the visual inspection of ~~products~~preparations for  
536 any particulate and/or foreign matter must be used as part of the inspection process, provided an  
537 alternate means of inspection shall be used if a visual inspection or exposure to the preparation  
538 may pose a health hazard.

539 (B) Risk Level 2: All Risk Level 1 requirements must be met.

540 (C) Risk Level 3: In addition to all Risk Level 1 requirements, the process validation procedure  
541 shall be supplemented with a program of end-~~product~~preparation sterility testing according to a  
542 formal sampling plan. Samples shall be statistically valid to ensure that batches are sterile. A  
543 method for recalling batch ~~products~~preparations shall be established if end-~~product~~preparation  
544 testing results are unacceptable. ~~All~~A sample from each sterile ~~products~~preparation/batch must  
545 be tested for sterility. ~~All~~A sample of each parenteral sterile ~~products~~preparation/batch must also  
546 be tested for pyrogenicity. ~~Sterile products compounded from nonsterile components~~Risk Level  
547 3 preparations must be quarantined and stored to maintain chemical and microbiological stability  
548 pending results of end-~~product~~preparation testing.

549 1. Sterility testing: Sampling for the sterility test shall occur promptly upon the completion of  
550 preparation. The sterility test, including the sampling scheme, shall be conducted according to  
551 ~~one (1) of the~~ a recognized USP methods for the preparation.

552 2. Pyrogen/Endotoxin testing: ~~Each~~ Sterile parenteral ~~product~~preparations prepared from  
553 non-sterile drug components shall be tested for pyrogen or endotoxin according to recommended  
554 USP methods.

555 3. Potency: The pharmacy shall have a procedure for a pre-release check of the potency of  
556 the active ingredients in the compounded sterile ~~product~~preparation prepared from non-sterile  
557 bulk active ingredients. The procedure shall include at least the following verifications by a  
558 pharmacist:

559 A. The lot of the active ingredients used for compounding have the necessary labeling,  
560 potency, purity, certificate of analysis and other relevant qualities;

561 B. All weighings, volumetric measurements, and additions of ingredients were carried out  
562 properly;

563 C. The compounding or control records include documentation that the fill volumes of all  
564 units available for release were checked and were correct; and

565 D. The final potency is confirmed by instrumental analysis for sterile ~~product~~preparations  
566 that have been assigned a beyond-use date of more than thirty (30) days.

567 (D) Emergency Dispensing of a Risk Level 3 Sterile ~~Product~~Preparation: When a compounded  
568 Risk Level 3 ~~product~~preparation must be released prior to the completion of -testing, the sterile  
569 ~~product~~preparation may be dispensed pending test results. Emergency dispensing shall be  
570 defined as, and comply with, section (1)(N) of this rule.

571 ~~(13) Handling Sterile Products Outside the Pharmacy.~~ (15) Storage, Handling and Transport.

572 ~~(A) Risk Level 1: Sterile preparations shall be packaged, stored, dispensed and distributed in a~~  
573 manner that will maintain the preparation's chemical and microbiological stability until the  
574 assigned beyond-use date or until delivery to the patient or intended recipient. The pharmacist-  
575 in-charge shall assure the environmental control of all sterile compounded ~~product~~preparations  
576 shipped. Sterile ~~product~~preparations shall be transported so as to be protected from excesses of  
577 temperatures and light within appropriate packaging or delivery containers that maintain  
578 necessary storage conditions to preserve the quality and integrity of sterile ~~product~~preparations.  
579 The pharmacy shall follow written procedures that specify packing techniques, configuration,

580 and materials for groups of ~~product~~preparations with common storage characteristics and for  
581 specific ~~product~~preparations where unique storage conditions are required to retain adequate  
582 stability and ~~product~~preparation quality.

583 ~~(B) Risk Level 2: All requirements for Risk Level 1 must be met.~~

584 ~~(C) Risk Level 3: All requirements for Risk Level 1 must be met.~~

585

586 (16) Point-of-Care Assembled Systems. Assembly of point-of-care assembled systems shall be  
587 considered Risk Level 1 compounding. Point-of-care assembled systems shall be assigned a  
588 beyond-use date which may exceed the beyond-use-date authorized for Risk Level 1 preparations  
589 provided the date is assigned in accordance with the manufacturer's recommendations or  
590 labeling.

591 (A) When dispensed, an assembled non-activated system shall be labeled with beyond-  
592 use dates for both activated and non-activated states. The compounding record must document  
593 both dates. The beyond-use date of an assembled non-activated system shall be limited to a  
594 maximum of fifteen (15) days unless the pharmacy has documentation from the system's  
595 manufacturer that a longer date is acceptable.

596 (B) Point of care assembled systems shall be assembled and stored in accordance with  
597 the manufacturer's labeling and recommendations.

598

599 (17) General Cleaning and Disinfection Requirements. Except as otherwise provided herein,  
600 cleaning and disinfection of controlled and buffer areas, supplies and equipment shall be  
601 performed and conducted in accordance with USP Chapter 797 timeframes and procedures.  
602 Controlled areas that do not meet ISO air classifications shall be cleaned and disinfected as  
603 required by USP Chapter 797 for segregated compounding areas. If compounding is done less  
604 frequently than the cleaning and disinfection timeframes specified in USP Chapter 797, cleaning  
605 and disinfection must occur before each compounding session begins.

606 (A) The pharmacy shall establish and follow written policies and procedures governing all  
607 aspects of cleaning and disinfection, including, approved cleaning/disinfecting agents  
608 and materials, schedules of use and methods of application.

609 (B) Individuals shall be trained in proper cleaning and disinfection procedures prior to  
610 performing such activities. Training shall include direct visual observation of the  
611 individual's cleaning and disinfecting process by qualified staff. The individual shall be  
612 annually reassessed for competency through direct visual observation. Documentation  
613 of the required training and training dates shall be maintained in the pharmacy's records.  
614 Individuals who fail to demonstrate competency shall be reinstructed and successfully  
615 reevaluated prior to any further cleaning or disinfection.

616 (C) Cleaning and disinfection activities shall be performed using approved  
617 cleaning/disinfection agents and procedures described in the pharmacy's written policies  
618 and procedures. Manufacturers' directions for minimum contact time shall be followed.

619 (D) All cleaning tools (e.g., wipes, sponges, and mop heads) must be low-lint and dedicated  
620 for use in the controlled area and buffer area.

621 (E) Primary engineering controls shall be cleaned with a germicidal agent followed by  
622 sterile alcohol. Sterile water for irrigation shall be used to dilute germicidal agents used  
623 inside the PEC that require dilution.

624 (F) At a minimum, the critical area shall be cleaned and disinfected prior to compounding,  
625 between batches and whenever contamination is suspected using sterile alcohol which is  
626 allowed to dry immediately prior to compounding.

627 ~~(14)~~

628 (18) Environmental Sampling/Testing. The pharmacy shall establish and follow proper controls  
629 to ensure environmental quality, prevent environmental contamination and maintain air quality in  
630 all ISO classified areas. Applicable environmental monitoring of air and surfaces must be  
631 conducted. Air monitoring must be conducted prior to initial compounding and every six (6)  
632 months thereafter. Surface sampling/monitoring must be conducted every six (6) months for  
633 Risk Level 2 and every thirty (30) days for Risk Level 3 compounding.

634 (19) Cytotoxic Drugs.

635 (A) The following additional requirements are necessary for those licensed pharmacies that  
636 prepare cytotoxic drugs to insure the protection of the personnel involved:

637 1. Cytotoxic drugs shall be compounded in a vertical flow, Class II biological safety cabinet  
638 or ~~an isolator~~ a CACI. If used for other ~~product~~ preparations, the cabinet must be thoroughly  
639 cleaned;

640 2. Protective apparel shall be worn by personnel compounding cytotoxic drugs which shall  
641 include disposable masks, gloves and gowns with tight cuffs;

642 3. Appropriate safety and containment techniques for compounding cytotoxic drugs shall be  
643 used in conjunction with the aseptic techniques required for preparing sterile  
644 ~~product~~preparations. Chemotherapy preparations should be compounded using a closed system  
645 drug transfer device;

646 4. Appropriate disposal containers for used needles, syringes, and if applicable, cytotoxic  
647 waste from the preparation of chemotherapy agents and infectious waste from patients' homes.  
648 Disposal of cytotoxic waste shall comply with all applicable local, state and federal  
649 requirements;

650 5. Written procedures for handling major and minor spills and generated waste of cytotoxic  
651 agents must be developed and must be included in the policy and procedure manual;

652 6. Prepared doses of cytotoxic drugs must be labeled with proper precautions inside and  
653 outside, and shipped in a manner to minimize the risk of accidental rupture of the primary  
654 container.

655 ~~(15) Exemption: Pharmacists and pharmacies where sterile compounding is provided may be~~  
656 ~~exempt from this rule when compounding is restricted to utilizing compounds or products that~~  
657 ~~are contained only in a closed or sealed system and can be transferred or compounded within this~~  
658 ~~self-contained system or topical products that require further transfer or combination in order to~~  
659 ~~achieve a finished product without further modification of the product.~~

660 ~~(16) In addition to the requirements outlined in this rule, all standards and requirements as~~  
661 ~~outlined in 20-CSR-2220-2.400 must be maintained. Pharmacies that are registered with the Food~~  
662 ~~and Drug Administration (FDA) are exempt from the distribution restrictions in 20-CSR-2220-~~  
663 ~~2.400(12) for compounded sterile pharmaceuticals distributed with FDA's knowledge and~~  
664 ~~enforcement discretion. This exemption applies only to a twenty four (24) hour course of~~  
665 ~~therapy which is needed:~~

666 ~~(A) To treat an emergency situation; or~~

667 ~~(B) For an unanticipated procedure for which a time delay would negatively affect a patient~~  
668 ~~outcome. In order to continue beyond twenty four (24) hours, the pharmacy must obtain a~~  
669 ~~prescription and comply with all record and labeling requirements as defined by law or~~  
670 ~~regulation.~~

671 (20) Remedial Investigations: A remedial investigation shall be required if: (1) any sampling or  
672 testing required by this rule demonstrates a colony forming unit (CFU) count that exceeds USP  
673 Chapter 797 recommended action levels for the type of sampling/testing or (2) if a highly  
674 pathogenic microorganism is detected in any preparation or ISO classified area (e.g., Gram-  
675 negative rods, coagulase positive staphylococcus, molds, fungus or yeasts).

676 (A) CSPs and any ingredients used within the compounding process that are part of the  
677 remedial investigation shall be quarantined until the results of the investigation are known. All  
678 affected areas shall be resampled to ensure a suitable state of microbial control prior to further  
679 compounding. The pharmacy shall ensure that no misbranded, contaminated or adulterated CSP  
680 is administered or dispensed for patient use.

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

684  
685 (21) Recalls. A recall must be initiated when a CSP is deemed to be misbranded, adulterated or  
686 non-sterile or if end-preparation testing results are out of specification. The pharmacy shall  
687 notify the prescriber of the nature of the recall, the problem(s) identified and any recommended  
688 actions to ensure public health and safety. In cases where the CSP has the potential to harm the  
689 patient, the same notification shall be provided to all patients that received the recalled CSP(s).  
690 Any recall initiated by a pharmacy shall be reported, in writing, to the board within three (3)  
691 business days. The pharmacy shall document their activities related to the recall.

692 *AUTHORITY: sections 338.140, 338.240, and 338.280, RSMo 2000 and section 338.010, RSMo*  
693 *Supp. 2007.\* This rule originally filed as 4 CSR 220-2.200. Original rule filed May 4, 1992,*  
694 *effective Feb. 26, 1993. Amended: Filed Oct. 28, 1994, effective May 28, 1995. Rescinded and*  
695 *readopted: Filed Dec. 3, 2002, effective July 30, 2003. Moved to 20 CSR 220-2.200, effective*  
696 *Aug. 28, 2006. Amended: Filed Feb. 6, 2008, effective Aug. 30, 2008.*

697 \*Original authority: 338.010, RSMo 1939, amended 1951, 1989, 1990, 2007; 338.140, RSMo  
698 1939, amended 1981, 1989, 1997; 338.240, RSMo 1951; and 338.280, RSMo 1951, amended  
699 1971, 1981.

700  
701 *PUBLIC COST: This proposed amendment will not cost state agencies or political more*  
702 *than five hundred dollars (\$ 500) in the aggregate.*

703  
704 *PRIVATE COST: This proposed amendment will cost private entities approximately*  
705 *\$\_\_\_\_\_ over the life of the rule.*

706