

## RULE ANALYSIS

**Introduction:** THE AMENDMENTS ARE SUBMITTED TO THE BOARD FOR CONSIDERATION AS A PROPOSED RULE

**Short Title:** Pharmacies Compounding Sterile Preparations

**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, clarify end process checking requirements to be consistent with other sections of the rules; clarify sterility testing requirements to be consistent with USP 797; and clarify requirements for blood products in nuclear pharmacies.

1 **TITLE 22 EXAMINING BOARDS**

2 **PART 15 TEXAS STATE BOARD OF PHARMACY**

3 **CHAPTER 291 PHARMACIES**

4 **SUBCHAPTER G SERVICES PROVIDED BY PHARMACIES**

5 **§291.133 Pharmacies Compounding Sterile Preparations**

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

10 (1) compounding of sterile preparations pursuant to a prescription or medication order for a  
11 patient from a practitioner in Class A-S, Class B, Class C-S, and Class E-S pharmacies;

12 (2) compounding, dispensing, and delivery of a reasonable quantity of a compounded sterile  
13 preparation in Class A-S, Class B, Class C-S, and Class E-S pharmacies to a practitioner's  
14 office for office use by the practitioner;

15 (3) compounding and distribution of compounded sterile preparations by a Class A-S  
16 pharmacy for a Class C-S pharmacy; and

17 (4) compounding of sterile preparations by a Class C-S pharmacy and the distribution of the  
18 compounded preparations to other Class C or Class C-S pharmacies under common  
19 ownership.

20 (b) Definitions. In addition to the definitions for specific license classifications, the following  
21 words and terms, when used in this section, shall have the following meanings, unless the  
22 context clearly indicates otherwise.

23 (1) ACPE--Accreditation Council for Pharmacy Education.

24 (2) Airborne particulate cleanliness class--The level of cleanliness specified by the maximum  
25 allowable number of particles per cubic meter of air as specified in the International  
26 Organization of Standardization (ISO) Classification Air Cleanliness (ISO 14644-1). For  
27 example:

28 (A) ISO Class 5 (formerly Class 100) is an atmospheric environment that contains less than  
29 3,520 particles 0.5 microns in diameter per cubic meter of air (formerly stated as 100  
30 particles 0.5 microns in diameter per cubic foot of air);

31 (B) ISO Class 7 (formerly Class 10,000) is an atmospheric environment that contains less  
32 than 352,000 particles 0.5 microns in diameter per cubic meter of air (formerly stated as  
33 10,000 particles 0.5 microns in diameter per cubic foot of air); and

34 (C) ISO Class 8 (formerly Class 100,000) is an atmospheric environment that contains less  
35 than 3,520,000 particles 0.5 microns in diameter per cubic meter of air (formerly stated as

- 36 100,000 particles 0.5 microns in diameter per cubic foot of air).
- 37 (3) Ancillary supplies--Supplies necessary for the preparation and administration of  
38 compounded sterile preparations.
- 39 (4) Ante-area--An ISO Class 8 or better area where personnel may perform hand hygiene and  
40 garbing procedures, staging of components, order entry, labeling, and other high-particulate  
41 generating activities. It is also a transition area that:
- 42 (A) provides assurance that pressure relationships are constantly maintained so that air flows  
43 from clean to dirty areas; and
- 44 (B) reduces the need for the heating, ventilating and air conditioning (HVAC) control system  
45 to respond to large disturbances.
- 46 (5) Aseptic Processing--A mode of processing pharmaceutical and medical preparations that  
47 involves the separate sterilization of the preparation and of the package (containers-closures  
48 or packaging material for medical devices) and the transfer of the preparation into the  
49 container and its closure under at least ISO Class 5 conditions.
- 50 (6) Automated compounding device--An automated device that compounds, measures, and/or  
51 packages a specified quantity of individual components in a predetermined sequence for a  
52 designated sterile preparation.
- 53 (7) Batch--A specific quantity of a drug or other material that is intended to have uniform  
54 character and quality, within specified limits, and is produced during a single preparation  
55 cycle.
- 56 (8) Batch preparation compounding--Compounding of multiple sterile preparation units, in a  
57 single discrete process, by the same individual(s), carried out during one limited time period.  
58 Batch preparation/compounding does not include the preparation of multiple sterile  
59 preparation units pursuant to patient specific medication orders.
- 60 (9) Beyond-use date--The date or time after which the compounded sterile preparation shall  
61 not be stored or transported or begin to be administered to a patient. The beyond-use date is  
62 determined from the date or time the preparation is compounded.
- 63 (10) Biological Safety Cabinet, Class II--A ventilated cabinet for personnel, product or  
64 preparation, and environmental protection having an open front with inward airflow for  
65 personnel protection, downward HEPA filtered laminar airflow for product protection, and  
66 HEPA filtered exhausted air for environmental protection.
- 67 (11) Buffer Area--An ISO Class 7 or, if a Class B pharmacy, ISO Class 8 or better, area  
68 where the primary engineering control area is physically located. Activities that occur in this  
69 area include the preparation and staging of components and supplies used when compounding  
70 sterile preparations.
- 71 (12) Clean room--A room in which the concentration of airborne particles is controlled to  
72 meet a specified airborne particulate cleanliness class. Microorganisms in the environment  
73 are monitored so that a microbial level for air, surface, and personnel gear are not exceeded

- 74 for a specified cleanliness class.
- 75 (13) Component--Any ingredient intended for use in the compounding of a drug preparation,  
76 including those that may not appear in such preparation.
- 77 (14) Compounding--The preparation, mixing, assembling, packaging, or labeling of a drug or  
78 device:
- 79 (A) as the result of a practitioner's prescription drug or medication order based on the  
80 practitioner-patient-pharmacist relationship in the course of professional practice;
- 81 (B) for administration to a patient by a practitioner as the result of a practitioner's initiative  
82 based on the practitioner-patient-pharmacist relationship in the course of professional  
83 practice;
- 84 (C) in anticipation of prescription drug or medication orders based on routine, regularly  
85 observed prescribing patterns; or
- 86 (D) for or as an incident to research, teaching, or chemical analysis and not for sale or  
87 dispensing, except as allowed under §562.154 or Chapter 563 of the Occupations Code.
- 88 (15) Compounding Aseptic Isolator--A form of barrier isolator specifically designed for  
89 compounding pharmaceutical ingredients or preparations. It is designed to maintain an  
90 aseptic compounding environment within the isolator throughout the compounding and  
91 material transfer processes. Air exchange into the isolator from the surrounding environment  
92 shall not occur unless it has first passed through a microbial retentive filter (HEPA  
93 minimum).
- 94 (16) Compounding Aseptic Containment Isolator--A compounding aseptic isolator designed  
95 to provide worker protection from exposure to undesirable levels of airborne drug throughout  
96 the compounding and material transfer processes and to provide an aseptic environment for  
97 compounding sterile preparations. Air exchange with the surrounding environment should not  
98 occur unless the air is first passed through a microbial retentive filter (HEPA minimum)  
99 system capable of containing airborne concentrations of the physical size and state of the  
100 drug being compounded. Where volatile hazardous drugs are prepared, the exhaust air from  
101 the isolator should be appropriately removed by properly designed building ventilation.
- 102 (17) Compounding Personnel--A pharmacist, pharmacy technician, or pharmacy technician  
103 trainee who performs the actual compounding; a pharmacist who supervises pharmacy  
104 technicians or pharmacy technician trainees compounding sterile preparations, and a  
105 pharmacist who performs an intermediate or final verification of a compounded sterile  
106 preparation.
- 107 (18) Critical Area--An ISO Class 5 environment.
- 108 (19) Critical Sites--A location that includes any component or fluid pathway surfaces (e.g.,  
109 vial septa, injection ports, beakers) or openings (e.g., opened ampules, needle hubs) exposed  
110 and at risk of direct contact with air (e.g., ambient room or HEPA filtered), moisture (e.g.,  
111 oral and mucosal secretions), or touch contamination. Risk of microbial particulate  
112 contamination of the critical site increases with the size of the openings and exposure time.

- 113 (20) Device--An instrument, apparatus, implement, machine, contrivance, implant, in-vitro  
114 reagent, or other similar or related article, including any component part or accessory, that is  
115 required under federal or state law to be ordered or prescribed by a practitioner.
- 116 (21) Direct Compounding Area--A critical area within the ISO Class 5 primary engineering  
117 control where critical sites are exposed to unidirectional HEPA-filtered air, also known as  
118 first air.
- 119 (22) Disinfectant--An agent that frees from infection, usually a chemical agent but sometimes  
120 a physical one, and that destroys disease-causing pathogens or other harmful microorganisms  
121 but may not kill bacterial and fungal spores. It refers to substances applied to inanimate  
122 objects.
- 123 (23) First Air--The air exiting the HEPA filter in a unidirectional air stream that is essentially  
124 particle free.
- 125 (24) Hazardous Drugs--Drugs that, studies in animals or humans indicate exposure to the  
126 drugs, have a potential for causing cancer, development or reproductive toxicity, or harm to  
127 organs. For the purposes of this chapter, radiopharmaceuticals are not considered hazardous  
128 drugs.
- 129 (25) Hot water--The temperature of water from the pharmacy's sink maintained at a minimum  
130 of 105 degrees F (41 degrees C).
- 131 (26) HVAC--Heating, ventilation, and air conditioning.
- 132 (27) Immediate use--A sterile preparation that is not prepared according to USP 797  
133 standards (i.e., outside the pharmacy and most likely not by pharmacy personnel) which shall  
134 be stored for no longer than one hour after completion of the preparation.
- 135 (28) IPA--Isopropyl alcohol (2-propanol).
- 136 (29) Labeling--All labels and other written, printed, or graphic matter on an immediate  
137 container of an article or preparation or on, or in, any package or wrapper in which it is  
138 enclosed, except any outer shipping container. The term "label" designates that part of the  
139 labeling on the immediate container.
- 140 (30) Media-Fill Test--A test used to qualify aseptic technique of compounding personnel or  
141 processes and to ensure that the processes used are able to produce sterile preparation without  
142 microbial contamination. During this test, a microbiological growth medium such as  
143 Soybean-Casein Digest Medium is substituted for the actual drug preparation to simulate  
144 admixture compounding. The issues to consider in the development of a media-fill test are  
145 the following: media-fill procedures, media selection, fill volume, incubation, time and  
146 temperature, inspection of filled units, documentation, interpretation of results, and possible  
147 corrective actions required.
- 148 (31) Multiple-Dose Container--A multiple-unit container for articles or preparations intended  
149 for potential administration only and usually contains antimicrobial preservatives. The  
150 beyond-use date for an opened or entered (e.g., needle-punctured) multiple-dose container  
151 with antimicrobial preservatives is 28 days, unless otherwise specified by the manufacturer.

- 152 (32) Negative Pressure Room--A room that is at a lower pressure compared to adjacent  
153 spaces and, therefore, the net flow of air is into the room.
- 154 (33) Office use--The administration of a compounded drug to a patient by a practitioner in the  
155 practitioner's office or by the practitioner in a health care facility or treatment setting,  
156 including a hospital, ambulatory surgical center, or pharmacy in accordance with Chapter 562  
157 of the Act, or for administration or provision by a veterinarian in accordance with §563.054  
158 of the Act.
- 159 (34) Pharmacy Bulk Package--A container of a sterile preparation for potential use that  
160 contains many single doses. The contents are intended for use in a pharmacy admixture  
161 program and are restricted to the preparation of admixtures for infusion or, through a sterile  
162 transfer device, for the filling of empty sterile syringes. The closure shall be penetrated only  
163 one time after constitution with a suitable sterile transfer device or dispensing set, which  
164 allows measured dispensing of the contents. The pharmacy bulk package is to be used only in  
165 a suitable work area such as a laminar flow hood (or an equivalent clean air compounding  
166 area).
- 167 (35) Prepackaging--The act of repackaging and relabeling quantities of drug products from a  
168 manufacturer's original container into unit dose packaging or a multiple dose container for  
169 distribution within a facility licensed as a Class C pharmacy or to other pharmacies under  
170 common ownership for distribution within those facilities. The term as defined does not  
171 prohibit the prepackaging of drug products for use within other pharmacy classes.
- 172 (36) Preparation or Compounded Sterile Preparation--A sterile admixture compounded in a  
173 licensed pharmacy or other healthcare-related facility pursuant to the order of a licensed  
174 prescriber. The components of the preparation may or may not be sterile products.
- 175 (37) Primary Engineering Control--A device or room that provides an ISO Class 5  
176 environment for the exposure of critical sites when compounding sterile preparations. Such  
177 devices include, but may not be limited to, laminar airflow workbenches, biological safety  
178 cabinets, compounding aseptic isolators, and compounding aseptic containment isolators.
- 179 (38) Product--A commercially manufactured sterile drug or nutrient that has been evaluated  
180 for safety and efficacy by the U.S. Food and Drug Administration (FDA). Products are  
181 accompanied by full prescribing information, which is commonly known as the FDA-  
182 approved manufacturer's labeling or product package insert.
- 183 (39) Positive Control--A quality assurance sample prepared to test positive for microbial  
184 growth.
- 185 (40) Quality assurance--The set of activities used to ensure that the process used in the  
186 preparation of sterile drug preparations lead to preparations that meet predetermined  
187 standards of quality.
- 188 (41) Quality control--The set of testing activities used to determine that the ingredients,  
189 components (e.g., containers), and final compounded sterile preparations prepared meet  
190 predetermined requirements with respect to identity, purity, non-pyrogenicity, and sterility.
- 191 (42) Reasonable quantity--An amount of a compounded drug that:

- 192 (A) does not exceed the amount a practitioner anticipates may be used in the practitioner's  
193 office or facility before the beyond use date of the drug;
- 194 (B) is reasonable considering the intended use of the compounded drug and the nature of the  
195 practitioner's practice; and
- 196 (C) for any practitioner and all practitioners as a whole, is not greater than an amount the  
197 pharmacy is capable of compounding in compliance with pharmaceutical standards for  
198 identity, strength, quality, and purity of the compounded drug that are consistent with United  
199 States Pharmacopoeia guidelines and accreditation practices.
- 200 (43) Segregated Compounding Area--A designated space, either a demarcated area or room,  
201 that is restricted to preparing low-risk level compounded sterile preparations with 12-hour or  
202 less beyond-use date. Such area shall contain a device that provides unidirectional airflow of  
203 ISO Class 5 air quality for preparation of compounded sterile preparations and shall be void  
204 of activities and materials that are extraneous to sterile compounding.
- 205 (44) Single-dose container--A single-unit container for articles or preparations intended for  
206 parenteral administration only. It is intended for a single use. A single-dose container is  
207 labeled as such. Examples of single-dose containers include pre-filled syringes, cartridges,  
208 fusion-sealed containers, and closure-sealed containers when so labeled.
- 209 (45) SOPs--Standard operating procedures.
- 210 (46) Sterilizing Grade Membranes--Membranes that are documented to retain 100% of a  
211 culture of 10<sup>7</sup> microorganisms of a strain of *Brevundimonas* (*Pseudomonas*) *diminuta* per  
212 square centimeter of membrane surface under a pressure of not less than 30 psi (2.0 bar).  
213 Such filter membranes are nominally at 0.22-micrometer or 0.2-micrometer nominal pore  
214 size, depending on the manufacturer's practice.
- 215 (47) Sterilization by Filtration--Passage of a fluid or solution through a sterilizing grade  
216 membrane to produce a sterile effluent.
- 217 (48) Terminal Sterilization--The application of a lethal process, e.g., steam under pressure or  
218 autoclaving, to sealed final preparation containers for the purpose of achieving a  
219 predetermined sterility assurance level of usually less than 10<sup>-6</sup> or a probability of less than  
220 one in one million of a non-sterile unit.
- 221 (49) Unidirectional Flow--An airflow moving in a single direction in a robust and uniform  
222 manner and at sufficient speed to reproducibly sweep particles away from the critical  
223 processing or testing area.
- 224 (50) USP/NF--The current edition of the United States Pharmacopoeia/National Formulary.
- 225 (c) Personnel.
- 226 (1) Pharmacist-in-charge.
- 227 (A) General. The pharmacy shall have a pharmacist-in-charge in compliance with the specific  
228 license classification of the pharmacy.

229 (B) Responsibilities. In addition to the responsibilities for the specific class of pharmacy, the  
230 pharmacist-in-charge shall have the responsibility for, at a minimum, the following  
231 concerning the compounding of sterile preparations:

232 (i) developing a system to ensure that all pharmacy personnel responsible for compounding  
233 and/or supervising the compounding of sterile preparations within the pharmacy receive  
234 appropriate education and training and competency evaluation;

235 (ii) determining that all personnel involved in compounding sterile preparations obtain  
236 continuing education appropriate for the type of compounding done by the personnel;

237 (iii) supervising a system to ensure appropriate procurement of drugs and devices and storage  
238 of all pharmaceutical materials including pharmaceuticals, components used in the  
239 compounding of sterile preparations, and drug delivery devices;

240 (iv) ensuring that the equipment used in compounding is properly maintained;

241 (v) developing a system for the disposal and distribution of drugs from the pharmacy;

242 (vi) developing a system for bulk compounding or batch preparation of drugs;

243 (vii) developing a system for the compounding, sterility assurance, quality assurance, and  
244 quality control of sterile preparations; and

245 (viii) if applicable, ensuring that the pharmacy has a system to dispose of hazardous waste in  
246 a manner so as not to endanger the public health.

247 (2) Pharmacists.

248 (A) General.

249 (i) A pharmacist is responsible for ensuring that compounded sterile preparations are  
250 accurately identified, measured, diluted, and mixed and are correctly purified, sterilized,  
251 packaged, sealed, labeled, stored, dispensed, and distributed.

252 (ii) A pharmacist shall inspect and approve all components, drug preparation containers,  
253 closures, labeling, and any other materials involved in the compounding process.

254 (iii) A pharmacist shall review all compounding records for accuracy and conduct periodic  
255 in-process checks as defined in the pharmacy's policy and procedures.

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

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

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

262 (B) Prior to September 1, 2015 - initial training and continuing education.

263 (i) All pharmacists who compound sterile preparations for administration to patients or  
264 supervise pharmacy technicians and pharmacy technician trainees compounding sterile  
265 preparations shall:

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

269 (-a-) completion of a structured on-the-job didactic and experiential training program at this  
270 pharmacy which provides 20 hours of instruction and experience. Such training may not be  
271 transferred to another pharmacy unless the pharmacies are under common ownership and  
272 control and use a common training program; or

273 (-b-) completion of a recognized course in an accredited college of pharmacy or a course  
274 sponsored by an ACPE accredited provider which provides 20 hours of instruction and  
275 experience;

276 (II) possess knowledge about:

277 (-a-) aseptic processing;

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

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

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

282 (-e-) sterilization techniques.

283 (ii) The required experiential portion of the training programs specified in this subparagraph  
284 must be supervised by an individual who has already completed training as specified in this  
285 paragraph or paragraph (3) of this subsection.

286 (iii) All pharmacists engaged in compounding sterile preparations shall obtain continuing  
287 education appropriate for the type of compounding done by the pharmacist.

288 (C) Effective September 1, 2015 - initial training and continuing education.

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

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

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

301 (III) possess knowledge about:

302 (-a-) aseptic processing;

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

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

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

307 (-e-) sterilization techniques.

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

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

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

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

320 (3) Pharmacy technicians and pharmacy technician trainees.

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

324 (B) Prior to September 1, 2015 - initial training and continuing education. In addition to  
325 specific qualifications for registration, all pharmacy technicians and pharmacy technician  
326 trainees who compound sterile preparations for administration to patients shall:

327 (i) have initial training obtained either through completion of:

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

330 (-a-) completion of a structured on-the-job didactic and experiential training program at this  
331 pharmacy which provides 40 hours of instruction and experience. Such training may not be  
332 transferred to another pharmacy unless the pharmacies are under common ownership and  
333 control and use a common training program; or

334 (-b-) completion of a course sponsored by an ACPE accredited provider which provides 40  
335 hours of instruction and experience; or

336 (II) a training program which is accredited by the American Society of Health-System  
337 Pharmacists. Individuals enrolled in training programs accredited by the American Society of  
338 Health-System Pharmacists may compound sterile preparations in a licensed pharmacy  
339 provided the:

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

343 (-b-) individual is under the direct supervision of and responsible to a pharmacist who has  
344 completed training as specified in paragraph (2) of this subsection; and

345 (-c-) supervising pharmacist conducts periodic in-process checks as defined in the pharmacy's  
346 policy and procedures; and

347 (-d-) supervising pharmacist conducts a final check.

348 (ii) acquire the required experiential portion of the training programs specified in this  
349 subparagraph under the supervision of an individual who has already completed training as  
350 specified in paragraph (2) of this subsection or this paragraph.

351 (C) Effective September 1, 2015 - initial training and continuing education.

352 (i) Pharmacy technicians and pharmacy technician trainees may compound sterile  
353 preparations provided the pharmacy technicians and/or pharmacy technician trainees are  
354 supervised by a pharmacist as ~~[who has completed the training]~~ specified in paragraph (2) of  
355 this subsection~~[- conducts in-process and final checks, and affixes his or her initials to the~~  
356 ~~appropriate quality control records].~~

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

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

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

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

366 (II) and

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

372 (-b-) possess knowledge about:

373 (-1-) aseptic processing;

374 (-2-) quality control and quality assurance as related to environmental, component, and  
375 finished preparation release checks and tests;

376 (-3-) chemical, pharmaceutical, and clinical properties of drugs;

377 (-4-) container, equipment, and closure system selection; and

378 (-5-) sterilization techniques.

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

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

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

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

388 (IV) supervising pharmacist conducts a final check.

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

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

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

398 (II) four hours of ACPE accredited continuing education relating to one or more of the areas  
399 listed in paragraph (4)(D) of this subsection if pharmacy technician is engaged in

400 compounding high risk sterile preparations.

401 (4) Evaluation and testing requirements.

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

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

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

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

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

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

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

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

420 (i) aseptic technique;

421 (ii) critical area contamination factors;

422 (iii) environmental monitoring;

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

424 (v) equipment and supplies;

425 (vi) sterile preparation calculations and terminology;

426 (vii) sterile preparation compounding documentation;

427 (viii) quality assurance procedures;

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

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

430 (xi) cleaning procedures; and

431 (xii) general conduct in the clean room.

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

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

444 (G) Media-fill tests procedures for assessing the preparation of specific types of sterile  
445 preparations shall be representative of the most challenging or stressful conditions  
446 encountered by the pharmacy personnel being evaluated and, if applicable, for sterilizing  
447 high-risk level compounded sterile preparations.

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

450 (I) Commercially available sterile fluid culture media, such as Soybean-Casein Digest  
451 Medium shall be able to promote exponential colonization of bacteria that are most likely to  
452 be transmitted to compounding sterile preparations from the compounding personnel and  
453 environment. Media-filled vials are generally incubated at 20 to 25 degrees Celsius or at 30 to  
454 35 degrees Celsius for a minimum of 14 days. If two temperatures are used for incubation of  
455 media-filled samples, then these filled containers should be incubated for at least 7 days at  
456 each temperature. Failure is indicated by visible turbidity in the medium on or before 14  
457 days.

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

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

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

463 (iii) whenever unacceptable techniques are observed; and

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

466 (K) The pharmacist-in-charge shall ensure that proper hand hygiene and garbing practices of  
467 compounding personnel are evaluated prior to compounding, supervising, or verifying sterile

468 preparations intended for patient use and whenever an aseptic media fill is performed.

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

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

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

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

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

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

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

507 (5) Documentation of Training. The pharmacy shall maintain a record of the training and  
508 continuing education on each person who compounds sterile preparations. The record shall  
509 contain, at a minimum, a written record of initial and in-service training, education, and the

510 results of written and practical testing and media-fill testing of pharmacy personnel. The  
511 record shall be maintained and available for inspection by the board and contain the  
512 following information:

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

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

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

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

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

522 (d) Operational Standards.

523 (1) General Requirements.

524 (A) Sterile preparations may be compounded:

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

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

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

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

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

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

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

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

542 (II) facility's lot number;

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

545 (IV) quantity or amount in the container;

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

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

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

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

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

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

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

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

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

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

580 (H) Compounded sterile preparations, including hazardous drugs and radiopharmaceuticals,

581 shall be prepared only under conditions that protect the pharmacy personnel in the  
582 preparation and storage areas.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

652 (V) For a medium-risk preparation, in the absence of **passing a** ~~[direct]~~ sterility **test** ~~[testing-~~  
653 ~~results]~~ the **storage periods cannot** ~~[beyond use dates may not]~~ exceed the following time  
654 periods: before administration, the compounded sterile preparations are properly stored and  
655 are exposed for not more than 30 hours at controlled room temperature, for not more than 9  
656 days at a cold temperature, and for 45 days in solid frozen state between minus 25 degrees  
657 Celsius and minus 10 degrees Celsius.

658 (ii) Examples of medium-risk compounding. Examples of medium-risk compounding include  
659 the following.

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

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

666 (III) Filling of reservoirs of injection and infusion devices with volumes of sterile drug  
667 solutions that will be administered over several days at ambient temperatures between 25 and  
668 40 degrees Celsius (77 and 104 degrees Fahrenheit).

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

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

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

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

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

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

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

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

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

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

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

690 (VI) For a sterilized high-risk level preparation, in the absence of passing a sterility test, the  
691 storage periods cannot exceed the following time periods: before administration, the  
692 compounded sterile preparations are properly stored and are exposed for not more than 24

693 hours at controlled room temperature, for not more than 3 days at a cold temperature, and for  
694 45 days in solid frozen state between minus 25 degrees Celsius and minus 10 degrees Celsius.

695 (VII) All non-sterile measuring, mixing, and purifying devices are rinsed thoroughly with  
696 sterile, pyrogen-free water, and then thoroughly drained or dried immediately before use for  
697 high-risk compounding. All high-risk compounded sterile solutions subjected to terminal  
698 sterilization are prefiltered by passing through a filter with a nominal pore size not larger than  
699 1.2 micron preceding or during filling into their final containers to remove particulate matter.  
700 Sterilization of high-risk level compounded sterile preparations by filtration shall be  
701 performed with a sterile 0.2 micrometer or 0.22 micrometer nominal pore size filter entirely  
702 within an ISO Class 5 or superior air quality environment.

703 (ii) Examples of high-risk compounding. Examples of high-risk compounding include the  
704 following.

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

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

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

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

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

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

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

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

- 733 surfaces.
- 734 (D) Administration begins not later than one hour following the completion of preparing the  
735 compounded sterile preparation.
- 736 (E) When the compounded sterile preparations is not administered by the person who  
737 prepared it, or its administration is not witnessed by the person who prepared it, the  
738 compounded sterile preparation shall bear a label listing patient identification information  
739 such as name and identification number(s), the names and amounts of all ingredients, the  
740 name or initials of the person who prepared the compounded sterile preparation, and the exact  
741 1-hour beyond-use time and date.
- 742 (F) If administration has not begun within one hour following the completion of preparing the  
743 compounded sterile preparation, the compounded sterile preparation is promptly and safely  
744 discarded. Immediate use compounded sterile preparations shall not be stored for later use.
- 745 (G) Hazardous drugs shall not be prepared as immediate use compounded sterile  
746 preparations.
- 747 (4) Single-dose and multiple dose containers.
- 748 (A) Opened or needle punctured single-dose containers, such as bags bottles, syringes, and  
749 vials of sterile products shall be used within one hour if opened in worse than ISO Class 5 air  
750 quality. Any remaining contents must be discarded.
- 751 (B) Single-dose containers, including single-dose large volume parenteral solutions and  
752 single-dose vials, exposed to ISO Class 5 or cleaner air may be used up to six hours after  
753 initial needle puncture.
- 754 (C) Opened single-dose fusion sealed containers shall not be stored for any time period.
- 755 (D) Multiple-dose containers may be used up to 28 days after initial needle puncture unless  
756 otherwise specified by the manufacturer.
- 757 (5) Library. In addition to the library requirements of the pharmacy's specific license  
758 classification, a pharmacy shall maintain current or updated copies in hard-copy or electronic  
759 format of each of the following:
- 760 (A) a reference text on injectable drug preparations, such as Handbook on Injectable Drug  
761 Products;
- 762 (B) a specialty reference text appropriate for the scope of pharmacy services provided by the  
763 pharmacy, e.g., if the pharmacy prepares hazardous drugs, a reference text on the preparation  
764 of hazardous drugs; and
- 765 (C) the United States Pharmacopeia/National Formulary containing USP Chapter 71, Sterility  
766 Tests, USP Chapter 85, Bacterial Endotoxins Test, Pharmaceutical Compounding--Nonsterile  
767 Preparations, USP Chapter 795, USP Chapter 797, Pharmaceutical Compounding--Sterile  
768 Preparations, and USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding;  
769 and

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

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

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

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

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

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

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

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

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

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

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

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

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

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

811 (II) The buffer area shall be segregated from surrounding, unclassified spaces to reduce the  
812 risk of contaminants being blown, dragged, or otherwise introduced into the filtered  
813 unidirectional 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  
815 principle of displacement airflow as defined in Chapter 797, Pharmaceutical Compounding--  
816 Sterile 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  
823 area that provides a physical separation, through the use of walls, doors and pass-throughs  
824 and has a 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  
829 to calibrate and verify the accuracy of automated compounding devices used in aseptic  
830 processing and document the calibration and verification on a daily basis, based on the  
831 manufacturer's 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  
834 by pharmacy technicians or pharmacy technician trainees under the direction and direct  
835 supervision of a pharmacist.

836 (II) The label of an automated compounding device container shall indicate the brand name  
837 and strength of the drug; or if no brand name, then the generic name, strength, and name of  
838 the manufacturer or distributor.

839 (III) Records of loading bulk drugs into an automated compounding device shall be  
840 maintained 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,  
861 including receiving, distribution, stocking, inventorying, preparation, for administration and  
862 disposal.

863 (iv) Appropriate safety and containment techniques for compounding hazardous drugs shall  
864 be used in conjunction with aseptic techniques required for preparing sterile preparations.

865 (v) Disposal of hazardous waste shall comply with all applicable local, state, and federal  
866 requirements.

867 (vi) Prepared doses of hazardous drugs must be dispensed, labeled with proper precautions  
868 inside and outside, and distributed in a manner to minimize patient contact with hazardous  
869 agents.

870 (E) Blood-labeling procedures. When compounding activities require the manipulation of a  
871 patient's blood-derived material (e.g., radiolabeling a patient's or donor's white blood cells),  
872 the manipulations shall **be performed in a primary engineering control device located in**  
873 **a buffer area that provides a physical separation, through the use of walls, doors and**  
874 **pass-throughs. The manipulations shall** be clearly separated from routine material-  
875 handling procedures and equipment used in preparation activities to avoid any cross-  
876 contamination. The preparations shall not require sterilization.

877 (F) Cleaning and disinfecting the sterile compounding areas. The following cleaning and  
878 disinfecting practices and frequencies apply to direct and contiguous compounding areas,  
879 which include ISO Class 5 compounding areas for exposure of critical sites as well as buffer  
880 areas, ante-areas, and segregated compounding areas.

881 (i) The pharmacist-in-charge is responsible for developing written procedures for cleaning  
882 and disinfecting the direct and contiguous compounding areas and assuring the procedures  
883 are followed.

884 (ii) These procedures shall be conducted at the beginning of each work shift, before each  
885 batch preparation is started, when there are spills, and when surface contamination is known  
886 or suspected resulting from procedural breaches, and every 30 minutes during continuous  
887 compounding of individual compounded sterile preparations, unless a particular  
888 compounding procedure requires more than 30 minutes to complete, in which case, the direct  
889 compounding area is to be cleaned immediately after the compounding activity is completed.

890 (iii) Before compounding is performed, all items shall be removed from the direct and  
891 contiguous compounding areas and all surfaces are cleaned by removing loose material and  
892 residue from spills, followed by an application of a residue-free disinfecting agent (e.g., IPA),  
893 which is allowed to dry before compounding begins. In a Class B pharmacy, objects used in  
894 preparing sterile radiopharmaceuticals (e.g., dose calibrator) which cannot be reasonably  
895 removed from the compounding area shall be sterilized with an application of a residue-free  
896 disinfection agent.

897 (iv) Work surfaces in the buffer areas and ante-areas, as well as segregated compounding  
898 areas, shall be cleaned and disinfected at least daily. Dust and debris shall be removed when  
899 necessary from storage sites for compounding ingredients and supplies using a method that  
900 does not degrade the ISO Class 7 or 8 air quality.

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

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

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

916 (viii) Supplies and equipment removed from shipping cartons must be wiped with a  
917 disinfecting agent, such as sterile IPA. After the disinfectant is sprayed or wiped on a surface  
918 to be disinfected, the disinfectant shall be allowed to dry, during which time the item shall not

919 be used for compounding purposes. However, if sterile supplies are received in sealed  
920 pouches, the pouches may be removed as the supplies are introduced into the ISO Class 5  
921 area without the need to disinfect the individual sterile supply items. No shipping or other  
922 external cartons may be taken into the buffer area or segregated compounding area.

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

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

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

928 (I) date and time of cleaning;

929 (II) type of cleaning performed; and

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

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

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

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

941 (ii) Beyond-use dating.

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

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

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

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

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

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

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

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

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

972 (iv) be located in a buffer area that has a minimum differential positive pressure of 0.02 to  
973 0.05 inches water column. A buffer area that is not physically separated from the ante-area  
974 shall employ the principle of displacement airflow as defined in Chapter 797, Pharmaceutical  
975 Compounding--Sterile Preparations, of the USP/NF, with limited access to personnel.

976 (B) Biological safety cabinet.

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

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

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

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

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

991 (I) be located in the buffer area and placed in the buffer area in a manner as to avoid  
992 conditions that could adversely affect its operation such as strong air currents from opened

- 993 doors, personnel traffic, or air streams from the heating, ventilating and air condition system;
- 994 (II) be certified by a qualified independent contractor according to the International  
995 Organization of Standardization (ISO) Classification of Particulate Matter in Room Air (ISO  
996 14644-1) for operational efficiency at least every six months and whenever the device or  
997 room is relocated or altered or major service to the facility is performed, in accordance with  
998 the manufacturer's specifications and test procedures specified in the Institute of  
999 Environmental Sciences and Technology (IEST) document IEST-RP-CC002.3;
- 1000 (III) have pre-filters inspected periodically and replaced as needed, in accordance with  
1001 written policies and procedures and the manufacturer's specification, and the inspection  
1002 and/or replacement date documented; and
- 1003 (IV) be located in a buffer area that has a minimum differential positive pressure of 0.02 to  
1004 0.05 inches water column.
- 1005 (C) Compounding aseptic isolator.
- 1006 (i) If the pharmacy is using a compounding aseptic isolator (CAI) as its PEC, the CAI shall  
1007 provide unidirectional airflow within the main processing and antechambers, and be placed in  
1008 an ISO Class 7 buffer area unless the isolator meets all of the following conditions:
- 1009 (I) The isolator must provide isolation from the room and maintain ISO Class 5 during  
1010 dynamic operating conditions including transferring ingredients, components, and devices  
1011 into and out of the isolator and during preparation of compounded sterile preparations.
- 1012 (II) Particle counts sampled approximately 6 to 12 inches upstream of the critical exposure  
1013 site must maintain ISO Class 5 levels during compounding operations.
- 1014 (III) The CAI must be validated according to CETA CAG-002-2006 standards.
- 1015 (IV) The pharmacy shall maintain documentation from the manufacturer that the isolator  
1016 meets this standard when located in worse than ISO Class 7 environments.
- 1017 (ii) If the isolator meets the requirements in clause (i) of this subparagraph, the CAI may be  
1018 placed in a non-ISO classified area of the pharmacy; however, the area shall be segregated  
1019 from other areas of the pharmacy and shall:
- 1020 (I) be clean, well lit, and of sufficient size;
- 1021 (II) be used only for the compounding of low- and medium-risk, non-hazardous sterile  
1022 preparations;
- 1023 (III) be located in an area of the pharmacy with non-porous and washable floors or floor  
1024 covering to enable regular disinfection; and
- 1025 (IV) be an area in which the CAI is placed in a manner as to avoid conditions that could  
1026 adversely affect its operation.
- 1027 (iii) In addition to the requirements specified in clauses (i) and (ii) of this subparagraph, if the

1028 CAI is used in the compounding of high-risk non-hazardous preparations, the CAI shall be  
1029 placed in an area or room with at least ISO 8 quality air so that high-risk powders weighed in  
1030 at least ISO-8 air quality conditions, compounding utensils for measuring and other  
1031 compounding equipment are not exposed to lesser air quality prior to the completion of  
1032 compounding and packaging of the high-risk preparation.

1033 (D) Compounding aseptic containment isolator.

1034 (i) If the pharmacy is using a compounding aseptic containment isolator as its PEC for the  
1035 preparation of low- and medium-risk hazardous drugs, the CACI shall be located in a  
1036 separate room away from other areas of the pharmacy and shall:

1037 (I) provide at least 0.01 inches water column negative pressure compared to the other areas of  
1038 the pharmacy;

1039 (II) provide unidirectional airflow within the main processing and antechambers, and be  
1040 placed in an ISO Class 7 buffer area, unless the CACI meets all of the following conditions.

1041 (-a-) The isolator must provide isolation from the room and maintain ISO Class 5 during  
1042 dynamic operating conditions including transferring ingredients, components, and devices  
1043 into and out of the isolator and during preparation of compounded sterile preparations.

1044 (-b-) Particle counts sampled approximately 6 to 12 inches upstream of the critical exposure  
1045 site must maintain ISO Class 5 levels during compounding operations.

1046 (-c-) The CACI must be validated according to CETA CAG-002-2006 standards.

1047 (-d-) The pharmacy shall maintain documentation from the manufacturer that the isolator  
1048 meets this standard when located in worse than ISO Class 7 environments.

1049 (ii) If the CACI meets all conditions specified in clause (i) of this subparagraph, the CACI  
1050 shall not be located in the same room as a CAI, but shall be located in a separate room in the  
1051 pharmacy, that is not required to maintain ISO classified air. The room in which the CACI is  
1052 located shall provide a minimum of 0.01 inches water column negative pressure compared  
1053 with the other areas of the pharmacy and shall meet the following requirements:

1054 (I) be clean, well lit, and of sufficient size;

1055 (II) be maintained at a **temperature of 20 degrees Celsius or cooler and a humidity below**  
1056 **60% at all times** [~~comfortable temperature (e.g., 20 degrees Celsius or cooler) allowing~~  
1057 ~~compounding personnel to perform flawlessly when attired in the required aseptic-~~  
1058 ~~compounding garb~~];

1059 (III) be used only for the compounding of hazardous sterile preparations;

1060 (IV) be located in an area of the pharmacy with walls, ceilings, floors, fixtures, shelving,  
1061 counters, and cabinets that are smooth, impervious, free from cracks and crevices, non-  
1062 shedding and resistant to damage by disinfectant agents; and

1063 (V) have non-porous and washable floors or floor covering to enable regular disinfection.

1064 (iii) If the CACI is used in the compounding of high-risk hazardous preparations, the CACI  
1065 shall be placed in an area or room with at least ISO 8 quality air so that high-risk powders,  
1066 weighed in at least ISO-8 air quality conditions, are not exposed to lesser air quality prior to  
1067 the completion of compounding and packaging of the high-risk preparation.

1068 (8) Additional Equipment and Supplies. Pharmacies compounding sterile preparations shall  
1069 have the following equipment and supplies:

1070 (A) a calibrated system or device (i.e., thermometer) to monitor the temperature to ensure that  
1071 proper storage requirements are met, if sterile preparations are stored in the refrigerator;

1072 (B) a calibrated system or device to monitor the temperature where bulk chemicals are stored;

1073 (C) a temperature-sensing mechanism suitably placed in the controlled temperature storage  
1074 space to reflect accurately the true temperature;

1075 (D) if applicable, a Class A prescription balance, or analytical balance and weights. Such  
1076 balance shall be properly maintained and subject to periodic inspection by the Texas State  
1077 Board of Pharmacy;

1078 (E) equipment and utensils necessary for the proper compounding of sterile preparations.  
1079 Such equipment and utensils used in the compounding process shall be:

1080 (i) of appropriate design, appropriate capacity, and be operated within designed operational  
1081 limits;

1082 (ii) of suitable composition so that surfaces that contact components, in-process material, or  
1083 drug products shall not be reactive, additive, or absorptive so as to alter the safety, identity,  
1084 strength, quality, or purity of the drug preparation beyond the desired result;

1085 (iii) cleaned and sanitized immediately prior to and after each use; and

1086 (iv) routinely inspected, calibrated (if necessary), or checked to ensure proper performance;

1087 (F) appropriate disposal containers for used needles, syringes, etc., and if applicable,  
1088 hazardous waste from the preparation of hazardous drugs and/or biohazardous waste;

1089 (G) appropriate packaging or delivery containers to maintain proper storage conditions for  
1090 sterile preparations;

1091 (H) infusion devices, if applicable; and

1092 (I) all necessary supplies, including:

1093 (i) disposable needles, syringes, and other supplies for aseptic mixing;

1094 (ii) disinfectant cleaning solutions;

1095 (iii) sterile 70% isopropyl alcohol;

- 1096 (iv) sterile gloves, both for hazardous and non-hazardous drug compounding;
- 1097 (v) sterile alcohol-based or water-less alcohol based surgical scrub;
- 1098 (vi) hand washing agents with bactericidal action;
- 1099 (vii) disposable, lint free towels or wipes;
- 1100 (viii) appropriate filters and filtration equipment;
- 1101 (ix) hazardous spill kits, if applicable; and
- 1102 (x) masks, caps, coveralls or gowns with tight cuffs, shoe covers, and gloves, as applicable.
- 1103 (9) Labeling.
- 1104 (A) Prescription drug or medication orders. In addition to the labeling requirements for the  
1105 pharmacy's specific license classification, the label dispensed or distributed pursuant to a  
1106 prescription drug or medication order shall contain the following:
- 1107 (i) the generic name(s) or the official name(s) of the principal active ingredient(s) of the  
1108 compounded sterile preparation;
- 1109 (ii) for outpatient prescription orders other than sterile radiopharmaceuticals, a statement that  
1110 the compounded sterile preparation has been compounded by the pharmacy. (An auxiliary  
1111 label may be used on the container to meet this requirement);
- 1112 (iii) a beyond-use date. The beyond-use date shall be determined as outlined in Chapter 797,  
1113 Pharmacy Compounding--Sterile Preparations of the USP/NF, and paragraph (7)(G) of this  
1114 subsection;
- 1115 (B) Batch. If the sterile preparation is compounded in a batch, the following shall also be  
1116 included on the batch label:
- 1117 (i) unique lot number assigned to the batch;
- 1118 (ii) quantity;
- 1119 (iii) appropriate ancillary instructions, such as storage instructions or cautionary statements,  
1120 including hazardous drug warning labels where appropriate; and
- 1121 (iv) device-specific instructions, where appropriate.
- 1122 (C) Pharmacy bulk package. The label of a pharmacy bulk package shall:
- 1123 (i) state prominently "Pharmacy Bulk Package--Not for Direct Infusion;"
- 1124 (ii) contain or refer to information on proper techniques to help ensure safe use of the  
1125 preparation; and

- 1126 (iii) bear a statement limiting the time frame in which the container may be used once it has  
1127 been entered, provided it is held under the labeled storage conditions.
- 1128 (10) Written drug information for prescription drug orders only. Written information about  
1129 the compounded preparation or its major active ingredient(s) shall be given to the patient at  
1130 the time of dispensing a prescription drug order. A statement which indicates that the  
1131 preparation was compounded by the pharmacy must be included in this written information.  
1132 If there is no written information available, the patient shall be advised that the drug has been  
1133 compounded and how to contact a pharmacist, and if appropriate, the prescriber, concerning  
1134 the drug. This paragraph does not apply to the preparation of radiopharmaceuticals.
- 1135 (11) Pharmaceutical Care Services. In addition to the pharmaceutical care requirements for  
1136 the pharmacy's specific license classification, the following requirements for sterile  
1137 preparations compounded pursuant to prescription drug orders must be met. This paragraph  
1138 does not apply to the preparation of radiopharmaceuticals.
- 1139 (A) Primary provider. There shall be a designated physician primarily responsible for the  
1140 patient's medical care. There shall be a clear understanding between the physician, the  
1141 patient, and the pharmacy of the responsibilities of each in the areas of the delivery of care,  
1142 and the monitoring of the patient. This shall be documented in the patient medication record  
1143 (PMR).
- 1144 (B) Patient training. The pharmacist-in-charge shall develop policies to ensure that the patient  
1145 and/or patient's caregiver receives information regarding drugs and their safe and appropriate  
1146 use, including instruction when applicable, regarding:
- 1147 (i) appropriate disposition of hazardous solutions and ancillary supplies;
- 1148 (ii) proper disposition of controlled substances in the home;
- 1149 (iii) self-administration of drugs, where appropriate;
- 1150 (iv) emergency procedures, including how to contact an appropriate individual in the event of  
1151 problems or emergencies related to drug therapy; and
- 1152 (v) if the patient or patient's caregiver prepares sterile preparations in the home, the following  
1153 additional information shall be provided:
- 1154 (I) safeguards against microbial contamination, including aseptic techniques for  
1155 compounding intravenous admixtures and aseptic techniques for injecting additives to  
1156 premixed intravenous solutions;
- 1157 (II) appropriate storage methods, including storage durations for sterile pharmaceuticals and  
1158 expirations of self-mixed solutions;
- 1159 (III) handling and disposition of premixed and self-mixed intravenous admixtures; and
- 1160 (IV) proper disposition of intravenous admixture compounding supplies such as syringes,  
1161 vials, ampules, and intravenous solution containers.

- 1162 (C) Pharmacist-patient relationship. It is imperative that a pharmacist-patient relationship be  
1163 established and maintained throughout the patient's course of therapy. This shall be  
1164 documented in the patient's medication record (PMR).
- 1165 (D) Patient monitoring. The pharmacist-in-charge shall develop policies to ensure that:
- 1166 (i) the patient's response to drug therapy is monitored and conveyed to the appropriate health  
1167 care provider;
- 1168 (ii) the first dose of any new drug therapy is administered in the presence of an individual  
1169 qualified to monitor for and respond to adverse drug reactions; and
- 1170 (iii) reports of adverse events with a compounded sterile preparation are reviewed promptly  
1171 and thoroughly to correct and prevent future occurrences.
- 1172 (12) Drugs, components, and materials used in sterile compounding.
- 1173 (A) Drugs used in sterile compounding shall be a USP/NF grade substances manufactured in  
1174 an FDA-registered facility.
- 1175 (B) If USP/NF grade substances are not available shall be of a chemical grade in one of the  
1176 following categories:
- 1177 (i) Chemically Pure (CP);
- 1178 (ii) Analytical Reagent (AR);
- 1179 (iii) American Chemical Society (ACS); or
- 1180 (iv) Food Chemical Codex.
- 1181 (C) If a drug, component or material is not purchased from a FDA-registered facility, the  
1182 pharmacist shall establish purity and stability by obtaining a Certificate of Analysis from the  
1183 supplier and the pharmacist shall compare the monograph of drugs in a similar class to the  
1184 Certificate of Analysis.
- 1185 (D) All components shall:
- 1186 (i) be manufactured in an FDA-registered facility; or
- 1187 (ii) in the professional judgment of the pharmacist, be of high quality and obtained from  
1188 acceptable and reliable alternative sources; and
- 1189 (iii) stored in properly labeled containers in a clean, dry area, under proper temperatures.
- 1190 (E) Drug preparation containers and closures shall not be reactive, additive, or absorptive so  
1191 as to alter the safety, identity, strength, quality, or purity of the compounded drug preparation  
1192 beyond the desired result.
- 1193 (F) Components, drug preparation containers, and closures shall be rotated so that the oldest

1194 stock is used first.

1195 (G) Container closure systems shall provide adequate protection against foreseeable external  
1196 factors in storage and use that can cause deterioration or contamination of the compounded  
1197 drug preparation.

1198 (H) A pharmacy may not compound a preparation that contains ingredients appearing on a  
1199 federal Food and Drug Administration list of drug products withdrawn or removed from the  
1200 market for safety reasons.

1201 (13) Compounding process.

1202 (A) Standard operating procedures (SOPs). All significant procedures performed in the  
1203 compounding area shall be covered by written SOPs designed to ensure accountability,  
1204 accuracy, quality, safety, and uniformity in the compounding process. At a minimum, SOPs  
1205 shall be developed and implemented for:

1206 (i) the facility;

1207 (ii) equipment;

1208 (iii) personnel;

1209 (iv) preparation evaluation;

1210 (v) quality assurance;

1211 (vi) preparation recall;

1212 (vii) packaging; and

1213 (viii) storage of compounded sterile preparations.

1214 (B) USP/NF. Any compounded formulation with an official monograph in the USP/NF shall  
1215 be compounded, labeled, and packaged in conformity with the USP/NF monograph for the  
1216 drug.

1217 (C) Personnel Cleansing and Garbing.

1218 (i) Any person with an apparent illness or open lesion, including rashes, sunburn, weeping  
1219 sores, conjunctivitis, and active respiratory infection, that may adversely affect the safety or  
1220 quality of a drug preparation being compounded shall be excluded from working in ISO Class  
1221 5, ISO Class 7, and ISO Class 8 compounding areas until the condition is remedied.

1222 (ii) Before entering the buffer area, compounding personnel must remove the following:

1223 (I) personal outer garments (e.g., bandanas, coats, hats, jackets, scarves, sweaters, vests);

1224 (II) all cosmetics, because they shed flakes and particles; and

- 1225 (III) all hand, wrist, and other body jewelry or piercings (e.g., earrings, lip or eyebrow  
1226 piercings) that can interfere with the effectiveness of personal protective equipment (e.g., fit  
1227 of gloves and cuffs of sleeves).
- 1228 (iii) The wearing of artificial nails or extenders is prohibited while working in the sterile  
1229 compounding environment. Natural nails shall be kept neat and trimmed.
- 1230 (iv) Personnel shall don personal protective equipment and perform hand hygiene in an order  
1231 that proceeds from the dirtiest to the cleanest activities as follows:
- 1232 (I) Activities considered the dirtiest include donning of dedicated shoes or shoe covers, head  
1233 and facial hair covers (e.g., beard covers in addition to face masks), and face mask/eye shield.  
1234 Eye shields are optional unless working with irritants like germicidal disinfecting agents or  
1235 when preparing hazardous drugs.
- 1236 (II) After donning dedicated shoes or shoe covers, head and facial hair covers, and face  
1237 masks, personnel shall perform a hand hygiene procedure by removing debris from  
1238 underneath fingernails using a nail cleaner under running warm water followed by vigorous  
1239 hand washing. Personnel shall begin washing arms at the hands and continue washing to  
1240 elbows for at least 30 seconds with either a plain (non-antimicrobial) soap, or antimicrobial  
1241 soap, and water while in the ante-area. Hands and forearms to the elbows shall be completely  
1242 dried using lint-free disposable towels, an electronic hands-free hand dryer, or a HEPA  
1243 filtered hand dryer.
- 1244 (III) After completion of hand washing, personnel shall don clean non-shedding gowns with  
1245 sleeves that fit snugly around the wrists and enclosed at the neck.
- 1246 (IV) Once inside the buffer area or segregated compounding area, and prior to donning sterile  
1247 powder-free gloves, antiseptic hand cleansing shall be performed using a waterless alcohol-  
1248 based surgical hand scrub with persistent activity following manufacturers' recommendations.  
1249 Hands shall be allowed to dry thoroughly before donning sterile gloves.
- 1250 (V) Sterile gloves that form a continuous barrier with the gown shall be the last item donned  
1251 before compounding begins. Sterile gloves shall be donned using proper technique to ensure  
1252 the sterility of the glove is not compromised while donning. The cuff of the sterile glove shall  
1253 cover the cuff of the gown at the wrist. When preparing hazardous preparations, the  
1254 compounder shall double glove or shall use single gloves ensuring that the gloves are sterile  
1255 powder-free chemotherapy-rated gloves. Routine application of sterile 70% IPA shall occur  
1256 throughout the compounding day and whenever non-sterile surfaces are touched.
- 1257 (v) When compounding personnel shall temporarily exit the buffer area during a work shift,  
1258 the exterior gown, if not visibly soiled, may be removed and retained in the ante-area, to be  
1259 re-donned during that same work shift only. However, shoe covers, hair and facial hair  
1260 covers, face mask/eye shield, and gloves shall be replaced with new ones before re-entering  
1261 the buffer area along with performing proper hand hygiene.
- 1262 (vi) During high-risk compounding activities that precede terminal sterilization, such as  
1263 weighing and mixing of non-sterile ingredients, compounding personnel shall be garbed and  
1264 gloved the same as when performing compounding in an ISO Class 5 environment. Properly  
1265 garbed and gloved compounding personnel who are exposed to air quality that is either

1266 known or suspected to be worse than ISO Class 7 shall re-garb personal protective equipment  
1267 along with washing their hands properly, performing antiseptic hand cleansing with a sterile  
1268 70% IPA-based or another suitable sterile alcohol-based surgical hand scrub, and donning  
1269 sterile gloves upon re-entering the ISO Class 7 buffer area.

1270 (vii) When compounding aseptic isolators or compounding aseptic containment isolators are  
1271 the source of the ISO Class 5 environment, at the start of each new compounding procedure,  
1272 a new pair of sterile gloves shall be donned within the CAI or CACI. In addition, the  
1273 compounding personnel should follow the requirements as specified in this subparagraph,  
1274 unless the isolator manufacturer can provide written documentation based on validated  
1275 environmental testing that any components of personal protective equipment or cleansing are  
1276 not required.

1277 (14) Quality Assurance.

1278 (A) Initial Formula Validation. Prior to routine compounding of a sterile preparation, a  
1279 pharmacy shall conduct an evaluation that shows that the pharmacy is capable of  
1280 compounding a preparation that is sterile and that contains the stated amount of active  
1281 ingredient(s).

1282 (i) Low risk preparations.

1283 (I) Quality assurance practices include, but are not limited to the following:

1284 (-a-) Routine disinfection and air quality testing of the direct compounding environment to  
1285 minimize microbial surface contamination and maintain ISO Class 5 air quality.

1286 (-b-) Visual confirmation that compounding personnel are properly donning and wearing  
1287 appropriate items and types of protective garments and goggles.

1288 (-c-) Review of all orders and packages of ingredients to ensure that the correct identity and  
1289 amounts of ingredients were compounded.

1290 (-d-) Visual inspection of compounded sterile preparations, except for sterile  
1291 radiopharmaceuticals, to ensure the absence of particulate matter in solutions, the absence of  
1292 leakage from vials and bags, and the accuracy and thoroughness of labeling.

1293 (II) Example of a Media-Fill Test Procedure. This, or an equivalent test, is performed at least  
1294 annually by each person authorized to compound in a low-risk level under conditions that  
1295 closely simulate the most challenging or stressful conditions encountered during  
1296 compounding of low-risk level sterile preparations. Once begun, this test is completed  
1297 without interruption within an ISO Class 5 air quality environment. Three sets of four 5-  
1298 milliliter aliquots of sterile Soybean-Casein Digest Medium are transferred with the same  
1299 sterile 10-milliliter syringe and vented needle combination into separate sealed, empty, sterile  
1300 30-milliliter clear vials (i.e., four 5-milliliter aliquots into each of three 30-milliliter vials).  
1301 Sterile adhesive seals are aseptically affixed to the rubber closures on the three filled vials.  
1302 The vials are incubated within a range of 20 - 35 degrees Celsius for a minimum of 14 days.  
1303 Failure is indicated by visible turbidity in the medium on or before 14 days. The media-fill  
1304 test must include a positive-control sample.

1305 (ii) Medium risk preparations.

1306 (I) Quality assurance procedures for medium-risk level compounded sterile preparations  
1307 include all those for low-risk level compounded sterile preparations, as well as a more  
1308 challenging media-fill test passed annually, or more frequently.

1309 (II) Example of a Media-Fill Test Procedure. This, or an equivalent test, is performed at least  
1310 annually under conditions that closely simulate the most challenging or stressful conditions  
1311 encountered during compounding. This test is completed without interruption within an ISO  
1312 Class 5 air quality environment. Six 100-milliliter aliquots of sterile Soybean-Casein Digest  
1313 Medium are aseptically transferred by gravity through separate tubing sets into separate  
1314 evacuated sterile containers. The six containers are then arranged as three pairs, and a sterile  
1315 10-milliliter syringe and 18-gauge needle combination is used to exchange two 5-milliliter  
1316 aliquots of medium from one container to the other container in the pair. For example, after a  
1317 5-milliliter aliquot from the first container is added to the second container in the pair, the  
1318 second container is agitated for 10 seconds, then a 5-milliliter aliquot is removed and  
1319 returned to the first container in the pair. The first container is then agitated for 10 seconds,  
1320 and the next 5-milliliter aliquot is transferred from it back to the second container in the pair.  
1321 Following the two 5-milliliter aliquot exchanges in each pair of containers, a 5-milliliter  
1322 aliquot of medium from each container is aseptically injected into a sealed, empty, sterile 10-  
1323 milliliter clear vial, using a sterile 10-milliliter syringe and vented needle. Sterile adhesive  
1324 seals are aseptically affixed to the rubber closures on the three filled vials. The vials are  
1325 incubated within a range of 20 - 35 degrees Celsius for a minimum of 14 days. Failure is  
1326 indicated by visible turbidity in the medium on or before 14 days. The media-fill test must  
1327 include a positive-control sample.

1328 (iii) High risk preparations.

1329 (I) Procedures for high-risk level compounded sterile preparations include all those for low-  
1330 risk level compounded sterile preparations. In addition, a media-fill test that represents high-  
1331 risk level compounding is performed twice a year by each person authorized to compound  
1332 high-risk level compounded sterile preparations.

1333 (II) Example of a Media-Fill Test Procedure Compounded Sterile Preparations Sterilized by  
1334 Filtration. This test, or an equivalent test, is performed under conditions that closely simulate  
1335 the most challenging or stressful conditions encountered when compounding high-risk level  
1336 compounded sterile preparations. Note: Sterility tests for autoclaved compounded sterile  
1337 preparations are not required unless they are prepared in batches of more than 25 units. This  
1338 test is completed without interruption in the following sequence:

1339 (-a-) Dissolve 3 grams of non-sterile commercially available Soybean-Casein Digest Medium  
1340 in 100 milliliters of non-bacteriostatic water to make a 3% non-sterile solution.

1341 (-b-) Draw 25 milliliters of the medium into each of three 30-milliliter sterile syringes.  
1342 Transfer 5 milliliters from each syringe into separate sterile 10-milliliter vials. These vials are  
1343 the positive controls to generate exponential microbial growth, which is indicated by visible  
1344 turbidity upon incubation.

1345 (-c-) Under aseptic conditions and using aseptic techniques, affix a sterile 0.2-micron porosity  
1346 filter unit and a 20-gauge needle to each syringe. Inject the next 10 milliliters from each

1347 syringe into three separate 10-milliliter sterile vials. Repeat the process for three more vials.  
1348 Label all vials, affix sterile adhesive seals to the closure of the nine vials, and incubate them  
1349 at 20 to 35 degrees Celsius for a minimum of 14 days. Inspect for microbial growth over 14  
1350 days as described in Chapter 797 Pharmaceutical Compounding--Sterile Preparations, of the  
1351 USP/NF.

1352 (III) Filter Integrity Testing. Filters need to undergo testing to evaluate the integrity of filters  
1353 used to sterilize high-risk preparations, such as Bubble Point Testing or comparable filter  
1354 integrity testing. Such testing is not a replacement for sterility testing and shall not be  
1355 interpreted as such. Such test shall be performed after a sterilization procedure on all filters  
1356 used to sterilize each high-risk preparation or batch preparation and the results documented.  
1357 The results should be compared with the filter manufacturer's specification for the specific  
1358 filter used. If a filter fails the integrity test, the preparation or batch must be sterilized again  
1359 using new unused filters.

1360 (B) Finished preparation release checks and tests.

1361 (i) All high-risk level compounded sterile preparations that are prepared in groups of more  
1362 than 25 identical individual single-dose packages (such as ampuls, bags, syringes, and vials),  
1363 or in multiple dose vials for administration to multiple patients, or are exposed longer than 12  
1364 hours at 2 - 8 degrees Celsius and longer than six hours at warmer than 8 degrees Celsius  
1365 before they are sterilized shall be tested to ensure they are sterile and do not contain excessive  
1366 bacterial endotoxins as specified in Chapter 71, Sterility Tests of the USP/NF before being  
1367 dispensed or administered.

1368 (ii) All compounded sterile preparations, except for sterile radiopharmaceuticals, that are  
1369 intended to be solutions must be visually examined for the presence of particulate matter and  
1370 not administered or dispensed when such matter is observed.

1371 (iii) The prescription drug and medication orders, written compounding procedure,  
1372 preparation records, and expended materials used to make compounded sterile preparations at  
1373 all contamination risk levels shall be inspected for accuracy of correct identities and amounts  
1374 of ingredients, aseptic mixing and sterilization, packaging, labeling, and expected physical  
1375 appearance before they are dispensed or administered.

1376 (iv) Written procedures for checking compounding accuracy shall be followed for every  
1377 compounded sterile preparation during preparation, in accordance with pharmacy's policies  
1378 and procedures, and immediately prior to release, including label accuracy and the accuracy  
1379 of the addition of all drug products or ingredients used to prepare the finished preparation and  
1380 their volumes or quantities. A pharmacist shall ensure that components used in compounding  
1381 are accurately weighed, measured, or subdivided as appropriate to conform to the formula  
1382 being prepared.

1383 (C) Environmental Testing.

1384 (i) Viable and nonviable environmental sampling testing. Environmental sampling shall  
1385 occur, at a minimum, every six months as part of a comprehensive quality management  
1386 program and under any of the following conditions:

1387 (I) as part of the commissioning and certification of new facilities and equipment;

- 1388 (II) following any servicing of facilities and equipment;
- 1389 (III) as part of the re-certification of facilities and equipment;
- 1390 (IV) in response to identified problems with end products or staff technique; or
- 1391 (V) in response to issues with compounded sterile preparations, observed compounding  
1392 personnel work practices, or patient-related infections (where the compounded sterile  
1393 preparation is being considered as a potential source of the infection).
- 1394 (ii) Total particle counts. Certification that each ISO classified area (e.g., ISO Class 5, 7, and  
1395 8), is within established guidelines shall be performed no less than every six months and  
1396 whenever the equipment is relocated or the physical structure of the buffer area or ante-area  
1397 has been altered. All certification records shall be maintained and reviewed to ensure that the  
1398 controlled environments comply with the proper air cleanliness, room pressures, and air  
1399 changes per hour. Testing shall be performed by qualified operators using current, state-of-  
1400 the-art equipment, with results of the following:
- 1401 (I) ISO Class 5 - not more than 3520 particles 0.5 micrometer and larger size per cubic meter  
1402 of air;
- 1403 (II) ISO Class 7 - not more than 352,000 particles of 0.5 micrometer and larger size per cubic  
1404 meter of air for any buffer area; and
- 1405 (III) ISO Class 8 - not more than 3,520,000 particles of 0.5 micrometer and larger size per  
1406 cubic meter of air for any ante-area.
- 1407 (iii) Pressure differential monitoring. A pressure gauge or velocity meter shall be installed to  
1408 monitor the pressure differential or airflow between the buffer area and the ante-area and  
1409 between the ante-area and the general environment outside the compounding area. The results  
1410 shall be reviewed and documented on a log at least every work shift (minimum frequency  
1411 shall be at least daily) or by a continuous recording device. The pressure between the ISO  
1412 Class 7 or ISO Class 8 and the general pharmacy area shall not be less than 0.02 inch water  
1413 column.
- 1414 (iv) Sampling plan. An appropriate environmental sampling plan shall be developed for  
1415 airborne viable particles based on a risk assessment of compounding activities performed.  
1416 Selected sampling sites shall include locations within each ISO Class 5 environment and in  
1417 the ISO Class 7 and 8 areas and in the segregated compounding areas at greatest risk of  
1418 contamination. The plan shall include sample location, method of collection, frequency of  
1419 sampling, volume of air sampled, and time of day as related to activity in the compounding  
1420 area and action levels.
- 1421 (v) Viable air sampling. Evaluation of airborne microorganisms using volumetric collection  
1422 methods in the controlled air environments shall be performed by properly trained individuals  
1423 for all compounding risk levels. For low-, medium-, and high-risk level compounding, air  
1424 sampling shall be performed at locations that are prone to contamination during compounding  
1425 activities and during other activities such as staging, labeling, gowning, and cleaning.  
1426 Locations shall include zones of air backwash turbulence within the laminar airflow  
1427 workbench and other areas where air backwash turbulence may enter the compounding area.

1428 For low-risk level compounded sterile preparations within 12-hour or less beyond-use-date  
1429 prepared in a primary engineering control that maintains an ISO Class 5, air sampling shall be  
1430 performed at locations inside the ISO Class 5 environment and other areas that are in close  
1431 proximity to the ISO Class 5 environment during the certification of the primary engineering  
1432 control.

1433 (vi) Air sampling frequency and process. Air sampling shall be performed at least every 6  
1434 months as a part of the re-certification of facilities and equipment. A sufficient volume of air  
1435 shall be sampled and the manufacturer's guidelines for use of the electronic air sampling  
1436 equipment followed. At the end of the designated sampling or exposure period for air  
1437 sampling activities, the microbial growth media plates are recovered and their covers secured  
1438 and they are inverted and incubated at a temperature and for a time period conducive to  
1439 multiplication of microorganisms. Sampling data shall be collected and reviewed on a  
1440 periodic basis as a means of evaluating the overall control of the compounding environment.  
1441 If an activity consistently shows elevated levels of microbial growth, competent microbiology  
1442 personnel shall be consulted.

1443 (vii) Compounding accuracy checks. Written procedures for checking compounding accuracy  
1444 shall be followed for every compounded sterile preparation during preparation and  
1445 immediately prior to release, including label accuracy and the accuracy of the addition of all  
1446 drug products or ingredients used to prepare the finished preparation and their volumes or  
1447 quantities. At each step of the compounding process, the pharmacist shall ensure that  
1448 components used in compounding are accurately weighed, measured, or subdivided as  
1449 appropriate to conform to the formula being prepared.

1450 (15) Quality control.

1451 (A) Quality control procedures. The pharmacy shall follow established quality control  
1452 procedures to monitor the compounding environment and quality of compounded drug  
1453 preparations for conformity with the quality indicators established for the preparation. When  
1454 developing these procedures, pharmacy personnel shall consider the provisions of USP  
1455 Chapter 71, Sterility Tests, USP Chapter 85, Bacterial Endotoxins Test, Pharmaceutical  
1456 Compounding-Non-sterile Preparations, USP Chapter 795, USP Chapter 797, Pharmaceutical  
1457 Compounding--Sterile Preparations, USP Chapter 800, Hazardous Drugs--Handling in  
1458 Healthcare Settings, USP Chapter 823, Positron Emission Tomography Drugs for  
1459 Compounding, Investigational, and Research Uses, USP Chapter 1160, Pharmaceutical  
1460 Calculations in Prescription Compounding, and USP Chapter 1163, Quality Assurance in  
1461 Pharmaceutical Compounding of the current USP/NF. Such procedures shall be documented  
1462 and be available for inspection.

1463 (B) Verification of compounding accuracy and sterility.

1464 (i) The accuracy of identities, concentrations, amounts, and purities of ingredients in  
1465 compounded sterile preparations shall be confirmed by reviewing labels on packages,  
1466 observing and documenting correct measurements with approved and correctly standardized  
1467 devices, and reviewing information in labeling and certificates of analysis provided by  
1468 suppliers.

1469 (ii) If the correct identity, purity, strength, and sterility of ingredients and components of  
1470 compounded sterile preparations cannot be confirmed such ingredients and components shall

1471 be discarded immediately. Any compounded sterile preparation that fails sterility testing  
1472 following sterilization by one method (e.g., filtration) is to be discarded and not subjected to a  
1473 second method of sterilization.

1474 (iii) If individual ingredients, such as bulk drug substances, are not labeled with expiration  
1475 dates, when the drug substances are stable indefinitely in their commercial packages under  
1476 labeled storage conditions, such ingredients may gain or lose moisture during storage and use  
1477 and shall require testing to determine the correct amount to weigh for accurate content of  
1478 active chemical moieties in compounded sterile preparations.

1479 (e) Records. Any testing, cleaning, procedures, or other activities required in this subsection  
1480 shall be documented and such documentation shall be maintained by the pharmacy.

1481 (1) Maintenance of records. Every record required under this section must be:

1482 (A) kept by the pharmacy and be available, for at least two years for inspecting and copying  
1483 by the board or its representative and to other authorized local, state, or federal law  
1484 enforcement agencies; and

1485 (B) supplied by the pharmacy within 72 hours, if requested by an authorized agent of the  
1486 Texas State Board of Pharmacy. If the pharmacy maintains the records in an electronic  
1487 format, the requested records must be provided in an electronic format. Failure to provide the  
1488 records set out in this section, either on site or within 72 hours, constitutes prima facie  
1489 evidence of failure to keep and maintain records in violation of the Act.

1490 (2) Compounding records.

1491 (A) Compounding pursuant to patient specific prescription drug orders. Compounding  
1492 records for all compounded preparations shall be maintained by the pharmacy electronically  
1493 or manually as part of the prescription drug or medication order, formula record, formula  
1494 book, or compounding log and shall include:

1495 (i) the date of preparation;

1496 (ii) a complete formula, including methodology and necessary equipment which includes the  
1497 brand name(s) of the raw materials, or if no brand name, the generic name(s) or official name  
1498 and name(s) of the manufacturer(s) or distributor of the raw materials and the quantities of  
1499 each;

1500 (iii) signature or initials of the pharmacist or pharmacy technician or pharmacy technician  
1501 trainee performing the compounding;

1502 (iv) signature or initials of the pharmacist responsible for supervising pharmacy technicians  
1503 or pharmacy technician trainees and conducting final checks of compounded  
1504 pharmaceuticals if pharmacy technicians or pharmacy technician trainees perform the  
1505 compounding function;

1506 (v) the quantity in units of finished preparation or amount of raw materials;

1507 (vi) the container used and the number of units prepared; and

1508 (vii) a reference to the location of the following documentation which may be maintained  
1509 with other records, such as quality control records:

1510 (I) the criteria used to determine the beyond-use date; and

1511 (II) documentation of performance of quality control procedures.

1512 (B) Compounding records when batch compounding or compounding in anticipation of  
1513 future prescription drug or medication orders.

1514 (i) Master work sheet. A master work sheet shall be developed and approved by a pharmacist  
1515 for preparations prepared in batch. Once approved, a duplicate of the master work sheet shall  
1516 be used as the preparation work sheet from which each batch is prepared and on which all  
1517 documentation for that batch occurs. The master work sheet shall contain at a minimum:

1518 (I) the formula;

1519 (II) the components;

1520 (III) the compounding directions;

1521 (IV) a sample label;

1522 (V) evaluation and testing requirements;

1523 (VI) specific equipment used during preparation; and

1524 (VII) storage requirements.

1525 (ii) Preparation work sheet. The preparation work sheet for each batch of preparations shall  
1526 document the following:

1527 (I) identity of all solutions and ingredients and their corresponding amounts, concentrations,  
1528 or volumes;

1529 (II) lot number for each component;

1530 (III) component manufacturer/distributor or suitable identifying number;

1531 (IV) container specifications (e.g., syringe, pump cassette);

1532 (V) unique lot or control number assigned to batch;

1533 (VI) expiration date of batch-prepared preparations;

1534 (VII) date of preparation;

1535 (VIII) name, initials, or electronic signature of the person(s) involved in the preparation;

1536 (IX) name, initials, or electronic signature of the responsible pharmacist;

- 1537 (X) finished preparation evaluation and testing specifications, if applicable; and
- 1538 (XI) comparison of actual yield to anticipated or theoretical yield, when appropriate.
- 1539 (f) Office Use Compounding and Distribution of Sterile Compounded Preparations
- 1540 (1) General.
- 1541 (A) A pharmacy may compound, dispense, deliver, and distribute a compounded sterile  
1542 preparation as specified in Subchapter D, Texas Pharmacy Act Chapter 562.
- 1543 (B) A Class A-S pharmacy is not required to register or be licensed under Chapter 431,  
1544 Health and Safety Code, to distribute sterile compounded preparations to a Class C or Class  
1545 C-S pharmacy.
- 1546 (C) A Class C-S pharmacy is not required to register or be licensed under Chapter 431,  
1547 Health and Safety Code, to distribute sterile compounded preparations that the Class C-S  
1548 pharmacy has compounded for other Class C or Class C-S pharmacies under common  
1549 ownership.
- 1550 (D) To compound and deliver a compounded preparation under this subsection, a pharmacy  
1551 must:
- 1552 (i) verify the source of the raw materials to be used in a compounded drug;
- 1553 (ii) comply with applicable United States Pharmacopoeia guidelines, including the testing  
1554 requirements, and the Health Insurance Portability and Accountability Act of 1996 (Pub. L.  
1555 No. 104-191);
- 1556 (iii) enter into a written agreement with a practitioner for the practitioner's office use of a  
1557 compounded preparation;
- 1558 (iv) comply with all applicable competency and accrediting standards as determined by the  
1559 board; and
- 1560 (v) comply with the provisions of this subsection.
- 1561 (E) This subsection does not apply to Class B pharmacies compounding sterile  
1562 radiopharmaceuticals that are furnished for departmental or physicians' use if such authorized  
1563 users maintain a Texas radioactive materials license.
- 1564 (2) Written Agreement. A pharmacy that provides sterile compounded preparations to  
1565 practitioners for office use or to another pharmacy shall enter into a written agreement with  
1566 the practitioner or pharmacy. The written agreement shall:
- 1567 (A) address acceptable standards of practice for a compounding pharmacy and a practitioner  
1568 and receiving pharmacy that enter into the agreement including a statement that the  
1569 compounded drugs may only be administered to the patient and may not be dispensed to the  
1570 patient or sold to any other person or entity except to a veterinarian as authorized by  
1571 §563.054 of the Act;

1572 (B) require the practitioner or receiving pharmacy to include on a patient's chart, medication  
1573 order or medication administration record the lot number and beyond-use date of a  
1574 compounded preparation administered to a patient;

1575 (C) describe the scope of services to be performed by the pharmacy and practitioner or  
1576 receiving pharmacy, including a statement of the process for:

1577 (i) a patient to report an adverse reaction or submit a complaint; and

1578 (ii) the pharmacy to recall batches of compounded preparations.

1579 (3) Recordkeeping.

1580 (A) Maintenance of Records.

1581 (i) Records of orders and distribution of sterile compounded preparations to a practitioner for  
1582 office use or to an institutional pharmacy for administration to a patient shall:

1583 (I) be kept by the pharmacy and be available, for at least two years from the date of the  
1584 record, for inspecting and copying by the board or its representative and to other authorized  
1585 local, state, or federal law enforcement agencies;

1586 (II) maintained separately from the records of preparations dispensed pursuant to a  
1587 prescription or medication order; and

1588 (III) supplied by the pharmacy within 72 hours, if requested by an authorized agent of the  
1589 Texas State Board of Pharmacy or its representative. If the pharmacy maintains the records in  
1590 an electronic format, the requested records must be provided in an electronic format. Failure  
1591 to provide the records set out in this subsection, either on site or within 72 hours for whatever  
1592 reason, constitutes prima facie evidence of failure to keep and maintain records.

1593 (ii) Records may be maintained in an alternative data retention system, such as a data  
1594 processing system or direct imaging system provided the data processing system is capable of  
1595 producing a hard copy of the record upon the request of the board, its representative, or other  
1596 authorized local, state, or federal law enforcement or regulatory agencies.

1597 (B) Orders. The pharmacy shall maintain a record of all sterile compounded preparations  
1598 ordered by a practitioner for office use or by an institutional pharmacy for administration to a  
1599 patient. The record shall include the following information:

1600 (i) date of the order;

1601 (ii) name, address, and phone number of the practitioner who ordered the preparation and if  
1602 applicable, the name, address and phone number of the institutional pharmacy ordering the  
1603 preparation; and

1604 (iii) name, strength, and quantity of the preparation ordered.

1605 (C) Distributions. The pharmacy shall maintain a record of all sterile compounded  
1606 preparations distributed pursuant to an order to a practitioner for office use or by an

1607 institutional pharmacy for administration to a patient. The record shall include the following  
1608 information:

1609 (i) date the preparation was compounded;

1610 (ii) date the preparation was distributed;

1611 (iii) name, strength and quantity in each container of the preparation;

1612 (iv) pharmacy's lot number;

1613 (v) quantity of containers shipped; and

1614 (vi) name, address, and phone number of the practitioner or institutional pharmacy to whom  
1615 the preparation is distributed.

1616 (D) Audit Trail.

1617 (i) The pharmacy shall store the order and distribution records of preparations for all sterile  
1618 compounded preparations ordered by and or distributed to a practitioner for office use or by a  
1619 pharmacy licensed to compound sterile preparations for administration to a patient in such a  
1620 manner as to be able to provide an audit trail for all orders and distributions of any of the  
1621 following during a specified time period:

1622 (I) any strength and dosage form of a preparation (by either brand or generic name or both);

1623 (II) any ingredient;

1624 (III) any lot number;

1625 (IV) any practitioner;

1626 (V) any facility; and

1627 (VI) any pharmacy, if applicable.

1628 (ii) The audit trail shall contain the following information:

1629 (I) date of order and date of the distribution;

1630 (II) practitioner's name, address, and name of the institutional pharmacy, if applicable;

1631 (III) name, strength and quantity of the preparation in each container of the preparation;

1632 (IV) name and quantity of each active ingredient;

1633 (V) quantity of containers distributed; and

1634 (VI) pharmacy's lot number.

- 1635 (4) Labeling. The pharmacy shall affix a label to the preparation containing the following  
1636 information:
- 1637 (A) name, address, and phone number of the compounding pharmacy;
- 1638 (B) the statement: "For Institutional or Office Use Only--Not for Resale"; or if the  
1639 preparation is distributed to a veterinarian the statement: "Compounded Preparation";
- 1640 (C) name and strength of the preparation or list of the active ingredients and strengths;
- 1641 (D) pharmacy's lot number;
- 1642 (E) beyond-use date as determined by the pharmacist using appropriate documented criteria;
- 1643 (F) quantity or amount in the container;
- 1644 (G) appropriate ancillary instructions, such as storage instructions or cautionary statements,  
1645 including hazardous drug warning labels where appropriate; and
- 1646 (H) device-specific instructions, where appropriate.
- 1647 (g) Recall Procedures.
- 1648 (1) The pharmacy shall have written procedures for the recall of any compounded sterile  
1649 preparation provided to a patient, to a practitioner for office use, or a pharmacy for  
1650 administration. Written procedures shall include, but not be limited to the requirements as  
1651 specified in paragraph (3) of this subsection.
- 1652 (2) The pharmacy shall immediately initiate a recall of any sterile preparation compounded  
1653 by the pharmacy upon identification of a potential or confirmed harm to a patient.
- 1654 (3) In the event of a recall, the pharmacist-in-charge shall ensure that:
- 1655 (A) each practitioner, facility, and/or pharmacy to which the preparation was distributed is  
1656 notified, in writing, of the recall;
- 1657 (B) each patient to whom the preparation was dispensed is notified, in writing, of the recall;
- 1658 (C) the board is notified of the recall, in writing, not later than 24 hours after the recall is  
1659 issued;
- 1660 (D) if the preparation is distributed for office use, the Texas Department of State Health  
1661 Services, Drugs and Medical Devices Group, is notified of the recall, in writing;
- 1662 (E) the preparation is quarantined; and
- 1663 (F) the pharmacy keeps a written record of the recall including all actions taken to notify all  
1664 parties and steps taken to ensure corrective measures.
- 1665 (4) If a pharmacy fails to initiate a recall, the board may require a pharmacy to initiate a recall

1666 if there is potential for or confirmed harm to a patient.

1667 (5) A pharmacy that compounds sterile preparations shall notify the board immediately of  
1668 any adverse effects reported to the pharmacy or that are known by the pharmacy to be  
1669 potentially attributable to a sterile preparation compounded by the pharmacy.

**From:** Sidney Phillips  
**Sent:** Tuesday, October 20, 2015 12:19 PM  
**To:** Allison Benz  
**Subject:** TSHP comments on Sterile Compounding rules

Allison,

Please see the attached comments and recommendations TSHP prepared on the sterile compounding rules.

TSHP will have a couple of leaders at the next board meeting to provide any clarity or further comments as requested by the board.

TSHP thanks the board of pharmacy for giving us this opportunity to provide some addition comments on these important rules and regulations.

Please let me know if you additional information or clarity.

Thank you,  
Sid

**Texas State Board of Pharmacy to consider clarifying the definition of compounding.** TSHP recognizes that this may require change in legislation. Interpretation of the definition as written, would require records for nearly every operational function that occurs within a health-system pharmacy. As an example, if a patient-specific label in placed on a commercially available product that is ready to administer, this could be considered compounding and would require records.

TSBP definition (Rule §291.133)

- (14) Compounding--The preparation, mixing, assembling, packaging, or labeling of a drug or device:
- (A) as the result of a practitioner's prescription drug or medication order based on the practitioner-patient-pharmacist relationship in the course of professional practice;
  - (B) for administration to a patient by a practitioner as the result of a practitioner's initiative based on the practitioner-patient-pharmacist relationship in the course of professional practice;
  - (C) in anticipation of prescription drug or medication orders based on routine, regularly observed prescribing patterns; or
  - (D) for or as an incident to research, teaching, or chemical analysis and not for sale or dispensing, except as allowed under §562.154 or Chapter 563 of the Occupations Code.

California State Board of Pharmacy definition

1735. Compounding in Licensed Pharmacies.

- (a) "Compounding" means any of the following activities occurring in a licensed pharmacy, by or under the supervision of a licensed pharmacist, pursuant to a prescription:
- (1) Altering the dosage form or delivery system of a drug
  - (2) Altering the strength of a drug
  - (3) Combining components or active ingredients
  - (4) Preparing a drug product from chemicals or bulk drug substances
- (b) "Compounding" does not include reconstitution of a drug pursuant to a manufacturer's direction(s) for oral, rectal topical, or injectable administration, nor does it include tablet splitting or the addition of flavoring agent(s) to enhance palatability.
- (c) "Compounding" does not include, except in small quantities under limited circumstances as justified by a specific, documented, medical need, preparation of a compounded drug product that is commercially available in the marketplace or that is essentially a copy of a drug product that is commercially available in the marketplace.

(d) The parameters and requirements stated by this Article 4.5 (Section 1735 et seq.) apply to all compounding practices. Additional parameters and requirements applicable solely to sterile injectable compounding are stated by Article 7 (Section 1751 et seq.).

**Texas State Board of Pharmacy to consider rewording the current regulation on compounding records in Rule §291.133 as follows:**

(2) Compounding records.

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

(i) the date of preparation;

(ii) ~~a complete~~ the formula, ~~including methodology and necessary equipment~~ which includes the methodology and equipment as necessary, ~~the brand name(s) and quantity of the raw materials, or if no brand name, the generic name(s) or official name and name(s) of the manufacturer(s) or distributor of the raw materials, and the container used, and the quantities of each;~~

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

(iv) ~~written or electronic~~ signature or initials of the pharmacist responsible for supervising pharmacy technicians or pharmacy technician trainees and conducting in-process and final checks of compounded pharmaceuticals ~~as defined by pharmacy policy~~ if pharmacy technicians or pharmacy technician trainees perform the compounding function;

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

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

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

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

(II) documentation of performance of quality control procedures.

**Texas State Board of Pharmacy to consider rewording the current regulation on media-fill testing in Rule §291.133 as follows:**

(F) Media-fill tests must be conducted at each pharmacy where an individual compounds sterile preparations ~~that is not under common ownership~~. No preparation intended for patient use shall be compounded by an individual until the on-site media-fill tests indicate that the individual can competently perform aseptic procedures, except that a pharmacist may temporarily compound sterile preparations and supervise pharmacy technicians compounding sterile preparations without media-fill tests provided the pharmacist completes the on-site media-fill tests within seven days of commencing work at the pharmacy.