

## RULE ANALYSIS

**Introduction:** THE AMENDMENTS ARE SUBMITTED TO THE BOARD FOR CONSIDERATION AS AN ADOPTED RULE

**Short Title:** Sterile Compounding

**Rule Numbers:** §291.133

**Statutory Authority:** Texas Pharmacy Act, Chapter 551-569, Occupations Code:

- (1) Section 551.002 specifies that the purpose of the Act is to protect the public through the effective control and regulation of the practice of pharmacy; and
- (2) Section 554.051 gives the Board the authority to adopt rules for the proper administration and enforcement of the Act.

**Purpose:** The amendments, if adopted, eliminate training requirements that are out-of-date; update the requirements for sterility testing; clarify the requirements for temperature and humidity; and clarify the requirements for blood labeling procedures.

**The Board reviewed and voted to propose the amendments during the February 2, 2016, meeting. The proposed amendments were published in the March 11, 2016, issue of the *Texas Register* at 41 TexReg 1799.**

1 **SUBCHAPTER G. SERVICES PROVIDED BY PHARMACIES**

2 **22 TAC §291.133**

3 The Texas State Board of Pharmacy proposes amendments to §291.133, concerning Pharmacies  
4 Compounding Sterile Preparations. The proposed amendments, if adopted, remove references to  
5 training requirements that are no longer necessary; update the requirements for sterility testing  
6 and temperature and humidity to be consistent with USP 797; clarify the requirements regarding  
7 blood labeling to specify that blood labeling occurs in a buffer area; and clarify recordkeeping  
8 requirements.

9 Gay Dodson, R.Ph., Executive Director/Secretary, has determined that, for the first five-year  
10 period the rule is in effect, there will be no fiscal implications for state or local government as a  
11 result of enforcing or administering the rule.

12 Ms. Dodson has determined that, for each year of the first five-year period the rule will be in  
13 effect, the public benefit anticipated as a result of enforcing the amendments will ensure  
14 pharmacies are compounding sterile preparations under appropriate conditions. There might be  
15 an adverse economic effect on micro, small, and large businesses or to other entities/persons who  
16 are required to comply with the rules for pharmacies compounding sterile preparations. Based on  
17 the significant variances in pharmacies' physical structure and layout, it is difficult for TSBP to  
18 determine the actual cost to businesses required to comply with this rule. These costs would  
19 involve bringing the sterile compounding area of pharmacies into compliance with the new  
20 provisions of the rules. In addition, TSBP is unable to reduce these costs because to do so would  
21 compromise the purposes of this rule which is intended to protect the health and safety of the  
22 public.

23 Written comments on the amendments may be submitted to Allison Vordenbaumen Benz, R.Ph.,  
24 M.S., Director of Professional Services, Texas State Board of Pharmacy, 333 Guadalupe Street,  
25 Suite 3-600, Austin, Texas 78701, FAX (512) 305-6778. Comments must be received by 5 p.m.,  
26 April 25, 2016.

27 The amendments are proposed under §551.002 and §554.051 of the Texas Pharmacy Act  
28 (Chapters 551 - 569, Texas Occupations Code). The Board interprets §551.002 as authorizing the  
29 agency to protect the public through the effective control and regulation of the practice of  
30 pharmacy. The Board interprets §554.051(a) as authorizing the agency to adopt rules for the  
31 proper administration and enforcement of the Act.

32 The statutes affected by these amendments: Texas Pharmacy Act, Chapters 551 - 569, Texas  
33 Occupations Code.

34 ***§291.133. Pharmacies Compounding Sterile Preparations.***

35 (a) Purpose. Pharmacies compounding sterile preparations, prepackaging pharmaceutical  
36 products, and distributing those products shall comply with all requirements for their specific  
37 license classification and this section. The purpose of this section is to provide standards for the:

- 38 (1) compounding of sterile preparations pursuant to a prescription or medication order for a  
39 patient from a practitioner in Class A-S, Class B, Class C-S, and Class E-S pharmacies;
- 40 (2) compounding, dispensing, and delivery of a reasonable quantity of a compounded sterile  
41 preparation in Class A-S, Class B, Class C-S, and Class E-S pharmacies to a practitioner's office  
42 for office use by the practitioner;
- 43 (3) compounding and distribution of compounded sterile preparations by a Class A-S pharmacy  
44 for a Class C-S pharmacy; and
- 45 (4) compounding of sterile preparations by a Class C-S pharmacy and the distribution of the  
46 compounded preparations to other Class C or Class C-S pharmacies under common ownership.
- 47 (b) Definitions. In addition to the definitions for specific license classifications, the following  
48 words and terms, when used in this section, shall have the following meanings, unless the  
49 context clearly indicates otherwise.
- 50 (1) ACPE--Accreditation Council for Pharmacy Education.
- 51 (2) Airborne particulate cleanliness class--The level of cleanliness specified by the maximum  
52 allowable number of particles per cubic meter of air as specified in the International  
53 Organization of Standardization (ISO) Classification Air Cleanliness (ISO 14644-1). For  
54 example:
- 55 (A) ISO Class 5 (formerly Class 100) is an atmospheric environment that contains less than  
56 3,520 particles 0.5 microns in diameter per cubic meter of air (formerly stated as 100 particles  
57 0.5 microns in diameter per cubic foot of air);
- 58 (B) ISO Class 7 (formerly Class 10,000) is an atmospheric environment that contains less than  
59 352,000 particles 0.5 microns in diameter per cubic meter of air (formerly stated as 10,000  
60 particles 0.5 microns in diameter per cubic foot of air); and
- 61 (C) ISO Class 8 (formerly Class 100,000) is an atmospheric environment that contains less than  
62 3,520,000 particles 0.5 microns in diameter per cubic meter of air (formerly stated as 100,000  
63 particles 0.5 microns in diameter per cubic foot of air).
- 64 (3) Ancillary supplies--Supplies necessary for the preparation and administration of compounded  
65 sterile preparations.
- 66 (4) Ante-area--An ISO Class 8 or better area where personnel may perform hand hygiene and  
67 garbing procedures, staging of components, order entry, labeling, and other high-particulate  
68 generating activities. It is also a transition area that:
- 69 (A) provides assurance that pressure relationships are constantly maintained so that air flows  
70 from clean to dirty areas; and

71 (B) reduces the need for the heating, ventilating and air conditioning (HVAC) control system to  
72 respond to large disturbances.

73 (5) Aseptic Processing--A mode of processing pharmaceutical and medical preparations that  
74 involves the separate sterilization of the preparation and of the package (containers-closures or  
75 packaging material for medical devices) and the transfer of the preparation into the container and  
76 its closure under at least ISO Class 5 conditions.

77 (6) Automated compounding device--An automated device that compounds, measures, and/or  
78 packages a specified quantity of individual components in a predetermined sequence for a  
79 designated sterile preparation.

80 (7) Batch--A specific quantity of a drug or other material that is intended to have uniform  
81 character and quality, within specified limits, and is produced during a single preparation cycle.

82 (8) Batch preparation compounding--Compounding of multiple sterile preparation units, in a  
83 single discrete process, by the same individual(s), carried out during one limited time period.  
84 Batch preparation/compounding does not include the preparation of multiple sterile preparation  
85 units pursuant to patient specific medication orders.

86 (9) Beyond-use date--The date or time after which the compounded sterile preparation shall not  
87 be stored or transported or begin to be administered to a patient. The beyond-use date is  
88 determined from the date or time the preparation is compounded.

89 (10) Biological Safety Cabinet, Class II--A ventilated cabinet for personnel, product or  
90 preparation, and environmental protection having an open front with inward airflow for  
91 personnel protection, downward HEPA filtered laminar airflow for product protection, and  
92 HEPA filtered exhausted air for environmental protection.

93 (11) Buffer Area--An ISO Class 7 or, if a Class B pharmacy, ISO Class 8 or better, area where  
94 the primary engineering control area is physically located. Activities that occur in this area  
95 include the preparation and staging of components and supplies used when compounding sterile  
96 preparations.

97 (12) Clean room--A room in which the concentration of airborne particles is controlled to meet a  
98 specified airborne particulate cleanliness class. Microorganisms in the environment are  
99 monitored so that a microbial level for air, surface, and personnel gear are not exceeded for a  
100 specified cleanliness class.

101 (13) Component--Any ingredient intended for use in the compounding of a drug preparation,  
102 including those that may not appear in such preparation.

103 (14) Compounding--The preparation, mixing, assembling, packaging, or labeling of a drug or  
104 device:

- 105 (A) as the result of a practitioner's prescription drug or medication order based on the  
106 practitioner-patient-pharmacist relationship in the course of professional practice;
- 107 (B) for administration to a patient by a practitioner as the result of a practitioner's initiative based  
108 on the practitioner-patient-pharmacist relationship in the course of professional practice;
- 109 (C) in anticipation of prescription drug or medication orders based on routine, regularly observed  
110 prescribing patterns; or
- 111 (D) for or as an incident to research, teaching, or chemical analysis and not for sale or  
112 dispensing, except as allowed under §562.154 or Chapter 563 of the Occupations Code.
- 113 (15) Compounding Aseptic Isolator--A form of barrier isolator specifically designed for  
114 compounding pharmaceutical ingredients or preparations. It is designed to maintain an aseptic  
115 compounding environment within the isolator throughout the compounding and material transfer  
116 processes. Air exchange into the isolator from the surrounding environment shall not occur  
117 unless it has first passed through a microbial retentive filter (HEPA minimum).
- 118 (16) Compounding Aseptic Containment Isolator--A compounding aseptic isolator designed to  
119 provide worker protection from exposure to undesirable levels of airborne drug throughout the  
120 compounding and material transfer processes and to provide an aseptic environment for  
121 compounding sterile preparations. Air exchange with the surrounding environment should not  
122 occur unless the air is first passed through a microbial retentive filter (HEPA minimum) system  
123 capable of containing airborne concentrations of the physical size and state of the drug being  
124 compounded. Where volatile hazardous drugs are prepared, the exhaust air from the isolator  
125 should be appropriately removed by properly designed building ventilation.
- 126 (17) Compounding Personnel--A pharmacist, pharmacy technician, or pharmacy technician  
127 trainee who performs the actual compounding; a pharmacist who supervises pharmacy  
128 technicians or pharmacy technician trainees compounding sterile preparations, and a pharmacist  
129 who performs an intermediate or final verification of a compounded sterile preparation.
- 130 (18) Critical Area--An ISO Class 5 environment.
- 131 (19) Critical Sites--A location that includes any component or fluid pathway surfaces (e.g., vial  
132 septa, injection ports, beakers) or openings (e.g., opened ampules, needle hubs) exposed and at  
133 risk of direct contact with air (e.g., ambient room or HEPA filtered), moisture (e.g., oral and  
134 mucosal secretions), or touch contamination. Risk of microbial particulate contamination of the  
135 critical site increases with the size of the openings and exposure time.
- 136 (20) Device--An instrument, apparatus, implement, machine, contrivance, implant, in-vitro  
137 reagent, or other similar or related article, including any component part or accessory, that is  
138 required under federal or state law to be ordered or prescribed by a practitioner.

- 139 (21) Direct Compounding Area--A critical area within the ISO Class 5 primary engineering  
140 control where critical sites are exposed to unidirectional HEPA-filtered air, also known as first  
141 air.
- 142 (22) Disinfectant--An agent that frees from infection, usually a chemical agent but sometimes a  
143 physical one, and that destroys disease-causing pathogens or other harmful microorganisms but  
144 may not kill bacterial and fungal spores. It refers to substances applied to inanimate objects.
- 145 (23) First Air--The air exiting the HEPA filter in a unidirectional air stream that is essentially  
146 particle free.
- 147 (24) Hazardous Drugs--Drugs that, studies in animals or humans indicate exposure to the drugs,  
148 have a potential for causing cancer, development or reproductive toxicity, or harm to organs. For  
149 the purposes of this chapter, radiopharmaceuticals are not considered hazardous drugs.
- 150 (25) Hot water--The temperature of water from the pharmacy's sink maintained at a minimum of  
151 105 degrees F (41 degrees C).
- 152 (26) HVAC--Heating, ventilation, and air conditioning.
- 153 (27) Immediate use--A sterile preparation that is not prepared according to USP 797 standards  
154 (i.e., outside the pharmacy and most likely not by pharmacy personnel) which shall be stored for  
155 no longer than one hour after completion of the preparation.
- 156 (28) IPA--Isopropyl alcohol (2-propanol).
- 157 (29) Labeling--All labels and other written, printed, or graphic matter on an immediate container  
158 of an article or preparation or on, or in, any package or wrapper in which it is enclosed, except  
159 any outer shipping container. The term "label" designates that part of the labeling on the  
160 immediate container.
- 161 (30) Media-Fill Test--A test used to qualify aseptic technique of compounding personnel or  
162 processes and to ensure that the processes used are able to produce sterile preparation without  
163 microbial contamination. During this test, a microbiological growth medium such as Soybean-  
164 Casein Digest Medium is substituted for the actual drug preparation to simulate admixture  
165 compounding. The issues to consider in the development of a media-fill test are the following:  
166 media-fill procedures, media selection, fill volume, incubation, time and temperature, inspection  
167 of filled units, documentation, interpretation of results, and possible corrective actions required.
- 168 (31) Multiple-Dose Container--A multiple-unit container for articles or preparations intended for  
169 potential administration only and usually contains antimicrobial preservatives. The beyond-use  
170 date for an opened or entered (e.g., needle-punctured) multiple-dose container with antimicrobial  
171 preservatives is 28 days, unless otherwise specified by the manufacturer.
- 172 (32) Negative Pressure Room--A room that is at a lower pressure compared to adjacent spaces  
173 and, therefore, the net flow of air is into the room.

174 (33) Office use--The administration of a compounded drug to a patient by a practitioner in the  
175 practitioner's office or by the practitioner in a health care facility or treatment setting, including a  
176 hospital, ambulatory surgical center, or pharmacy in accordance with Chapter 562 of the Act, or  
177 for administration or provision by a veterinarian in accordance with §563.054 of the Act.

178 (34) Pharmacy Bulk Package--A container of a sterile preparation for potential use that contains  
179 many single doses. The contents are intended for use in a pharmacy admixture program and are  
180 restricted to the preparation of admixtures for infusion or, through a sterile transfer device, for  
181 the filling of empty sterile syringes. The closure shall be penetrated only one time after  
182 constitution with a suitable sterile transfer device or dispensing set, which allows measured  
183 dispensing of the contents. The pharmacy bulk package is to be used only in a suitable work area  
184 such as a laminar flow hood (or an equivalent clean air compounding area).

185 (35) Prepackaging--The act of repackaging and relabeling quantities of drug products from a  
186 manufacturer's original container into unit dose packaging or a multiple dose container for  
187 distribution within a facility licensed as a Class C pharmacy or to other pharmacies under  
188 common ownership for distribution within those facilities. The term as defined does not prohibit  
189 the prepackaging of drug products for use within other pharmacy classes.

190 (36) Preparation or Compounded Sterile Preparation--A sterile admixture compounded in a  
191 licensed pharmacy or other healthcare-related facility pursuant to the order of a licensed  
192 prescriber. The components of the preparation may or may not be sterile products.

193 (37) Primary Engineering Control--A device or room that provides an ISO Class 5 environment  
194 for the exposure of critical sites when compounding sterile preparations. Such devices include,  
195 but may not be limited to, laminar airflow workbenches, biological safety cabinets, compounding  
196 aseptic isolators, and compounding aseptic containment isolators.

197 (38) Product--A commercially manufactured sterile drug or nutrient that has been evaluated for  
198 safety and efficacy by the U.S. Food and Drug Administration (FDA). Products are accompanied  
199 by full prescribing information, which is commonly known as the FDA-approved manufacturer's  
200 labeling or product package insert.

201 (39) Positive Control--A quality assurance sample prepared to test positive for microbial growth.

202 (40) Quality assurance--The set of activities used to ensure that the process used in the  
203 preparation of sterile drug preparations lead to preparations that meet predetermined standards of  
204 quality.

205 (41) Quality control--The set of testing activities used to determine that the ingredients,  
206 components (e.g., containers), and final compounded sterile preparations prepared meet  
207 predetermined requirements with respect to identity, purity, non-pyrogenicity, and sterility.

208 (42) Reasonable quantity--An amount of a compounded drug that:

209 (A) does not exceed the amount a practitioner anticipates may be used in the practitioner's office  
210 or facility before the beyond use date of the drug;

211 (B) is reasonable considering the intended use of the compounded drug and the nature of the  
212 practitioner's practice; and

213 (C) for any practitioner and all practitioners as a whole, is not greater than an amount the  
214 pharmacy is capable of compounding in compliance with pharmaceutical standards for identity,  
215 strength, quality, and purity of the compounded drug that are consistent with United States  
216 Pharmacopoeia guidelines and accreditation practices.

217 (43) Segregated Compounding Area--A designated space, either a demarcated area or room, that  
218 is restricted to preparing low-risk level compounded sterile preparations with 12-hour or less  
219 beyond-use date. Such area shall contain a device that provides unidirectional airflow of ISO  
220 Class 5 air quality for preparation of compounded sterile preparations and shall be void of  
221 activities and materials that are extraneous to sterile compounding.

222 (44) Single-dose container--A single-unit container for articles or preparations intended for  
223 parenteral administration only. It is intended for a single use. A single-dose container is labeled  
224 as such. Examples of single-dose containers include pre-filled syringes, cartridges, fusion-sealed  
225 containers, and closure-sealed containers when so labeled.

226 (45) SOPs--Standard operating procedures.

227 (46) Sterilizing Grade Membranes--Membranes that are documented to retain 100% of a culture  
228 of 10<sup>7</sup> microorganisms of a strain of *Brevundimonas* (*Pseudomonas*) *diminuta* per square  
229 centimeter of membrane surface under a pressure of not less than 30 psi (2.0 bar). Such filter  
230 membranes are nominally at 0.22-micrometer or 0.2-micrometer nominal pore size, depending  
231 on the manufacturer's practice.

232 (47) Sterilization by Filtration--Passage of a fluid or solution through a sterilizing grade  
233 membrane to produce a sterile effluent.

234 (48) Terminal Sterilization--The application of a lethal process, e.g., steam under pressure or  
235 autoclaving, to sealed final preparation containers for the purpose of achieving a predetermined  
236 sterility assurance level of usually less than 10<sup>-6</sup> or a probability of less than one in one million  
237 of a non-sterile unit.

238 (49) Unidirectional Flow--An airflow moving in a single direction in a robust and uniform  
239 manner and at sufficient speed to reproducibly sweep particles away from the critical processing  
240 or testing area.

241 (50) USP/NF--The current edition of the United States Pharmacopoeia/National Formulary.

242 (c) Personnel.

- 243 (1) Pharmacist-in-charge.
- 244 (A) General. The pharmacy shall have a pharmacist-in-charge in compliance with the specific  
245 license classification of the pharmacy.
- 246 (B) Responsibilities. In addition to the responsibilities for the specific class of pharmacy, the  
247 pharmacist-in-charge shall have the responsibility for, at a minimum, the following concerning  
248 the compounding of sterile preparations:
- 249 (i) developing a system to ensure that all pharmacy personnel responsible for compounding  
250 and/or supervising the compounding of sterile preparations within the pharmacy receive  
251 appropriate education and training and competency evaluation;
- 252 (ii) determining that all personnel involved in compounding sterile preparations obtain  
253 continuing education appropriate for the type of compounding done by the personnel;
- 254 (iii) supervising a system to ensure appropriate procurement of drugs and devices and storage of  
255 all pharmaceutical materials including pharmaceuticals, components used in the compounding of  
256 sterile preparations, and drug delivery devices;
- 257 (iv) ensuring that the equipment used in compounding is properly maintained;
- 258 (v) developing a system for the disposal and distribution of drugs from the pharmacy;
- 259 (vi) developing a system for bulk compounding or batch preparation of drugs;
- 260 (vii) developing a system for the compounding, sterility assurance, quality assurance, and quality  
261 control of sterile preparations; and
- 262 (viii) if applicable, ensuring that the pharmacy has a system to dispose of hazardous waste in a  
263 manner so as not to endanger the public health.
- 264 (2) Pharmacists.
- 265 (A) General.
- 266 (i) A pharmacist is responsible for ensuring that compounded sterile preparations are accurately  
267 identified, measured, diluted, and mixed and are correctly purified, sterilized, packaged, sealed,  
268 labeled, stored, dispensed, and distributed.
- 269 (ii) A pharmacist shall inspect and approve all components, drug preparation containers,  
270 closures, labeling, and any other materials involved in the compounding process.
- 271 (iii) A pharmacist shall review all compounding records for accuracy and conduct periodic in-  
272 process checks as defined in the pharmacy's policy and procedures.

273 (iv) A pharmacist shall review all compounding records for accuracy and conduct a final check.

274 (v) A pharmacist is responsible for ensuring the proper maintenance, cleanliness, and use of all  
275 equipment used in the compounding process.

276 (vi) A pharmacist shall be accessible at all times, 24 hours a day, to respond to patients' and other  
277 health professionals' questions and needs.

278 ~~{(B) Prior to September 1, 2015—initial training and continuing education.}~~

279 ~~{(i) All pharmacists who compound sterile preparations for administration to patients or  
280 supervise pharmacy technicians and pharmacy technician trainees compounding sterile  
281 preparations shall:}~~

282 ~~{(I) complete through a single course, a minimum of 20 hours of instruction and experience in  
283 the areas listed in paragraph (4)(D) of this subsection. Such training may be obtained through:}~~

284 ~~{(a) completion of a structured on-the-job didactic and experiential training program at this  
285 pharmacy which provides 20 hours of instruction and experience. Such training may not be  
286 transferred to another pharmacy unless the pharmacies are under common ownership and control  
287 and use a common training program; or}~~

288 ~~{(b) completion of a recognized course in an accredited college of pharmacy or a course  
289 sponsored by an ACPE accredited provider which provides 20 hours of instruction and  
290 experience;}~~

291 ~~{(II) possess knowledge about:}~~

292 ~~{(a) aseptic processing;}~~

293 ~~{(b) quality control and quality assurance as related to environmental, component, and finished  
294 preparation release checks and tests;}~~

295 ~~{(c) chemical, pharmaceutical, and clinical properties of drugs;}~~

296 ~~{(d) container, equipment, and closure system selection; and}~~

297 ~~{(e) sterilization techniques.}~~

298 ~~{(ii) The required experiential portion of the training programs specified in this subparagraph  
299 must be supervised by an individual who has already completed training as specified in this  
300 paragraph or paragraph (3) of this subsection.}~~

301 ~~{(iii) All pharmacists engaged in compounding sterile preparations shall obtain continuing  
302 education appropriate for the type of compounding done by the pharmacist.}~~

303 (B) [~~(C)~~] Initial [~~Effective September 1, 2015~~—initial] training and continuing education.

304 (i) All pharmacists who compound sterile preparations or supervise pharmacy technicians and  
305 pharmacy technician trainees compounding sterile preparations shall comply with the following:

306 (I) complete through a single course, a minimum of 20 hours of instruction and experience in the  
307 areas listed in paragraph (4)(D) of this subsection. Such training shall be obtained through  
308 completion of a recognized course in an accredited college of pharmacy or a course sponsored by  
309 an ACPE accredited provider;

310 (II) complete a structured on-the-job didactic and experiential training program at this pharmacy  
311 which provides sufficient hours of instruction and experience in the facility's sterile  
312 compounding processes and procedures. Such training may not be transferred to another  
313 pharmacy unless the pharmacies are under common ownership and control and use a common  
314 training program; and

315 (III) possess knowledge about:

316 (-a-) aseptic processing;

317 (-b-) quality control and quality assurance as related to environmental, component, and finished  
318 preparation release checks and tests;

319 (-c-) chemical, pharmaceutical, and clinical properties of drugs;

320 (-d-) container, equipment, and closure system selection; and

321 (-e-) sterilization techniques.

322 (ii) The required experiential portion of the training programs specified in this subparagraph  
323 must be supervised by an individual who is actively engaged in performing sterile compounding  
324 and is qualified and has completed training as specified in this paragraph or paragraph (3) of this  
325 subsection.

326 (iii) In order to renew a license to practice pharmacy, during the previous licensure period, a  
327 pharmacist engaged in sterile compounding shall complete a minimum of:

328 (I) two hours of ACPE-accredited continuing education relating to one or more of the areas listed  
329 in paragraph (4)(D) of this subsection if the pharmacist is engaged in compounding low and  
330 medium risk sterile preparations; or

331 (II) four hours of ACPE-accredited continuing education relating to one or more of the areas  
332 listed in paragraph (4)(D) of this subsection if the pharmacist is engaged in compounding high  
333 risk sterile preparations.

334 (3) Pharmacy technicians and pharmacy technician trainees.

335 (A) General. All pharmacy technicians and pharmacy technician trainees shall meet the training  
336 requirements specified in §297.6 of this title (relating to Pharmacy Technician and Pharmacy  
337 Technician Trainee Training).

338 ~~[(B) Prior to September 1, 2015—initial training and continuing education. In addition to specific  
339 qualifications for registration, all pharmacy technicians and pharmacy technician trainees who  
340 compound sterile preparations for administration to patients shall:]~~

341 ~~[(i) have initial training obtained either through completion of:]~~

342 ~~[(I) a single course, a minimum of 40 hours of instruction and experience in the areas listed in  
343 paragraph (4)(D) of this subsection. Such training may be obtained through:]~~

344 ~~[(a) completion of a structured on-the-job didactic and experiential training program at this  
345 pharmacy which provides 40 hours of instruction and experience. Such training may not be  
346 transferred to another pharmacy unless the pharmacies are under common ownership and control  
347 and use a common training program; or]~~

348 ~~[(b) completion of a course sponsored by an ACPE accredited provider which provides 40  
349 hours of instruction and experience; or]~~

350 ~~[(II) a training program which is accredited by the American Society of Health-System  
351 Pharmacists. Individuals enrolled in training programs accredited by the American Society of  
352 Health-System Pharmacists may compound sterile preparations in a licensed pharmacy provided  
353 the:]~~

354 ~~[(a) compounding occurs only during times the individual is assigned to a pharmacy as a part of  
355 the experiential component of the American Society of Health-System Pharmacists training  
356 program;]~~

357 ~~[(b) individual is under the direct supervision of and responsible to a pharmacist who has  
358 completed training as specified in paragraph (2) of this subsection; and]~~

359 ~~[(c) supervising pharmacist conducts periodic in-process checks as defined in the pharmacy's  
360 policy and procedures; and]~~

361 ~~[(d) supervising pharmacist conducts a final check.]~~

362 ~~[(ii) acquire the required experiential portion of the training programs specified in this  
363 subparagraph under the supervision of an individual who has already completed training as  
364 specified in paragraph (2) of this subsection or this paragraph.]~~

365 (B) ~~[(C)]~~ Initial ~~[Effective September 1, 2015—initial]~~ training and continuing education.

366 (i) Pharmacy technicians and pharmacy technician trainees may compound sterile preparations  
367 provided the pharmacy technicians and/or pharmacy technician trainees are supervised by a

368 pharmacist ~~as [who has completed the training]~~ specified in paragraph (2) of this subsection[;   
369 ~~conducts in-process and final checks, and affixes his or her initials to the appropriate quality~~   
370 ~~control records].~~

371 (ii) All pharmacy technicians and pharmacy technician trainees who compound sterile   
372 preparations for administration to patients shall:

373 (I) have initial training obtained either through completion of:

374 (-a-) a single course, a minimum of 40 hours of instruction and experience in the areas listed in   
375 paragraph (4)(D) of this subsection. Such training shall be obtained through completion of a   
376 course sponsored by an ACPE accredited provider which provides 40 hours of instruction and   
377 experience; or

378 (-b-) a training program which is accredited by the American Society of Health-System   
379 Pharmacists.

380 (II) and

381 (-a-) complete a structured on-the-job didactic and experiential training program at this pharmacy   
382 which provides sufficient hours of instruction and experience in the facility's sterile   
383 compounding processes and procedures. Such training may not be transferred to another   
384 pharmacy unless the pharmacies are under common ownership and control and use a common   
385 training program; and

386 (-b-) possess knowledge about:

387 (-1-) aseptic processing;

388 (-2-) quality control and quality assurance as related to environmental, component, and finished   
389 preparation release checks and tests;

390 (-3-) chemical, pharmaceutical, and clinical properties of drugs;

391 (-4-) container, equipment, and closure system selection; and

392 (-5-) sterilization techniques.

393 (iii) Individuals enrolled in training programs accredited by the American Society of Health-   
394 System Pharmacists may compound sterile preparations in a licensed pharmacy provided the:

395 (I) compounding occurs only during times the individual is assigned to a pharmacy as a part of   
396 the experiential component of the American Society of Health-System Pharmacists training   
397 program;

398 (II) individual is under the direct supervision of and responsible to a pharmacist who has  
399 completed training as specified in paragraph (2) of this subsection; and

400 (III) supervising pharmacist conducts periodic in-process checks as defined in the pharmacy's  
401 policy and procedures; and

402 (IV) supervising pharmacist conducts a final check.

403 (iv) The required experiential portion of the training programs specified in this subparagraph  
404 must be supervised by an individual who is actively engaged in performing sterile compounding,  
405 is qualified and has completed training as specified in paragraph (2) of this subsection or this  
406 paragraph.

407 (v) In order to renew a registration as a pharmacy technician, during the previous registration  
408 period, a pharmacy technician engaged in sterile compounding shall complete a minimum of:

409 (I) two hours of ACPE accredited continuing education relating to one or more of the areas listed  
410 in paragraph (4)(D) of this subsection if the pharmacy technician is engaged in compounding low  
411 and medium risk sterile preparations; or

412 (II) four hours of ACPE accredited continuing education relating to one or more of the areas  
413 listed in paragraph (4)(D) of this subsection if pharmacy technician is engaged in compounding  
414 high risk sterile preparations.

415 (4) Evaluation and testing requirements.

416 (A) All pharmacy personnel preparing sterile preparations shall be trained conscientiously and  
417 skillfully by expert personnel through multimedia instructional sources and professional  
418 publications in the theoretical principles and practical skills of aseptic manipulations, garbing  
419 procedures, aseptic work practices, achieving and maintaining ISO Class 5 environmental  
420 conditions, and cleaning and disinfection procedures before beginning to prepare compounded  
421 sterile preparations.

422 (B) All pharmacy personnel preparing sterile preparations shall perform didactic review and pass  
423 written and media-fill testing of aseptic manipulative skills initially followed by:

424 (i) every 12 months for low- and medium-risk level compounding; and

425 (ii) every six months for high-risk level compounding.

426 (C) Pharmacy personnel who fail written tests or whose media-fill test vials result in gross  
427 microbial colonization shall:

428 (i) be immediately re-instructed and re-evaluated by expert compounding personnel to ensure  
429 correction of all aseptic practice deficiencies; and

430 (ii) not be allowed to compound sterile preparations for patient use until passing results are  
431 achieved.

432 (D) The didactic and experiential training shall include instruction, experience, and demonstrated  
433 proficiency in the following areas:

434 (i) aseptic technique;

435 (ii) critical area contamination factors;

436 (iii) environmental monitoring;

437 (iv) structure and engineering controls related to facilities;

438 (v) equipment and supplies;

439 (vi) sterile preparation calculations and terminology;

440 (vii) sterile preparation compounding documentation;

441 (viii) quality assurance procedures;

442 (ix) aseptic preparation procedures including proper gowning and gloving technique;

443 (x) handling of hazardous drugs, if applicable;

444 (xi) cleaning procedures; and

445 (xii) general conduct in the clean room.

446 (E) The aseptic technique of each person compounding or responsible for the direct supervision  
447 of personnel compounding sterile preparations shall be observed and evaluated by expert  
448 personnel as satisfactory through written and practical tests, and challenge testing, and such  
449 evaluation documented. Compounding personnel shall not evaluate their own aseptic technique  
450 or results of their own media-fill challenge testing.

451 (F) Media-fill tests must be conducted at each pharmacy where an individual compounds sterile  
452 preparations. No preparation intended for patient use shall be compounded by an individual until  
453 the on-site media-fill tests indicate that the individual can competently perform aseptic  
454 procedures, except that a pharmacist may temporarily compound sterile preparations and  
455 supervise pharmacy technicians compounding sterile preparations without media-fill tests  
456 provided the pharmacist completes the on-site media-fill tests within seven days of commencing  
457 work at the pharmacy.

458 (G) Media-fill tests procedures for assessing the preparation of specific types of sterile  
459 preparations shall be representative of the most challenging or stressful conditions encountered

460 by the pharmacy personnel being evaluated and, if applicable, for sterilizing high-risk level  
461 compounded sterile preparations.

462 (H) Media-fill challenge tests simulating high-risk level compounding shall be used to verify the  
463 capability of the compounding environment and process to produce a sterile preparation.

464 (I) Commercially available sterile fluid culture media, such as Soybean-Casein Digest Medium  
465 shall be able to promote exponential colonization of bacteria that are most likely to be  
466 transmitted to compounding sterile preparations from the compounding personnel and  
467 environment. Media-filled vials are generally incubated at 20 to 25 degrees Celsius or at 30 to 35  
468 degrees Celsius for a minimum of 14 days. If two temperatures are used for incubation of media-  
469 filled samples, then these filled containers should be incubated for at least 7 days at each  
470 temperature. Failure is indicated by visible turbidity in the medium on or before 14 days.

471 (J) The pharmacist-in-charge shall ensure continuing competency of pharmacy personnel through  
472 in-service education, training, and media-fill tests to supplement initial training. Personnel  
473 competency shall be evaluated:

474 (i) during orientation and training prior to the regular performance of those tasks;

475 (ii) whenever the quality assurance program yields an unacceptable result;

476 (iii) whenever unacceptable techniques are observed; and

477 (iv) at least on an annual basis for low- and medium-risk level compounding, and every six  
478 months for high-risk level compounding.

479 (K) The pharmacist-in-charge shall ensure that proper hand hygiene and garbing practices of  
480 compounding personnel are evaluated prior to compounding, supervising, or verifying sterile  
481 preparations intended for patient use and whenever an aseptic media fill is performed.

482 (i) Sampling of compounding personnel glove fingertips shall be performed for all risk level  
483 compounding.

484 (ii) All compounding personnel shall demonstrate competency in proper hand hygiene and  
485 garbing procedures and in aseptic work practices (e.g., disinfection of component surfaces,  
486 routine disinfection of gloved hands).

487 (iii) Sterile contact agar plates shall be used to sample the gloved fingertips of compounding  
488 personnel after garbing in order to assess garbing competency and after completing the media-fill  
489 preparation (without applying sterile 70% IPA).

490 (iv) The visual observation shall be documented and maintained to provide a permanent record  
491 and long-term assessment of personnel competency.

492 (v) All compounding personnel shall successfully complete an initial competency evaluation and  
493 gloved fingertip/thumb sampling procedure no less than three times before initially being  
494 allowed to compound sterile preparations for patient use. Immediately after the compounding  
495 personnel completes the hand hygiene and garbing procedure (i.e., after donning of sterile gloves  
496 and before any disinfecting with sterile 70% IPA), the evaluator will collect a gloved fingertip  
497 and thumb sample from both hands of the compounding personnel onto agar plates or media test  
498 paddles by having the individual lightly touching each fingertip onto the agar. The test plates or  
499 test paddles will be incubated for the appropriate incubation period and at the appropriate  
500 temperature. Results of the initial gloved fingertip evaluations shall indicate zero colony-forming  
501 units (0 CFU) growth on the agar plates or media test paddles, or the test shall be considered a  
502 failure. In the event of a failed gloved fingertip test, the evaluation shall be repeated until the  
503 individual can successfully don sterile gloves and pass the gloved fingertip evaluation, defined as  
504 zero CFUs growth. No preparation intended for patient use shall be compounded by an  
505 individual until the results of the initial gloved fingertip evaluation indicate that the individual  
506 can competently perform aseptic procedures except that a pharmacist may temporarily supervise  
507 pharmacy technicians compounding sterile preparations while waiting for the results of the  
508 evaluation for no more than three days.

509 (vi) Re-evaluation of all compounding personnel shall occur at least annually for compounding  
510 personnel who compound low and medium risk level preparations and every six months for  
511 compounding personnel who compound high risk level preparations. Results of gloved fingertip  
512 tests conducted immediately after compounding personnel complete a compounding procedure  
513 shall indicate no more than 3 CFUs growth, or the test shall be considered a failure, in which  
514 case, the evaluation shall be repeated until an acceptable test can be achieved (i.e., the results  
515 indicated no more than 3 CFUs growth).

516 (L) The pharmacist-in-charge shall ensure surface sampling shall be conducted in all ISO  
517 classified areas on a periodic basis. Sampling shall be accomplished using contact plates at the  
518 conclusion of compounding. The sample area shall be gently touched with the agar surface by  
519 rolling the plate across the surface to be sampled.

520 (5) Documentation of Training. The pharmacy shall maintain a record of the training and  
521 continuing education on each person who compounds sterile preparations. The record shall  
522 contain, at a minimum, a written record of initial and in-service training, education, and the  
523 results of written and practical testing and media-fill testing of pharmacy personnel. The record  
524 shall be maintained and available for inspection by the board and contain the following  
525 information:

526 (A) name of the person receiving the training or completing the testing or media-fill tests;

527 (B) date(s) of the training, testing, or media-fill challenge testing;

528 (C) general description of the topics covered in the training or testing or of the process validated;

529 (D) name of the person supervising the training, testing, or media-fill challenge testing; and

530 (E) signature or initials of the person receiving the training or completing the testing or media-  
531 fill challenge testing and the pharmacist-in-charge or other pharmacist employed by the  
532 pharmacy and designated by the pharmacist-in-charge as responsible for training, testing, or  
533 media-fill challenge testing of personnel.

534 (d) Operational Standards.

535 (1) General Requirements.

536 (A) Sterile preparations may be compounded:

537 (i) upon presentation of a practitioner's prescription drug or medication order based on a valid  
538 pharmacist/patient/prescriber relationship;

539 (ii) in anticipation of future prescription drug or medication orders based on routine, regularly  
540 observed prescribing patterns; or

541 (iii) in reasonable quantities for office use by a practitioner and for use by a veterinarian.

542 (B) Sterile compounding in anticipation of future prescription drug or medication orders must be  
543 based upon a history of receiving valid prescriptions issued within an established  
544 pharmacist/patient/prescriber relationship, provided that in the pharmacist's professional  
545 judgment the quantity prepared is stable for the anticipated shelf time.

546 (i) The pharmacist's professional judgment shall be based on the criteria used to determine a  
547 beyond-use date outlined in paragraph (6)(G) of this subsection.

548 (ii) Documentation of the criteria used to determine the stability for the anticipated shelf time  
549 must be maintained and be available for inspection.

550 (iii) Any preparation compounded in anticipation of future prescription drug or medication  
551 orders shall be labeled. Such label shall contain:

552 (I) name and strength of the compounded preparation or list of the active ingredients and  
553 strengths;

554 (II) facility's lot number;

555 (III) beyond-use date as determined by the pharmacist using appropriate documented criteria as  
556 outlined in paragraph (6)(G) of this subsection;

557 (IV) quantity or amount in the container;

558 (V) appropriate ancillary instructions, such as storage instructions or cautionary statements,  
559 including hazardous drug warning labels where appropriate; and

560 (VI) device-specific instructions, where appropriate.

561 (C) Commercially available products may be compounded for dispensing to individual patients  
562 or for office use provided the following conditions are met:

563 (i) the commercial product is not reasonably available from normal distribution channels in a  
564 timely manner to meet individual patient's needs;

565 (ii) the pharmacy maintains documentation that the product is not reasonably available due to a  
566 drug shortage or unavailability from the manufacturer; and

567 (iii) the prescribing practitioner has requested that the drug be compounded as described in  
568 subparagraph (D) of this paragraph.

569 (D) A pharmacy may not compound preparations that are essentially copies of commercially  
570 available products (e.g., the preparation is dispensed in a strength that is only slightly different  
571 from a commercially available product) unless the prescribing practitioner specifically orders the  
572 strength or dosage form and specifies why the individual patient needs the particular strength or  
573 dosage form of the preparation or why the preparation for office use is needed in the particular  
574 strength or dosage form of the preparation. The prescribing practitioner shall provide  
575 documentation of a patient specific medical need and the preparation produces a clinically  
576 significant therapeutic response (e.g., the physician requests an alternate preparation due to  
577 hypersensitivity to excipients or preservative in the FDA-approved product, or the physician  
578 requests an effective alternate dosage form) or if the drug product is not commercially available.  
579 The unavailability of such drug product must be documented prior to compounding. The  
580 methodology for documenting unavailability includes maintaining a copy of the wholesaler's  
581 notification showing back-ordered, discontinued, or out-of-stock items. This documentation must  
582 be available in hard-copy or electronic format for inspection by the board.

583 (E) A pharmacy may enter into an agreement to compound and dispense prescription/medication  
584 orders for another pharmacy provided the pharmacy complies with the provisions of §291.125 of  
585 this title (relating to Centralized Prescription Dispensing).

586 (F) Compounding pharmacies/pharmacists may advertise and promote the fact that they provide  
587 sterile prescription compounding services, which may include specific drug preparations and  
588 classes of drugs.

589 (G) A pharmacy may not compound veterinary preparations for use in food producing animals  
590 except in accordance with federal guidelines.

591 (H) Compounded sterile preparations, including hazardous drugs and radiopharmaceuticals, shall  
592 be prepared only under conditions that protect the pharmacy personnel in the preparation and  
593 storage areas.

594 (2) Microbial Contamination Risk Levels. Risk Levels for sterile compounded preparations shall  
595 be as outlined in Chapter 797, Pharmacy Compounding--Sterile Preparations of the USP/NF and  
596 as listed in this paragraph.

597 (A) Low-risk level compounded sterile preparations.

598 (i) Low-Risk conditions. Low-risk level compounded sterile preparations are those compounded  
599 under all of the following conditions.

600 (I) The compounded sterile preparations are compounded with aseptic manipulations entirely  
601 within ISO Class 5 or better air quality using only sterile ingredients, products, components, and  
602 devices.

603 (II) The compounding involves only transfer, measuring, and mixing manipulations using not  
604 more than three commercially manufactured packages of sterile products and not more than two  
605 entries into any one sterile container or package (e.g., bag, vial) of sterile product or  
606 administration container/device to prepare the compounded sterile preparation.

607 (III) Manipulations are limited to aseptically opening ampuls, penetrating disinfected stoppers on  
608 vials with sterile needles and syringes, and transferring sterile liquids in sterile syringes to sterile  
609 administration devices, package containers of other sterile products, and containers for storage  
610 and dispensing.

611 (IV) For a low-risk preparation, in the absence of passing a [direct] sterility test [~~testing results or~~  
612 ~~appropriate information sources that justify different limits,~~] the storage periods cannot [~~may~~  
613 ~~not~~] exceed the following periods: before administration the compounded sterile preparation is  
614 stored properly and are exposed for not more than 48 hours at controlled room temperature, for  
615 not more than 14 days if stored at a cold temperature, and for 45 days if stored in a frozen state  
616 between minus 25 degrees Celsius and minus 10 degrees Celsius. For delayed activation device  
617 systems, the storage period begins when the device is activated.

618 (ii) Examples of Low-Risk Compounding. Examples of low-risk compounding include the  
619 following.

620 (I) Single volume transfers of sterile dosage forms from ampuls, bottles, bags, and vials using  
621 sterile syringes with sterile needles, other administration devices, and other sterile containers.  
622 The solution content of ampules shall be passed through a sterile filter to remove any particles.

623 (II) Simple aseptic measuring and transferring with not more than three packages of  
624 manufactured sterile products, including an infusion or diluent solution to compound drug  
625 admixtures and nutritional solutions.

626 (B) Low-Risk Level compounded sterile preparations with 12-hour or less beyond-use date.  
627 Low-risk level compounded sterile preparations are those compounded pursuant to a physician's  
628 order for a specific patient under all of the following conditions.

629 (i) The compounded sterile preparations are compounded in compounding aseptic isolator or  
630 compounding aseptic containment isolator that does not meet the requirements described in  
631 paragraph (7)(C) or (D) of this subsection (relating to Primary Engineering Control Device) or  
632 the compounded sterile preparations are compounded in laminar airflow workbench or a  
633 biological safety cabinet that cannot be located within the buffer area.

634 (ii) The primary engineering control device shall be certified and maintain ISO Class 5 for  
635 exposure of critical sites and shall be located in a segregated compounding area restricted to  
636 sterile compounding activities that minimizes the risk of contamination of the compounded  
637 sterile preparation.

638 (iii) The segregated compounding area shall not be in a location that has unsealed windows or  
639 doors that connect to the outdoors or high traffic flow, or that is adjacent to construction sites,  
640 warehouses, or food preparation.

641 (iv) For a low-risk preparation compounded as described in clauses (i) - (iii) of this  
642 subparagraph, administration of such compounded sterile preparations must commence within 12  
643 hours of preparation or as recommended in the manufacturers' package insert, whichever is less.  
644 However, the administration of sterile radiopharmaceuticals, with documented testing of  
645 chemical stability, may be administered beyond 12 hours of preparation.

646 (C) Medium-risk level compounded sterile preparations.

647 (i) Medium-Risk Conditions. Medium-risk level compounded sterile preparations, are those  
648 compounded aseptically under low-risk conditions and one or more of the following conditions  
649 exists.

650 (I) Multiple individual or small doses of sterile products are combined or pooled to prepare a  
651 compounded sterile preparation that will be administered either to multiple patients or to one  
652 patient on multiple occasions.

653 (II) The compounding process includes complex aseptic manipulations other than the single-  
654 volume transfer.

655 (III) The compounding process requires unusually long duration, such as that required to  
656 complete the dissolution or homogenous mixing (e.g., reconstitution of intravenous  
657 immunoglobulin or other intravenous protein products).

658 (IV) The compounded sterile preparations do not contain broad spectrum bacteriostatic  
659 substances and they are administered over several days (e.g., an externally worn infusion  
660 device).

661 (V) For a medium-risk preparation, in the absence of passing a [direct] sterility test [testing  
662 results] the storage periods cannot [beyond use dates may not] exceed the following time  
663 periods: before administration, the compounded sterile preparations are properly stored and are  
664 exposed for not more than 30 hours at controlled room temperature, for not more than 9 days at a

665 cold temperature, and for 45 days in solid frozen state between minus 25 degrees Celsius and  
666 minus 10 degrees Celsius.

667 (ii) Examples of medium-risk compounding. Examples of medium-risk compounding include the  
668 following.

669 (I) Compounding of total parenteral nutrition fluids using a manual or automated device during  
670 which there are multiple injections, detachments, and attachments of nutrient source products to  
671 the device or machine to deliver all nutritional components to a final sterile container.

672 (II) Filling of reservoirs of injection and infusion devices with more than three sterile drug  
673 products and evacuations of air from those reservoirs before the filled device is dispensed.

674 (III) Filling of reservoirs of injection and infusion devices with volumes of sterile drug solutions  
675 that will be administered over several days at ambient temperatures between 25 and 40 degrees  
676 Celsius (77 and 104 degrees Fahrenheit).

677 (IV) Transfer of volumes from multiple ampuls or vials into a single, final sterile container or  
678 product.

679 (D) High-risk level compounded sterile preparations.

680 (i) High-risk Conditions. High-risk level compounded sterile preparations are those compounded  
681 under any of the following conditions.

682 (I) Non-sterile ingredients, including manufactured products not intended for sterile routes of  
683 administration (e.g., oral) are incorporated or a non-sterile device is employed before terminal  
684 sterilization.

685 (II) Any of the following are exposed to air quality worse than ISO Class 5 for more than 1 hour:

686 (-a-) sterile contents of commercially manufactured products;

687 (-b-) CSPs that lack effective antimicrobial preservatives; and

688 (-c-) sterile surfaces of devices and containers for the preparation, transfer, sterilization, and  
689 packaging of CSPs.

690 (III) Compounding personnel are improperly garbed and gloved.

691 (IV) Non-sterile water-containing preparations are exposed no more than 6 hours before being  
692 sterilized.

693 (V) It is assumed, and not verified by examination of labeling and documentation from suppliers  
694 or by direct determination, that the chemical purity and content strength of ingredients meet their  
695 original or compendial specifications in unopened or in opened packages of bulk ingredients.

696 (VI) For a sterilized high-risk level preparation, in the absence of passing a sterility test, the  
697 storage periods cannot exceed the following time periods: before administration, the  
698 compounded sterile preparations are properly stored and are exposed for not more than 24 hours  
699 at controlled room temperature, for not more than 3 days at a cold temperature, and for 45 days  
700 in solid frozen state between minus 25 degrees Celsius and minus 10 degrees Celsius.

701 (VII) All non-sterile measuring, mixing, and purifying devices are rinsed thoroughly with sterile,  
702 pyrogen-free water, and then thoroughly drained or dried immediately before use for high-risk  
703 compounding. All high-risk compounded sterile solutions subjected to terminal sterilization are  
704 prefiltered by passing through a filter with a nominal pore size not larger than 1.2 micron  
705 preceding or during filling into their final containers to remove particulate matter. Sterilization of  
706 high-risk level compounded sterile preparations by filtration shall be performed with a sterile 0.2  
707 micrometer or 0.22 micrometer nominal pore size filter entirely within an ISO Class 5 or  
708 superior air quality environment.

709 (ii) Examples of high-risk compounding. Examples of high-risk compounding include the  
710 following.

711 (I) Dissolving non-sterile bulk drug powders to make solutions, which will be terminally  
712 sterilized.

713 (II) Exposing the sterile ingredients and components used to prepare and package compounded  
714 sterile preparations to room air quality worse than ISO Class 5 for more than one hour.

715 (III) Measuring and mixing sterile ingredients in non-sterile devices before sterilization is  
716 performed.

717 (IV) Assuming, without appropriate evidence or direct determination, that packages of bulk  
718 ingredients contain at least 95% by weight of their active chemical moiety and have not been  
719 contaminated or adulterated between uses.

720 (3) Immediate Use Compounded Sterile Preparations. For the purpose of emergency or  
721 immediate patient care, such situations may include cardiopulmonary resuscitation, emergency  
722 room treatment, preparation of diagnostic agents, or critical therapy where the preparation of the  
723 compounded sterile preparation under low-risk level conditions would subject the patient to  
724 additional risk due to delays in therapy. Compounded sterile preparations are exempted from the  
725 requirements described in this paragraph for low-risk level compounded sterile preparations  
726 when all of the following criteria are met.

727 (A) Only simple aseptic measuring and transfer manipulations are performed with not more than  
728 three sterile non-hazardous commercial drug and diagnostic radiopharmaceutical drug products,  
729 including an infusion or diluent solution, from the manufacturers' original containers and not  
730 more than two entries into any one container or package of sterile infusion solution or  
731 administration container/device.

732 (B) Unless required for the preparation, the compounding procedure occurs continuously without  
733 delays or interruptions and does not exceed 1 hour.

734 (C) During preparation, aseptic technique is followed and, if not immediately administered, the  
735 finished compounded sterile preparation is under continuous supervision to minimize the  
736 potential for contact with nonsterile surfaces, introduction of particulate matter of biological  
737 fluids, mix-ups with other compounded sterile preparations, and direct contact of outside  
738 surfaces.

739 (D) Administration begins not later than one hour following the completion of preparing the  
740 compounded sterile preparation.

741 (E) When the compounded sterile preparations is not administered by the person who prepared it,  
742 or its administration is not witnessed by the person who prepared it, the compounded sterile  
743 preparation shall bear a label listing patient identification information such as name and  
744 identification number(s), the names and amounts of all ingredients, the name or initials of the  
745 person who prepared the compounded sterile preparation, and the exact 1-hour beyond-use time  
746 and date.

747 (F) If administration has not begun within one hour following the completion of preparing the  
748 compounded sterile preparation, the compounded sterile preparation is promptly and safely  
749 discarded. Immediate use compounded sterile preparations shall not be stored for later use.

750 (G) Hazardous drugs shall not be prepared as immediate use compounded sterile preparations.

751 (4) Single-dose and multiple dose containers.

752 (A) Opened or needle punctured single-dose containers, such as bags bottles, syringes, and vials  
753 of sterile products shall be used within one hour if opened in worse than ISO Class 5 air quality.  
754 Any remaining contents must be discarded.

755 (B) Single-dose containers, including single-dose large volume parenteral solutions and single-  
756 dose vials, exposed to ISO Class 5 or cleaner air may be used up to six hours after initial needle  
757 puncture.

758 (C) Opened single-dose fusion sealed containers shall not be stored for any time period.

759 (D) Multiple-dose containers may be used up to 28 days after initial needle puncture unless  
760 otherwise specified by the manufacturer.

761 (5) Library. In addition to the library requirements of the pharmacy's specific license  
762 classification, a pharmacy shall maintain current or updated copies in hard-copy or electronic  
763 format of each of the following:

764 (A) a reference text on injectable drug preparations, such as Handbook on Injectable Drug  
765 Products;

766 (B) a specialty reference text appropriate for the scope of pharmacy services provided by the  
767 pharmacy, e.g., if the pharmacy prepares hazardous drugs, a reference text on the preparation of  
768 hazardous drugs; and

769 (C) the United States Pharmacopeia/National Formulary containing USP Chapter 71, Sterility  
770 Tests, USP Chapter 85, Bacterial Endotoxins Test, Pharmaceutical Compounding--Nonsterile  
771 Preparations, USP Chapter 795, USP Chapter 797, Pharmaceutical Compounding--Sterile  
772 Preparations, and USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding; and

773 (D) any additional USP/NF chapters applicable to the practice of the pharmacy (e.g., USP  
774 Chapter 800, Hazardous Drugs--Handling in Healthcare Settings, USP Chapter 823, Positron  
775 Emission Tomography Drugs for Compounding, Investigational, and Research Uses).

776 (6) Environment. Compounding facilities shall be physically designed and environmentally  
777 controlled to minimize airborne contamination from contacting critical sites.

778 (A) Low and Medium Risk Preparations. A pharmacy that prepares low- and medium-risk  
779 preparations shall have a clean room for the compounding of sterile preparations that is  
780 constructed to minimize the opportunities for particulate and microbial contamination. The clean  
781 room shall:

782 (i) be clean, well lit, and of sufficient size to support sterile compounding activities;

783 (ii) be maintained at a temperature of 20 degrees Celsius or cooler and at a humidity below 60%  
784 ~~[a comfortable temperature (e.g., 20 degrees Celsius or cooler) allowing compounding personnel~~  
785 ~~to perform flawlessly when attired in the required aseptic compounding garb];~~

786 (iii) be used only for the compounding of sterile preparations;

787 (iv) be designed such that hand sanitizing and gowning occurs outside the buffer area but allows  
788 hands-free access by compounding personnel to the buffer area;

789 (v) have non-porous and washable floors or floor covering to enable regular disinfection;

790 (vi) be ventilated in a manner to avoid disruption from the HVAC system and room cross-drafts;

791 (vii) have walls, ceilings, floors, fixtures, shelving, counters, and cabinets that are smooth,  
792 impervious, free from cracks and crevices (e.g., coved), non-shedding and resistant to damage by  
793 disinfectant agents;

794 (viii) have junctures of ceilings to walls coved or caulked to avoid cracks and crevices;

795 (ix) have drugs and supplies stored on shelving areas above the floor to permit adequate floor  
796 cleaning;

797 (x) contain only the appropriate compounding supplies and not be used for bulk storage for  
798 supplies and materials. Objects that shed particles shall not be brought into the clean room. A  
799 Class B pharmacy may use low-linting absorbent materials in the primary engineering control  
800 device;

801 (xi) contain an ante-area that contains a sink with hot and cold running water that enables hands-  
802 free use with a closed system of soap dispensing to minimize the risk of extrinsic contamination.  
803 A Class B pharmacy may have a sink with hot and cold running water that enables hands-free  
804 use with a closed system of soap dispensing immediately outside the ante-area if antiseptic hand  
805 cleansing is performed using a waterless alcohol-based surgical hand scrub with persistent  
806 activity following manufacturers' recommendations once inside the ante-area; and

807 (xii) contain a buffer area. The following is applicable for the buffer area.

808 (I) There shall be some demarcation designation that delineates the ante-area from the buffer  
809 area. The demarcation shall be such that it does not create conditions that could adversely affect  
810 the cleanliness of the area.

811 (II) The buffer area shall be segregated from surrounding, unclassified spaces to reduce the risk  
812 of contaminants being blown, dragged, or otherwise introduced into the filtered unidirectional  
813 airflow environment, and this segregation should be continuously monitored.

814 (III) A buffer area that is not physically separated from the ante-area shall employ the principle  
815 of displacement airflow as defined in Chapter 797, Pharmaceutical Compounding--Sterile  
816 Preparations, of the USP/NF, with limited access to personnel.

817 (IV) The buffer area shall not contain sources of water (i.e., sinks) or floor drains other than  
818 distilled or sterile water introduced for facilitating the use of heat block wells for  
819 radiopharmaceuticals.

820 (B) High-risk Preparations.

821 (i) In addition to the requirements in subparagraph (A) of this paragraph, when high-risk  
822 preparations are compounded, the primary engineering control shall be located in a buffer area  
823 that provides a physical separation, through the use of walls, doors and pass-throughs and has a  
824 minimum differential positive pressure of 0.02 to 0.05 inches water column.

825 (ii) Presterilization procedures for high-risk level compounded sterile preparations, such as  
826 weighing and mixing, shall be completed in no worse than an ISO Class 8 environment.

827 (C) Automated compounding device.

828 (i) General. If automated compounding devices are used, the pharmacy shall have a method to  
829 calibrate and verify the accuracy of automated compounding devices used in aseptic processing  
830 and document the calibration and verification on a daily basis, based on the manufacturer's  
831 recommendations, and review the results at least weekly.

- 832 (ii) Loading bulk drugs into automated compounding devices.
- 833 (I) Automated compounding device may be loaded with bulk drugs only by a pharmacist or by  
834 pharmacy technicians or pharmacy technician trainees under the direction and direct supervision  
835 of a pharmacist.
- 836 (II) The label of an automated compounding device container shall indicate the brand name and  
837 strength of the drug; or if no brand name, then the generic name, strength, and name of the  
838 manufacturer or distributor.
- 839 (III) Records of loading bulk drugs into an automated compounding device shall be maintained  
840 to show:
- 841 (-a-) name of the drug, strength, and dosage form;
- 842 (-b-) manufacturer or distributor;
- 843 (-c-) manufacturer's lot number;
- 844 (-d-) manufacturer's expiration date;
- 845 (-e-) quantity added to the automated compounding device;
- 846 (-f-) date of loading;
- 847 (-g-) name, initials, or electronic signature of the person loading the automated compounding  
848 device; and
- 849 (-h-) name, initials, or electronic signature of the responsible pharmacist.
- 850 (IV) The automated compounding device shall not be used until a pharmacist verifies that the  
851 system is properly loaded and affixes his or her signature or electronic signature to the record  
852 specified in subclause (III) of this clause.
- 853 (D) Hazardous drugs. If the preparation is hazardous, the following is also applicable.
- 854 (i) Hazardous drugs shall be prepared only under conditions that protect personnel during  
855 preparation and storage.
- 856 (ii) Hazardous drugs shall be stored separately from other inventory in a manner to prevent  
857 contamination and personnel exposure.
- 858 (iii) All personnel involved in the compounding of hazardous drugs shall wear appropriate  
859 protective apparel, such as gowns, face masks, eye protection, hair covers, shoe covers or  
860 dedicated shoes, and appropriate gloving at all times when handling hazardous drugs, including  
861 receiving, distribution, stocking, inventorying, preparation, for administration and disposal.

- 862 (iv) Appropriate safety and containment techniques for compounding hazardous drugs shall be  
863 used in conjunction with aseptic techniques required for preparing sterile preparations.
- 864 (v) Disposal of hazardous waste shall comply with all applicable local, state, and federal  
865 requirements.
- 866 (vi) Prepared doses of hazardous drugs must be dispensed, labeled with proper precautions inside  
867 and outside, and distributed in a manner to minimize patient contact with hazardous agents.
- 868 (E) Blood-labeling procedures. When compounding activities require the manipulation of a  
869 patient's blood-derived material (e.g., radiolabeling a patient's or donor's white blood cells), the  
870 manipulations shall be performed in a ISO Class 5 biological safety cabinet located in a buffer  
871 area and shall be clearly separated from routine material-handling procedures and equipment  
872 used in preparation activities to avoid any cross-contamination. The preparations shall not  
873 require sterilization.
- 874 (F) Cleaning and disinfecting the sterile compounding areas. The following cleaning and  
875 disinfecting practices and frequencies apply to direct and contiguous compounding areas, which  
876 include ISO Class 5 compounding areas for exposure of critical sites as well as buffer areas,  
877 ante-areas, and segregated compounding areas.
- 878 (i) The pharmacist-in-charge is responsible for developing written procedures for cleaning and  
879 disinfecting the direct and contiguous compounding areas and assuring the procedures are  
880 followed.
- 881 (ii) These procedures shall be conducted at the beginning of each work shift, before each batch  
882 preparation is started, when there are spills, and when surface contamination is known or  
883 suspected resulting from procedural breaches, and every 30 minutes during continuous  
884 compounding of individual compounded sterile preparations, unless a particular compounding  
885 procedure requires more than 30 minutes to complete, in which case, the direct compounding  
886 area is to be cleaned immediately after the compounding activity is completed.
- 887 (iii) Before compounding is performed, all items shall be removed from the direct and  
888 contiguous compounding areas and all surfaces are cleaned by removing loose material and  
889 residue from spills, followed by an application of a residue-free disinfecting agent (e.g., IPA),  
890 which is allowed to dry before compounding begins. In a Class B pharmacy, objects used in  
891 preparing sterile radiopharmaceuticals (e.g., dose calibrator) which cannot be reasonably  
892 removed from the compounding area shall be sterilized with an application of a residue-free  
893 disinfection agent.
- 894 (iv) Work surfaces in the buffer areas and ante-areas, as well as segregated compounding areas,  
895 shall be cleaned and disinfected at least daily. Dust and debris shall be removed when necessary  
896 from storage sites for compounding ingredients and supplies using a method that does not  
897 degrade the ISO Class 7 or 8 air quality.

898 (v) Floors in the buffer area, ante-area, and segregated compounding area are cleaned by  
899 mopping with a cleaning and disinfecting agent at least once daily when no aseptic operations  
900 are in progress. Mopping shall be performed by trained personnel using approved agents and  
901 procedures described in the written SOPs. It is incumbent on compounding personnel to ensure  
902 that such cleaning is performed properly.

903 (vi) In the buffer area, ante-area, and segregated compounding area, walls, ceilings, and shelving  
904 shall be cleaned and disinfected monthly. Cleaning and disinfecting agents shall be used with  
905 careful consideration of compatibilities, effectiveness, and inappropriate or toxic residues.

906 (vii) All cleaning materials, such as wipers, sponges, and mops, shall be non-shedding, and  
907 dedicated to use in the buffer area, ante-area, and segregated compounding areas and shall not be  
908 removed from these areas except for disposal. Floor mops may be used in both the buffer area  
909 and ante-area, but only in that order. If cleaning materials are reused, procedures shall be  
910 developed that ensure that the effectiveness of the cleaning device is maintained and that  
911 repeated use does not add to the bio-burden of the area being cleaned.

912 (viii) Supplies and equipment removed from shipping cartons must be wiped with a disinfecting  
913 agent, such as sterile IPA. After the disinfectant is sprayed or wiped on a surface to be  
914 disinfected, the disinfectant shall be allowed to dry, during which time the item shall not be used  
915 for compounding purposes. However, if sterile supplies are received in sealed pouches, the  
916 pouches may be removed as the supplies are introduced into the ISO Class 5 area without the  
917 need to disinfect the individual sterile supply items. No shipping or other external cartons may be  
918 taken into the buffer area or segregated compounding area.

919 (ix) Storage shelving emptied of all supplies, walls, and ceilings are cleaned and disinfected at  
920 planned intervals, monthly, if not more frequently.

921 (x) Cleaning must be done by personnel trained in appropriate cleaning techniques.

922 (xi) Proper documentation and frequency of cleaning must be maintained and shall contain the  
923 following:

924 (I) date and time of cleaning;

925 (II) type of cleaning performed; and

926 (III) name of individual who performed the cleaning.

927 (G) Security requirements. The pharmacist-in-charge may authorize personnel to gain access to  
928 that area of the pharmacy containing dispensed sterile preparations, in the absence of the  
929 pharmacist, for the purpose of retrieving dispensed prescriptions to deliver to patients. If the  
930 pharmacy allows such after-hours access, the area containing the dispensed sterile preparations  
931 shall be an enclosed and lockable area separate from the area containing undispensed  
932 prescription drugs. A list of the authorized personnel having such access shall be in the  
933 pharmacy's policy and procedure manual.

934 (H) Storage requirements and beyond-use dating.

935 (i) Storage requirements. All drugs shall be stored at the proper temperature and conditions, as  
936 defined in the USP/NF and in §291.15 of this title (relating to Storage of Drugs).

937 (ii) Beyond-use dating.

938 (I) Beyond-use dates for compounded sterile preparations shall be assigned based on professional  
939 experience, which shall include careful interpretation of appropriate information sources for the  
940 same or similar formulations.

941 (II) Beyond-use dates for compounded sterile preparations that are prepared strictly in  
942 accordance with manufacturers' product labeling must be those specified in that labeling, or from  
943 appropriate literature sources or direct testing.

944 (III) When assigning a beyond-use date, compounding personnel shall consult and apply drug-  
945 specific and general stability documentation and literature where available, and they should  
946 consider the nature of the drug and its degradation mechanism, the container in which it is  
947 packaged, the expected storage conditions, and the intended duration of therapy.

948 (IV) The sterility and storage and stability beyond-use date for attached and activated container  
949 pairs of drug products for intravascular administration shall be applied as indicated by the  
950 manufacturer.

951 (7) Primary engineering control device. The pharmacy shall prepare sterile preparations in a  
952 primary engineering control device (PEC), such as a laminar air flow hood, biological safety  
953 cabinet, compounding aseptic isolator (CAI), or compounding aseptic containment isolator  
954 (CACI) which is capable of maintaining at least ISO Class 5 conditions for 0.5 micrometer  
955 particles while compounding sterile preparations.

956 (A) Laminar air flow hood. If the pharmacy is using a laminar air flow hood as its PEC, the  
957 laminar air flow hood shall:

958 (i) be located in the buffer area and placed in the buffer area in a manner as to avoid conditions  
959 that could adversely affect its operation such as strong air currents from opened doors, personnel  
960 traffic, or air streams from the heating, ventilating and air condition system;

961 (ii) be certified by a qualified independent contractor according to the appropriate Controlled  
962 Environment Testing Association (CETA) standard (CAG-003-2006) for operational efficiency  
963 at least every six months and whenever the device or room is relocated or altered or major  
964 service to the facility is performed;

965 (iii) have pre-filters inspected periodically and replaced as needed, in accordance with written  
966 policies and procedures and the manufacturer's specification, and the inspection and/or  
967 replacement date documented; and

968 (iv) be located in a buffer area that has a minimum differential positive pressure of 0.02 to 0.05  
969 inches water column. A buffer area that is not physically separated from the ante-area shall  
970 employ the principle of displacement airflow as defined in Chapter 797, Pharmaceutical  
971 Compounding--Sterile Preparations, of the USP/NF, with limited access to personnel.

972 (B) Biological safety cabinet.

973 (i) If the pharmacy is using a biological safety cabinet as its PEC for the preparation of  
974 hazardous sterile compounded preparations, the biological safety cabinet shall be a Class II or III  
975 vertical flow biological safety cabinet located in an ISO Class 7 area that is physically separated  
976 from other preparation areas. The area for preparation of sterile chemotherapeutic preparations  
977 shall:

978 (I) have not less than 0.01 inches water column negative pressure to the adjacent positive  
979 pressure ISO Class 7 or better ante-area; and

980 (II) have a pressure indicator that can be readily monitored for correct room pressurization.

981 (ii) Pharmacies that prepare a low volume of hazardous drugs, are not required to comply with  
982 the provisions of clause (i) of this subparagraph if the pharmacy uses a device that provides two  
983 tiers of containment (e.g., closed-system vial transfer device within a BSC or CACI that is  
984 located in a non-negative pressure room).

985 (iii) If the pharmacy is using a biological safety cabinet as its PEC for the preparation of non-  
986 hazardous sterile compounded preparations, the biological safety cabinet shall:

987 (I) be located in the buffer area and placed in the buffer area in a manner as to avoid conditions  
988 that could adversely affect its operation such as strong air currents from opened doors, personnel  
989 traffic, or air streams from the heating, ventilating and air condition system;

990 (II) be certified by a qualified independent contractor according to the International Organization  
991 of Standardization (ISO) Classification of Particulate Matter in Room Air (ISO 14644-1) for  
992 operational efficiency at least every six months and whenever the device or room is relocated or  
993 altered or major service to the facility is performed, in accordance with the manufacturer's  
994 specifications and test procedures specified in the Institute of Environmental Sciences and  
995 Technology (IEST) document IEST-RP-CC002.3;

996 (III) have pre-filters inspected periodically and replaced as needed, in accordance with written  
997 policies and procedures and the manufacturer's specification, and the inspection and/or  
998 replacement date documented; and

999 (IV) be located in a buffer area that has a minimum differential positive pressure of 0.02 to 0.05  
1000 inches water column.

1001 (C) Compounding aseptic isolator.

1002 (i) If the pharmacy is using a compounding aseptic isolator (CAI) as its PEC, the CAI shall  
1003 provide unidirectional airflow within the main processing and antechambers, and be placed in an  
1004 ISO Class 7 buffer area unless the isolator meets all of the following conditions:

1005 (I) The isolator must provide isolation from the room and maintain ISO Class 5 during dynamic  
1006 operating conditions including transferring ingredients, components, and devices into and out of  
1007 the isolator and during preparation of compounded sterile preparations.

1008 (II) Particle counts sampled approximately 6 to 12 inches upstream of the critical exposure site  
1009 must maintain ISO Class 5 levels during compounding operations.

1010 (III) The CAI must be validated according to CETA CAG-002-2006 standards.

1011 (IV) The pharmacy shall maintain documentation from the manufacturer that the isolator meets  
1012 this standard when located in worse than ISO Class 7 environments.

1013 (ii) If the isolator meets the requirements in clause (i) of this subparagraph, the CAI may be  
1014 placed in a non-ISO classified area of the pharmacy; however, the area shall be segregated from  
1015 other areas of the pharmacy and shall:

1016 (I) be clean, well lit, and of sufficient size;

1017 (II) be used only for the compounding of low- and medium-risk, non-hazardous sterile  
1018 preparations;

1019 (III) be located in an area of the pharmacy with non-porous and washable floors or floor covering  
1020 to enable regular disinfection; and

1021 (IV) be an area in which the CAI is placed in a manner as to avoid conditions that could  
1022 adversely affect its operation.

1023 (iii) In addition to the requirements specified in clauses (i) and (ii) of this subparagraph, if the  
1024 CAI is used in the compounding of high-risk non-hazardous preparations, the CAI shall be  
1025 placed in an area or room with at least ISO 8 quality air so that high-risk powders weighed in at  
1026 least ISO-8 air quality conditions, compounding utensils for measuring and other compounding  
1027 equipment are not exposed to lesser air quality prior to the completion of compounding and  
1028 packaging of the high-risk preparation.

1029 (D) Compounding aseptic containment isolator.

1030 (i) If the pharmacy is using a compounding aseptic containment isolator as its PEC for the  
1031 preparation of low- and medium-risk hazardous drugs, the CACI shall be located in a separate  
1032 room away from other areas of the pharmacy and shall:

1033 (I) provide at least 0.01 inches water column negative pressure compared to the other areas of the  
1034 pharmacy;

1035 (II) provide unidirectional airflow within the main processing and antechambers, and be placed  
1036 in an ISO Class 7 buffer area, unless the CACI meets all of the following conditions.

1037 (-a-) The isolator must provide isolation from the room and maintain ISO Class 5 during  
1038 dynamic operating conditions including transferring ingredients, components, and devices into  
1039 and out of the isolator and during preparation of compounded sterile preparations.

1040 (-b-) Particle counts sampled approximately 6 to 12 inches upstream of the critical exposure site  
1041 must maintain ISO Class 5 levels during compounding operations.

1042 (-c-) The CACI must be validated according to CETA CAG-002-2006 standards.

1043 (-d-) The pharmacy shall maintain documentation from the manufacturer that the isolator meets  
1044 this standard when located in worse than ISO Class 7 environments.

1045 (ii) If the CACI meets all conditions specified in clause (i) of this subparagraph, the CACI shall  
1046 not be located in the same room as a CAI, but shall be located in a separate room in the  
1047 pharmacy, that is not required to maintain ISO classified air. The room in which the CACI is  
1048 located shall provide a minimum of 0.01 inches water column negative pressure compared with  
1049 the other areas of the pharmacy and shall meet the following requirements:

1050 (I) be clean, well lit, and of sufficient size;

1051 (II) be maintained at a temperature of 20 degrees Celsius or cooler and a humidity below 60%  
1052 ~~[comfortable temperature (e.g., 20 degrees Celsius or cooler) allowing compounding personnel~~  
1053 ~~to perform flawlessly when attired in the required aseptic compounding garb];~~

1054 (III) be used only for the compounding of hazardous sterile preparations;

1055 (IV) be located in an area of the pharmacy with walls, ceilings, floors, fixtures, shelving,  
1056 counters, and cabinets that are smooth, impervious, free from cracks and crevices, non-shedding  
1057 and resistant to damage by disinfectant agents; and

1058 (V) have non-porous and washable floors or floor covering to enable regular disinfection.

1059 (iii) If the CACI is used in the compounding of high-risk hazardous preparations, the CACI shall  
1060 be placed in an area or room with at least ISO 8 quality air so that high-risk powders, weighed in  
1061 at least ISO-8 air quality conditions, are not exposed to lesser air quality prior to the completion  
1062 of compounding and packaging of the high-risk preparation.

1063 (8) Additional Equipment and Supplies. Pharmacies compounding sterile preparations shall have  
1064 the following equipment and supplies:

1065 (A) a calibrated system or device (i.e., thermometer) to monitor the temperature to ensure that  
1066 proper storage requirements are met, if sterile preparations are stored in the refrigerator;

- 1067 (B) a calibrated system or device to monitor the temperature where bulk chemicals are stored;
- 1068 (C) a temperature-sensing mechanism suitably placed in the controlled temperature storage space  
1069 to reflect accurately the true temperature;
- 1070 (D) if applicable, a Class A prescription balance, or analytical balance and weights. Such balance  
1071 shall be properly maintained and subject to periodic inspection by the Texas State Board of  
1072 Pharmacy;
- 1073 (E) equipment and utensils necessary for the proper compounding of sterile preparations. Such  
1074 equipment and utensils used in the compounding process shall be:
- 1075 (i) of appropriate design, appropriate capacity, and be operated within designed operational  
1076 limits;
- 1077 (ii) of suitable composition so that surfaces that contact components, in-process material, or drug  
1078 products shall not be reactive, additive, or absorptive so as to alter the safety, identity, strength,  
1079 quality, or purity of the drug preparation beyond the desired result;
- 1080 (iii) cleaned and sanitized immediately prior to and after each use; and
- 1081 (iv) routinely inspected, calibrated (if necessary), or checked to ensure proper performance;
- 1082 (F) appropriate disposal containers for used needles, syringes, etc., and if applicable, hazardous  
1083 waste from the preparation of hazardous drugs and/or biohazardous waste;
- 1084 (G) appropriate packaging or delivery containers to maintain proper storage conditions for sterile  
1085 preparations;
- 1086 (H) infusion devices, if applicable; and
- 1087 (I) all necessary supplies, including:
- 1088 (i) disposable needles, syringes, and other supplies for aseptic mixing;
- 1089 (ii) disinfectant cleaning solutions;
- 1090 (iii) sterile 70% isopropyl alcohol;
- 1091 (iv) sterile gloves, both for hazardous and non-hazardous drug compounding;
- 1092 (v) sterile alcohol-based or water-less alcohol based surgical scrub;
- 1093 (vi) hand washing agents with bactericidal action;
- 1094 (vii) disposable, lint free towels or wipes;

- 1095 (viii) appropriate filters and filtration equipment;
- 1096 (ix) hazardous spill kits, if applicable; and
- 1097 (x) masks, caps, coveralls or gowns with tight cuffs, shoe covers, and gloves, as applicable.
- 1098 (9) Labeling.
- 1099 (A) Prescription drug or medication orders. In addition to the labeling requirements for the  
1100 pharmacy's specific license classification, the label dispensed or distributed pursuant to a  
1101 prescription drug or medication order shall contain the following:
- 1102 (i) the generic name(s) or the official name(s) of the principal active ingredient(s) of the  
1103 compounded sterile preparation;
- 1104 (ii) for outpatient prescription orders other than sterile radiopharmaceuticals, a statement that the  
1105 compounded sterile preparation has been compounded by the pharmacy. (An auxiliary label may  
1106 be used on the container to meet this requirement);
- 1107 (iii) a beyond-use date. The beyond-use date shall be determined as outlined in Chapter 797,  
1108 Pharmacy Compounding--Sterile Preparations of the USP/NF, and paragraph (7)(G) of this  
1109 subsection;
- 1110 (B) Batch. If the sterile preparation is compounded in a batch, the following shall also be  
1111 included on the batch label:
- 1112 (i) unique lot number assigned to the batch;
- 1113 (ii) quantity;
- 1114 (iii) appropriate ancillary instructions, such as storage instructions or cautionary statements,  
1115 including hazardous drug warning labels where appropriate; and
- 1116 (iv) device-specific instructions, where appropriate.
- 1117 (C) Pharmacy bulk package. The label of a pharmacy bulk package shall:
- 1118 (i) state prominently "Pharmacy Bulk Package--Not for Direct Infusion;"
- 1119 (ii) contain or refer to information on proper techniques to help ensure safe use of the  
1120 preparation; and
- 1121 (iii) bear a statement limiting the time frame in which the container may be used once it has been  
1122 entered, provided it is held under the labeled storage conditions.

1123 (10) Written drug information for prescription drug orders only. Written information about the  
1124 compounded preparation or its major active ingredient(s) shall be given to the patient at the time  
1125 of dispensing a prescription drug order. A statement which indicates that the preparation was  
1126 compounded by the pharmacy must be included in this written information. If there is no written  
1127 information available, the patient shall be advised that the drug has been compounded and how  
1128 to contact a pharmacist, and if appropriate, the prescriber, concerning the drug. This paragraph  
1129 does not apply to the preparation of radiopharmaceuticals.

1130 (11) Pharmaceutical Care Services. In addition to the pharmaceutical care requirements for the  
1131 pharmacy's specific license classification, the following requirements for sterile preparations  
1132 compounded pursuant to prescription drug orders must be met. This paragraph does not apply to  
1133 the preparation of radiopharmaceuticals.

1134 (A) Primary provider. There shall be a designated physician primarily responsible for the  
1135 patient's medical care. There shall be a clear understanding between the physician, the patient,  
1136 and the pharmacy of the responsibilities of each in the areas of the delivery of care, and the  
1137 monitoring of the patient. This shall be documented in the patient medication record (PMR).

1138 (B) Patient training. The pharmacist-in-charge shall develop policies to ensure that the patient  
1139 and/or patient's caregiver receives information regarding drugs and their safe and appropriate  
1140 use, including instruction when applicable, regarding:

1141 (i) appropriate disposition of hazardous solutions and ancillary supplies;

1142 (ii) proper disposition of controlled substances in the home;

1143 (iii) self-administration of drugs, where appropriate;

1144 (iv) emergency procedures, including how to contact an appropriate individual in the event of  
1145 problems or emergencies related to drug therapy; and

1146 (v) if the patient or patient's caregiver prepares sterile preparations in the home, the following  
1147 additional information shall be provided:

1148 (I) safeguards against microbial contamination, including aseptic techniques for compounding  
1149 intravenous admixtures and aseptic techniques for injecting additives to premixed intravenous  
1150 solutions;

1151 (II) appropriate storage methods, including storage durations for sterile pharmaceuticals and  
1152 expirations of self-mixed solutions;

1153 (III) handling and disposition of premixed and self-mixed intravenous admixtures; and

1154 (IV) proper disposition of intravenous admixture compounding supplies such as syringes, vials,  
1155 ampules, and intravenous solution containers.

1156 (C) Pharmacist-patient relationship. It is imperative that a pharmacist-patient relationship be  
1157 established and maintained throughout the patient's course of therapy. This shall be documented  
1158 in the patient's medication record (PMR).

1159 (D) Patient monitoring. The pharmacist-in-charge shall develop policies to ensure that:

1160 (i) the patient's response to drug therapy is monitored and conveyed to the appropriate health  
1161 care provider;

1162 (ii) the first dose of any new drug therapy is administered in the presence of an individual  
1163 qualified to monitor for and respond to adverse drug reactions; and

1164 (iii) reports of adverse events with a compounded sterile preparation are reviewed promptly and  
1165 thoroughly to correct and prevent future occurrences.

1166 (12) Drugs, components, and materials used in sterile compounding.

1167 (A) Drugs used in sterile compounding shall be a USP/NF grade substances manufactured in an  
1168 FDA-registered facility.

1169 (B) If USP/NF grade substances are not available shall be of a chemical grade in one of the  
1170 following categories:

1171 (i) Chemically Pure (CP);

1172 (ii) Analytical Reagent (AR);

1173 (iii) American Chemical Society (ACS); or

1174 (iv) Food Chemical Codex.

1175 (C) If a drug, component or material is not purchased from a FDA-registered facility, the  
1176 pharmacist shall establish purity and stability by obtaining a Certificate of Analysis from the  
1177 supplier and the pharmacist shall compare the monograph of drugs in a similar class to the  
1178 Certificate of Analysis.

1179 (D) All components shall:

1180 (i) be manufactured in an FDA-registered facility; or

1181 (ii) in the professional judgment of the pharmacist, be of high quality and obtained from  
1182 acceptable and reliable alternative sources; and

1183 (iii) stored in properly labeled containers in a clean, dry area, under proper temperatures.

1184 (E) Drug preparation containers and closures shall not be reactive, additive, or absorptive so as to  
1185 alter the safety, identity, strength, quality, or purity of the compounded drug preparation beyond  
1186 the desired result.

1187 (F) Components, drug preparation containers, and closures shall be rotated so that the oldest  
1188 stock is used first.

1189 (G) Container closure systems shall provide adequate protection against foreseeable external  
1190 factors in storage and use that can cause deterioration or contamination of the compounded drug  
1191 preparation.

1192 (H) A pharmacy may not compound a preparation that contains ingredients appearing on a  
1193 federal Food and Drug Administration list of drug products withdrawn or removed from the  
1194 market for safety reasons.

1195 (13) Compounding process.

1196 (A) Standard operating procedures (SOPs). All significant procedures performed in the  
1197 compounding area shall be covered by written SOPs designed to ensure accountability, accuracy,  
1198 quality, safety, and uniformity in the compounding process. At a minimum, SOPs shall be  
1199 developed and implemented for:

1200 (i) the facility;

1201 (ii) equipment;

1202 (iii) personnel;

1203 (iv) preparation evaluation;

1204 (v) quality assurance;

1205 (vi) preparation recall;

1206 (vii) packaging; and

1207 (viii) storage of compounded sterile preparations.

1208 (B) USP/NF. Any compounded formulation with an official monograph in the USP/NF shall be  
1209 compounded, labeled, and packaged in conformity with the USP/NF monograph for the drug.

1210 (C) Personnel Cleansing and Garbing.

1211 (i) Any person with an apparent illness or open lesion, including rashes, sunburn, weeping sores,  
1212 conjunctivitis, and active respiratory infection, that may adversely affect the safety or quality of a

1213 drug preparation being compounded shall be excluded from working in ISO Class 5, ISO Class  
1214 7, and ISO Class 8 compounding areas until the condition is remedied.

1215 (ii) Before entering the buffer area, compounding personnel must remove the following:

1216 (I) personal outer garments (e.g., bandanas, coats, hats, jackets, scarves, sweaters, vests);

1217 (II) all cosmetics, because they shed flakes and particles; and

1218 (III) all hand, wrist, and other body jewelry or piercings (e.g., earrings, lip or eyebrow piercings)  
1219 that can interfere with the effectiveness of personal protective equipment (e.g., fit of gloves and  
1220 cuffs of sleeves).

1221 (iii) The wearing of artificial nails or extenders is prohibited while working in the sterile  
1222 compounding environment. Natural nails shall be kept neat and trimmed.

1223 (iv) Personnel shall don personal protective equipment and perform hand hygiene in an order that  
1224 proceeds from the dirtiest to the cleanest activities as follows:

1225 (I) Activities considered the dirtiest include donning of dedicated shoes or shoe covers, head and  
1226 facial hair covers (e.g., beard covers in addition to face masks), and face mask/eye shield. Eye  
1227 shields are optional unless working with irritants like germicidal disinfecting agents or when  
1228 preparing hazardous drugs.

1229 (II) After donning dedicated shoes or shoe covers, head and facial hair covers, and face masks,  
1230 personnel shall perform a hand hygiene procedure by removing debris from underneath  
1231 fingernails using a nail cleaner under running warm water followed by vigorous hand washing.  
1232 Personnel shall begin washing arms at the hands and continue washing to elbows for at least 30  
1233 seconds with either a plain (non-antimicrobial) soap, or antimicrobial soap, and water while in  
1234 the ante-area. Hands and forearms to the elbows shall be completely dried using lint-free  
1235 disposable towels, an electronic hands-free hand dryer, or a HEPA filtered hand dryer.

1236 (III) After completion of hand washing, personnel shall don clean non-shedding gowns with  
1237 sleeves that fit snugly around the wrists and enclosed at the neck.

1238 (IV) Once inside the buffer area or segregated compounding area, and prior to donning sterile  
1239 powder-free gloves, antiseptic hand cleansing shall be performed using a waterless alcohol-based  
1240 surgical hand scrub with persistent activity following manufacturers' recommendations. Hands  
1241 shall be allowed to dry thoroughly before donning sterile gloves.

1242 (V) Sterile gloves that form a continuous barrier with the gown shall be the last item donned  
1243 before compounding begins. Sterile gloves shall be donned using proper technique to ensure the  
1244 sterility of the glove is not compromised while donning. The cuff of the sterile glove shall cover  
1245 the cuff of the gown at the wrist. When preparing hazardous preparations, the compounder shall  
1246 double glove or shall use single gloves ensuring that the gloves are sterile powder-free

1247 chemotherapy-rated gloves. Routine application of sterile 70% IPA shall occur throughout the  
1248 compounding day and whenever non-sterile surfaces are touched.

1249 (v) When compounding personnel shall temporarily exit the buffer area during a work shift, the  
1250 exterior gown, if not visibly soiled, may be removed and retained in the ante-area, to be re-  
1251 donned during that same work shift only. However, shoe covers, hair and facial hair covers, face  
1252 mask/eye shield, and gloves shall be replaced with new ones before re-entering the buffer area  
1253 along with performing proper hand hygiene.

1254 (vi) During high-risk compounding activities that precede terminal sterilization, such as  
1255 weighing and mixing of non-sterile ingredients, compounding personnel shall be garbed and  
1256 gloved the same as when performing compounding in an ISO Class 5 environment. Properly  
1257 garbed and gloved compounding personnel who are exposed to air quality that is either known or  
1258 suspected to be worse than ISO Class 7 shall re-garb personal protective equipment along with  
1259 washing their hands properly, performing antiseptic hand cleansing with a sterile 70% IPA-based  
1260 or another suitable sterile alcohol-based surgical hand scrub, and donning sterile gloves upon re-  
1261 entering the ISO Class 7 buffer area.

1262 (vii) When compounding aseptic isolators or compounding aseptic containment isolators are the  
1263 source of the ISO Class 5 environment, at the start of each new compounding procedure, a new  
1264 pair of sterile gloves shall be donned within the CAI or CACI. In addition, the compounding  
1265 personnel should follow the requirements as specified in this subparagraph, unless the isolator  
1266 manufacturer can provide written documentation based on validated environmental testing that  
1267 any components of personal protective equipment or cleansing are not required.

1268 (14) Quality Assurance.

1269 (A) Initial Formula Validation. Prior to routine compounding of a sterile preparation, a pharmacy  
1270 shall conduct an evaluation that shows that the pharmacy is capable of compounding a  
1271 preparation that is sterile and that contains the stated amount of active ingredient(s).

1272 (i) Low risk preparations.

1273 (I) Quality assurance practices include, but are not limited to the following:

1274 (-a-) Routine disinfection and air quality testing of the direct compounding environment to  
1275 minimize microbial surface contamination and maintain ISO Class 5 air quality.

1276 (-b-) Visual confirmation that compounding personnel are properly donning and wearing  
1277 appropriate items and types of protective garments and goggles.

1278 (-c-) Review of all orders and packages of ingredients to ensure that the correct identity and  
1279 amounts of ingredients were compounded.

1280 (-d-) Visual inspection of compounded sterile preparations, except for sterile  
1281 radiopharmaceuticals, to ensure the absence of particulate matter in solutions, the absence of  
1282 leakage from vials and bags, and the accuracy and thoroughness of labeling.

1283 (II) Example of a Media-Fill Test Procedure. This, or an equivalent test, is performed at least  
1284 annually by each person authorized to compound in a low-risk level under conditions that closely  
1285 simulate the most challenging or stressful conditions encountered during compounding of low-  
1286 risk level sterile preparations. Once begun, this test is completed without interruption within an  
1287 ISO Class 5 air quality environment. Three sets of four 5-milliliter aliquots of sterile Soybean-  
1288 Casein Digest Medium are transferred with the same sterile 10-milliliter syringe and vented  
1289 needle combination into separate sealed, empty, sterile 30-milliliter clear vials (i.e., four 5-  
1290 milliliter aliquots into each of three 30-milliliter vials). Sterile adhesive seals are aseptically  
1291 affixed to the rubber closures on the three filled vials. The vials are incubated within a range of  
1292 20 - 35 degrees Celsius for a minimum of 14 days. Failure is indicated by visible turbidity in the  
1293 medium on or before 14 days. The media-fill test must include a positive-control sample.

1294 (ii) Medium risk preparations.

1295 (I) Quality assurance procedures for medium-risk level compounded sterile preparations include  
1296 all those for low-risk level compounded sterile preparations, as well as a more challenging  
1297 media-fill test passed annually, or more frequently.

1298 (II) Example of a Media-Fill Test Procedure. This, or an equivalent test, is performed at least  
1299 annually under conditions that closely simulate the most challenging or stressful conditions  
1300 encountered during compounding. This test is completed without interruption within an ISO  
1301 Class 5 air quality environment. Six 100-milliliter aliquots of sterile Soybean-Casein Digest  
1302 Medium are aseptically transferred by gravity through separate tubing sets into separate  
1303 evacuated sterile containers. The six containers are then arranged as three pairs, and a sterile 10-  
1304 milliliter syringe and 18-gauge needle combination is used to exchange two 5-milliliter aliquots  
1305 of medium from one container to the other container in the pair. For example, after a 5-milliliter  
1306 aliquot from the first container is added to the second container in the pair, the second container  
1307 is agitated for 10 seconds, then a 5-milliliter aliquot is removed and returned to the first container  
1308 in the pair. The first container is then agitated for 10 seconds, and the next 5-milliliter aliquot is  
1309 transferred from it back to the second container in the pair. Following the two 5-milliliter aliquot  
1310 exchanges in each pair of containers, a 5-milliliter aliquot of medium from each container is  
1311 aseptically injected into a sealed, empty, sterile 10-milliliter clear vial, using a sterile 10-  
1312 milliliter syringe and vented needle. Sterile adhesive seals are aseptically affixed to the rubber  
1313 closures on the three filled vials. The vials are incubated within a range of 20 - 35 degrees  
1314 Celsius for a minimum of 14 days. Failure is indicated by visible turbidity in the medium on or  
1315 before 14 days. The media-fill test must include a positive-control sample.

1316 (iii) High risk preparations.

1317 (I) Procedures for high-risk level compounded sterile preparations include all those for low-risk  
1318 level compounded sterile preparations. In addition, a media-fill test that represents high-risk level

1319 compounding is performed twice a year by each person authorized to compound high-risk level  
1320 compounded sterile preparations.

1321 (II) Example of a Media-Fill Test Procedure Compounded Sterile Preparations Sterilized by  
1322 Filtration. This test, or an equivalent test, is performed under conditions that closely simulate the  
1323 most challenging or stressful conditions encountered when compounding high-risk level  
1324 compounded sterile preparations. Note: Sterility tests for autoclaved compounded sterile  
1325 preparations are not required unless they are prepared in batches of more than 25 units. This test  
1326 is completed without interruption in the following sequence:

1327 (-a-) Dissolve 3 grams of non-sterile commercially available Soybean-Casein Digest Medium in  
1328 100 milliliters of non-bacteriostatic water to make a 3% non-sterile solution.

1329 (-b-) Draw 25 milliliters of the medium into each of three 30-milliliter sterile syringes. Transfer 5  
1330 milliliters from each syringe into separate sterile 10-milliliter vials. These vials are the positive  
1331 controls to generate exponential microbial growth, which is indicated by visible turbidity upon  
1332 incubation.

1333 (-c-) Under aseptic conditions and using aseptic techniques, affix a sterile 0.2-micron porosity  
1334 filter unit and a 20-gauge needle to each syringe. Inject the next 10 milliliters from each syringe  
1335 into three separate 10-milliliter sterile vials. Repeat the process for three more vials. Label all  
1336 vials, affix sterile adhesive seals to the closure of the nine vials, and incubate them at 20 to 35  
1337 degrees Celsius for a minimum of 14 days. Inspect for microbial growth over 14 days as  
1338 described in Chapter 797 Pharmaceutical Compounding--Sterile Preparations, of the USP/NF.

1339 (III) Filter Integrity Testing. Filters need to undergo testing to evaluate the integrity of filters  
1340 used to sterilize high-risk preparations, such as Bubble Point Testing or comparable filter  
1341 integrity testing. Such testing is not a replacement for sterility testing and shall not be interpreted  
1342 as such. Such test shall be performed after a sterilization procedure on all filters used to sterilize  
1343 each high-risk preparation or batch preparation and the results documented. The results should be  
1344 compared with the filter manufacturer's specification for the specific filter used. If a filter fails  
1345 the integrity test, the preparation or batch must be sterilized again using new unused filters.

1346 (B) Finished preparation release checks and tests.

1347 (i) All high-risk level compounded sterile preparations that are prepared in groups of more than  
1348 25 identical individual single-dose packages (such as ampuls, bags, syringes, and vials), or in  
1349 multiple dose vials for administration to multiple patients, or are exposed longer than 12 hours at  
1350 2 - 8 degrees Celsius and longer than six hours at warmer than 8 degrees Celsius before they are  
1351 sterilized shall be tested to ensure they are sterile and do not contain excessive bacterial  
1352 endotoxins as specified in Chapter 71, Sterility Tests of the USP/NF before being dispensed or  
1353 administered.

1354 (ii) All compounded sterile preparations, except for sterile radiopharmaceuticals, that are  
1355 intended to be solutions must be visually examined for the presence of particulate matter and not  
1356 administered or dispensed when such matter is observed.

1357 (iii) The prescription drug and medication orders, written compounding procedure, preparation  
1358 records, and expended materials used to make compounded sterile preparations at all  
1359 contamination risk levels shall be inspected for accuracy of correct identities and amounts of  
1360 ingredients, aseptic mixing and sterilization, packaging, labeling, and expected physical  
1361 appearance before they are dispensed or administered.

1362 (iv) Written procedures for checking compounding accuracy shall be followed for every  
1363 compounded sterile preparation during preparation, in accordance with pharmacy's policies and  
1364 procedures, and immediately prior to release, including label accuracy and the accuracy of the  
1365 addition of all drug products or ingredients used to prepare the finished preparation and their  
1366 volumes or quantities. A pharmacist shall ensure that components used in compounding are  
1367 accurately weighed, measured, or subdivided as appropriate to conform to the formula being  
1368 prepared.

1369 (C) Environmental Testing.

1370 (i) Viable and nonviable environmental sampling testing. Environmental sampling shall occur, at  
1371 a minimum, every six months as part of a comprehensive quality management program and  
1372 under any of the following conditions:

1373 (I) as part of the commissioning and certification of new facilities and equipment;

1374 (II) following any servicing of facilities and equipment;

1375 (III) as part of the re-certification of facilities and equipment;

1376 (IV) in response to identified problems with end products or staff technique; or

1377 (V) in response to issues with compounded sterile preparations, observed compounding  
1378 personnel work practices, or patient-related infections (where the compounded sterile preparation  
1379 is being considered as a potential source of the infection).

1380 (ii) Total particle counts. Certification that each ISO classified area (e.g., ISO Class 5, 7, and 8),  
1381 is within established guidelines shall be performed no less than every six months and whenever  
1382 the equipment is relocated or the physical structure of the buffer area or ante-area has been  
1383 altered. All certification records shall be maintained and reviewed to ensure that the controlled  
1384 environments comply with the proper air cleanliness, room pressures, and air changes per hour.  
1385 Testing shall be performed by qualified operators using current, state-of-the-art equipment, with  
1386 results of the following:

1387 (I) ISO Class 5 - not more than 3520 particles 0.5 micrometer and larger size per cubic meter of  
1388 air;

1389 (II) ISO Class 7 - not more than 352,000 particles of 0.5 micrometer and larger size per cubic  
1390 meter of air for any buffer area; and

1391 (III) ISO Class 8 - not more than 3,520,000 particles of 0.5 micrometer and larger size per cubic  
1392 meter of air for any ante-area.

1393 (iii) Pressure differential monitoring. A pressure gauge or velocity meter shall be installed to  
1394 monitor the pressure differential or airflow between the buffer area and the ante-area and  
1395 between the ante-area and the general environment outside the compounding area. The results  
1396 shall be reviewed and documented on a log at least every work shift (minimum frequency shall  
1397 be at least daily) or by a continuous recording device. The pressure between the ISO Class 7 or  
1398 ISO Class 8 and the general pharmacy area shall not be less than 0.02 inch water column.

1399 (iv) Sampling plan. An appropriate environmental sampling plan shall be developed for airborne  
1400 viable particles based on a risk assessment of compounding activities performed. Selected  
1401 sampling sites shall include locations within each ISO Class 5 environment and in the ISO Class  
1402 7 and 8 areas and in the segregated compounding areas at greatest risk of contamination. The  
1403 plan shall include sample location, method of collection, frequency of sampling, volume of air  
1404 sampled, and time of day as related to activity in the compounding area and action levels.

1405 (v) Viable air sampling. Evaluation of airborne microorganisms using volumetric collection  
1406 methods in the controlled air environments shall be performed by properly trained individuals for  
1407 all compounding risk levels. For low-, medium-, and high-risk level compounding, air sampling  
1408 shall be performed at locations that are prone to contamination during compounding activities  
1409 and during other activities such as staging, labeling, gowning, and cleaning. Locations shall  
1410 include zones of air backwash turbulence within the laminar airflow workbench and other areas  
1411 where air backwash turbulence may enter the compounding area. For low-risk level compounded  
1412 sterile preparations within 12-hour or less beyond-use-date prepared in a primary engineering  
1413 control that maintains an ISO Class 5, air sampling shall be performed at locations inside the ISO  
1414 Class 5 environment and other areas that are in close proximity to the ISO Class 5 environment  
1415 during the certification of the primary engineering control.

1416 (vi) Air sampling frequency and process. Air sampling shall be performed at least every 6  
1417 months as a part of the re-certification of facilities and equipment. A sufficient volume of air  
1418 shall be sampled and the manufacturer's guidelines for use of the electronic air sampling  
1419 equipment followed. At the end of the designated sampling or exposure period for air sampling  
1420 activities, the microbial growth media plates are recovered and their covers secured and they are  
1421 inverted and incubated at a temperature and for a time period conducive to multiplication of  
1422 microorganisms. Sampling data shall be collected and reviewed on a periodic basis as a means of  
1423 evaluating the overall control of the compounding environment. If an activity consistently shows  
1424 elevated levels of microbial growth, competent microbiology personnel shall be consulted.

1425 (vii) Compounding accuracy checks. Written procedures for checking compounding accuracy  
1426 shall be followed for every compounded sterile preparation during preparation and immediately  
1427 prior to release, including label accuracy and the accuracy of the addition of all drug products or  
1428 ingredients used to prepare the finished preparation and their volumes or quantities. At each step  
1429 of the compounding process, the pharmacist shall ensure that components used in compounding  
1430 are accurately weighed, measured, or subdivided as appropriate to conform to the formula being  
1431 prepared.

1432 (15) Quality control.

1433 (A) Quality control procedures. The pharmacy shall follow established quality control  
1434 procedures to monitor the compounding environment and quality of compounded drug  
1435 preparations for conformity with the quality indicators established for the preparation. When  
1436 developing these procedures, pharmacy personnel shall consider the provisions of USP Chapter  
1437 71, Sterility Tests, USP Chapter 85, Bacterial Endotoxins Test, Pharmaceutical Compounding--  
1438 Non-sterile Preparations, USP Chapter 795, USP Chapter 797, Pharmaceutical Compounding--  
1439 Sterile Preparations, USP Chapter 800, Hazardous Drugs--Handling in Healthcare Settings, USP  
1440 Chapter 823, Positron Emission Tomography Drugs for Compounding, Investigational, and  
1441 Research Uses, USP Chapter 1160, Pharmaceutical Calculations in Prescription Compounding,  
1442 and USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding of the current  
1443 USP/NF. Such procedures shall be documented and be available for inspection.

1444 (B) Verification of compounding accuracy and sterility.

1445 (i) The accuracy of identities, concentrations, amounts, and purities of ingredients in  
1446 compounded sterile preparations shall be confirmed by reviewing labels on packages, observing  
1447 and documenting correct measurements with approved and correctly standardized devices, and  
1448 reviewing information in labeling and certificates of analysis provided by suppliers.

1449 (ii) If the correct identity, purity, strength, and sterility of ingredients and components of  
1450 compounded sterile preparations cannot be confirmed such ingredients and components shall be  
1451 discarded immediately. Any compounded sterile preparation that fails sterility testing following  
1452 sterilization by one method (e.g., filtration) is to be discarded and not subjected to a second  
1453 method of sterilization.

1454 (iii) If individual ingredients, such as bulk drug substances, are not labeled with expiration dates,  
1455 when the drug substances are stable indefinitely in their commercial packages under labeled  
1456 storage conditions, such ingredients may gain or lose moisture during storage and use and shall  
1457 require testing to determine the correct amount to weigh for accurate content of active chemical  
1458 moieties in compounded sterile preparations.

1459 (e) Records. Any testing, cleaning, procedures, or other activities required in this subsection shall  
1460 be documented and such documentation shall be maintained by the pharmacy.

1461 (1) Maintenance of records. Every record required under this section must be:

1462 (A) kept by the pharmacy and be available, for at least two years for inspecting and copying by  
1463 the board or its representative and to other authorized local, state, or federal law enforcement  
1464 agencies; and

1465 (B) supplied by the pharmacy within 72 hours, if requested by an authorized agent of the Texas  
1466 State Board of Pharmacy. If the pharmacy maintains the records in an electronic format, the  
1467 requested records must be provided in an electronic format. Failure to provide the records set out

1468 in this section, either on site or within 72 hours, constitutes prima facie evidence of failure to  
1469 keep and maintain records in violation of the Act.

1470 (2) Compounding records.

1471 (A) Compounding pursuant to patient specific prescription drug orders. Compounding records  
1472 for all compounded preparations shall be maintained by the pharmacy electronically or manually  
1473 as part of the prescription drug or medication order, formula record, formula book, or  
1474 compounding log and shall include:

1475 (i) the date and time of preparation;

1476 (ii) a complete formula, including methodology and necessary equipment which includes the  
1477 brand name(s) of the raw materials, or if no brand name, the generic name(s) or official name  
1478 and name(s) of the manufacturer(s) or distributor of the raw materials and the quantities of each;

1479 (iii) written or electronic signature or initials of the pharmacist or pharmacy technician or  
1480 pharmacy technician trainee performing the compounding;

1481 (iv) written or electronic signature or initials of the pharmacist responsible for supervising  
1482 pharmacy technicians or pharmacy technician trainees and conducting final checks of  
1483 compounded pharmaceuticals if pharmacy technicians or pharmacy technician trainees perform  
1484 the compounding function;

1485 (v) the quantity in units of finished preparation or amount of raw materials;

1486 (vi) the container used and the number of units prepared; and

1487 (vii) a reference to the location of the following documentation which may be maintained with  
1488 other records, such as quality control records:

1489 (I) the criteria used to determine the beyond-use date; and

1490 (II) documentation of performance of quality control procedures.

1491 (B) Compounding records when batch compounding or compounding in anticipation of future  
1492 prescription drug or medication orders.

1493 (i) Master work sheet. A master work sheet shall be developed and approved by a pharmacist for  
1494 preparations prepared in batch. Once approved, a duplicate of the master work sheet shall be  
1495 used as the preparation work sheet from which each batch is prepared and on which all  
1496 documentation for that batch occurs. The master work sheet shall contain at a minimum:

1497 (I) the formula;

1498 (II) the components;

- 1499 (III) the compounding directions;
- 1500 (IV) a sample label;
- 1501 (V) evaluation and testing requirements;
- 1502 (VI) specific equipment used during preparation; and
- 1503 (VII) storage requirements.
- 1504 (ii) Preparation work sheet. The preparation work sheet for each batch of preparations shall  
1505 document the following:
- 1506 (I) identity of all solutions and ingredients and their corresponding amounts, concentrations, or  
1507 volumes;
- 1508 (II) lot number for each component;
- 1509 (III) component manufacturer/distributor or suitable identifying number;
- 1510 (IV) container specifications (e.g., syringe, pump cassette);
- 1511 (V) unique lot or control number assigned to batch;
- 1512 (VI) expiration date of batch-prepared preparations;
- 1513 (VII) date of preparation;
- 1514 (VIII) name, initials, or electronic signature of the person(s) involved in the preparation;
- 1515 (IX) name, initials, or electronic signature of the responsible pharmacist;
- 1516 (X) finished preparation evaluation and testing specifications, if applicable; and
- 1517 (XI) comparison of actual yield to anticipated or theoretical yield, when appropriate.
- 1518 (f) Office Use Compounding and Distribution of Sterile Compounded Preparations
- 1519 (1) General.
- 1520 (A) A pharmacy may compound, dispense, deliver, and distribute a compounded sterile  
1521 preparation as specified in Subchapter D, Texas Pharmacy Act Chapter 562.
- 1522 (B) A Class A-S pharmacy is not required to register or be licensed under Chapter 431, Health  
1523 and Safety Code, to distribute sterile compounded preparations to a Class C or Class C-S  
1524 pharmacy.

1525 (C) A Class C-S pharmacy is not required to register or be licensed under Chapter 431, Health  
1526 and Safety Code, to distribute sterile compounded preparations that the Class C-S pharmacy has  
1527 compounded for other Class C or Class C-S pharmacies under common ownership.

1528 (D) To compound and deliver a compounded preparation under this subsection, a pharmacy  
1529 must:

1530 (i) verify the source of the raw materials to be used in a compounded drug;

1531 (ii) comply with applicable United States Pharmacopoeia guidelines, including the testing  
1532 requirements, and the Health Insurance Portability and Accountability Act of 1996 (Pub. L. No.  
1533 104-191);

1534 (iii) enter into a written agreement with a practitioner for the practitioner's office use of a  
1535 compounded preparation;

1536 (iv) comply with all applicable competency and accrediting standards as determined by the  
1537 board; and

1538 (v) comply with the provisions of this subsection.

1539 (E) This subsection does not apply to Class B pharmacies compounding sterile  
1540 radiopharmaceuticals that are furnished for departmental or physicians' use if such authorized  
1541 users maintain a Texas radioactive materials license.

1542 (2) Written Agreement. A pharmacy that provides sterile compounded preparations to  
1543 practitioners for office use or to another pharmacy shall enter into a written agreement with the  
1544 practitioner or pharmacy. The written agreement shall:

1545 (A) address acceptable standards of practice for a compounding pharmacy and a practitioner and  
1546 receiving pharmacy that enter into the agreement including a statement that the compounded  
1547 drugs may only be administered to the patient and may not be dispensed to the patient or sold to  
1548 any other person or entity except to a veterinarian as authorized by §563.054 of the Act;

1549 (B) require the practitioner or receiving pharmacy to include on a patient's chart, medication  
1550 order or medication administration record the lot number and beyond-use date of a compounded  
1551 preparation administered to a patient;

1552 (C) describe the scope of services to be performed by the pharmacy and practitioner or receiving  
1553 pharmacy, including a statement of the process for:

1554 (i) a patient to report an adverse reaction or submit a complaint; and

1555 (ii) the pharmacy to recall batches of compounded preparations.

1556 (3) Recordkeeping.

1557 (A) Maintenance of Records.

1558 (i) Records of orders and distribution of sterile compounded preparations to a practitioner for  
1559 office use or to an institutional pharmacy for administration to a patient shall:

1560 (I) be kept by the pharmacy and be available, for at least two years from the date of the record,  
1561 for inspecting and copying by the board or its representative and to other authorized local, state,  
1562 or federal law enforcement agencies;

1563 (II) maintained separately from the records of preparations dispensed pursuant to a prescription  
1564 or medication order; and

1565 (III) supplied by the pharmacy within 72 hours, if requested by an authorized agent of the Texas  
1566 State Board of Pharmacy or its representative. If the pharmacy maintains the records in an  
1567 electronic format, the requested records must be provided in an electronic format. Failure to  
1568 provide the records set out in this subsection, either on site or within 72 hours for whatever  
1569 reason, constitutes prima facie evidence of failure to keep and maintain records.

1570 (ii) Records may be maintained in an alternative data retention system, such as a data processing  
1571 system or direct imaging system provided the data processing system is capable of producing a  
1572 hard copy of the record upon the request of the board, its representative, or other authorized  
1573 local, state, or federal law enforcement or regulatory agencies.

1574 (B) Orders. The pharmacy shall maintain a record of all sterile compounded preparations ordered  
1575 by a practitioner for office use or by an institutional pharmacy for administration to a patient.  
1576 The record shall include the following information:

1577 (i) date of the order;

1578 (ii) name, address, and phone number of the practitioner who ordered the preparation and if  
1579 applicable, the name, address and phone number of the institutional pharmacy ordering the  
1580 preparation; and

1581 (iii) name, strength, and quantity of the preparation ordered.

1582 (C) Distributions. The pharmacy shall maintain a record of all sterile compounded preparations  
1583 distributed pursuant to an order to a practitioner for office use or by an institutional pharmacy for  
1584 administration to a patient. The record shall include the following information:

1585 (i) date the preparation was compounded;

1586 (ii) date the preparation was distributed;

1587 (iii) name, strength and quantity in each container of the preparation;

1588 (iv) pharmacy's lot number;

1589 (v) quantity of containers shipped; and

1590 (vi) name, address, and phone number of the practitioner or institutional pharmacy to whom the  
1591 preparation is distributed.

1592 (D) Audit Trail.

1593 (i) The pharmacy shall store the order and distribution records of preparations for all sterile  
1594 compounded preparations ordered by and or distributed to a practitioner for office use or by a  
1595 pharmacy licensed to compound sterile preparations for administration to a patient in such a  
1596 manner as to be able to provide an audit trail for all orders and distributions of any of the  
1597 following during a specified time period:

1598 (I) any strength and dosage form of a preparation (by either brand or generic name or both);

1599 (II) any ingredient;

1600 (III) any lot number;

1601 (IV) any practitioner;

1602 (V) any facility; and

1603 (VI) any pharmacy, if applicable.

1604 (ii) The audit trail shall contain the following information:

1605 (I) date of order and date of the distribution;

1606 (II) practitioner's name, address, and name of the institutional pharmacy, if applicable;

1607 (III) name, strength and quantity of the preparation in each container of the preparation;

1608 (IV) name and quantity of each active ingredient;

1609 (V) quantity of containers distributed; and

1610 (VI) pharmacy's lot number.

1611 (4) Labeling. The pharmacy shall affix a label to the preparation containing the following  
1612 information:

1613 (A) name, address, and phone number of the compounding pharmacy;

1614 (B) the statement: "For Institutional or Office Use Only--Not for Resale"; or if the preparation is  
1615 distributed to a veterinarian the statement: "Compounded Preparation";

- 1616 (C) name and strength of the preparation or list of the active ingredients and strengths;
- 1617 (D) pharmacy's lot number;
- 1618 (E) beyond-use date as determined by the pharmacist using appropriate documented criteria;
- 1619 (F) quantity or amount in the container;
- 1620 (G) appropriate ancillary instructions, such as storage instructions or cautionary statements,  
1621 including hazardous drug warning labels where appropriate; and
- 1622 (H) device-specific instructions, where appropriate.
- 1623 (g) Recall Procedures.
- 1624 (1) The pharmacy shall have written procedures for the recall of any compounded sterile  
1625 preparation provided to a patient, to a practitioner for office use, or a pharmacy for  
1626 administration. Written procedures shall include, but not be limited to the requirements as  
1627 specified in paragraph (3) of this subsection.
- 1628 (2) The pharmacy shall immediately initiate a recall of any sterile preparation compounded by  
1629 the pharmacy upon identification of a potential or confirmed harm to a patient.
- 1630 (3) In the event of a recall, the pharmacist-in-charge shall ensure that:
- 1631 (A) each practitioner, facility, and/or pharmacy to which the preparation was distributed is  
1632 notified, in writing, of the recall;
- 1633 (B) each patient to whom the preparation was dispensed is notified, in writing, of the recall;
- 1634 (C) the board is notified of the recall, in writing, not later than 24 hours after the recall is issued;
- 1635 (D) if the preparation is distributed for office use, the Texas Department of State Health  
1636 Services, Drugs and Medical Devices Group, is notified of the recall, in writing;
- 1637 (E) the preparation is quarantined; and
- 1638 (F) the pharmacy keeps a written record of the recall including all actions taken to notify all  
1639 parties and steps taken to ensure corrective measures.
- 1640 (4) If a pharmacy fails to initiate a recall, the board may require a pharmacy to initiate a recall if  
1641 there is potential for or confirmed harm to a patient.
- 1642 (5) A pharmacy that compounds sterile preparations shall notify the board immediately of any  
1643 adverse effects reported to the pharmacy or that are known by the pharmacy to be potentially  
1644 attributable to a sterile preparation compounded by the pharmacy.



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April 4, 2016

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Hello Ms. Benz:

This letter is to express Cardinal Health's support of the proposed language in 22 TAC §291.133 as it relates to Class B radiopharmacy blood labeling procedures. This language was proposed and adopted by a working committee of radiopharmacists over a year ago.

The proposed language is;

(E) Blood-labeling procedures. When compounding activities require the manipulation of a patient's blood-derived material (e.g., radiolabeling a patient's or donor's white blood cells), the manipulations shall be performed in a ISO Class 5 biological safety cabinet located in a buffer area and shall be clearly separated from routine material-handling procedures and equipment used in preparation activities to avoid any cross-contamination. The preparations shall not require sterilization.

Cardinal Health supports the rule as proposed because it adequately protects public health and reflects current practices at most nuclear pharmacies. As you are no doubt aware, this is the second attempt to reach a compromise on this subject. And yet there are still some parties who are trying to establish an even higher standard (ISO Class 7) for rooms in which blood products are handled. The finished radiolabeled dose going to a patient is not sterile and to characterize it as a high risk compounded sterile product simply makes no sense.

Please do not misconstrue this as a Texas gunfight between competing companies. We are concerned that any language requiring an ISO Class 7 room where blood labeling occurs will have an adverse impact on both large companies and smaller independent nuclear pharmacies in Texas who will no longer be able to provide this service as they are not likely to have ISO Class 7 conditions or a "separate buffer room" since that is not required for nuclear pharmacy practice. This would put a severe restriction on the number of Texas citizens who could possibly receive this important diagnostic procedure that helps physicians manage critical patient care.

Once again, we are supportive of the Board's current language as published in the Texas Register and encourage the Board to adopt the rule without any changes.

Best regards,

A handwritten signature in black ink, appearing to read "Richard L. Green".

Richard L. Green, R.Ph., BCNP  
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Vice Chair, BPS Specialty Council on Nuclear Pharmacy  
Nuclear Pharmacist on the NRC Advisory Committee on the Medical Uses of Isotopes (ACMUI)

cc: Michael A. Moné, BSP Pharm, J.D., FAPhA