

RULE ANALYSIS

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

Short Title: Sterile Compounding

Rule Numbers: §291.133

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

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

Purpose: The amendments, if adopted, eliminate training requirements that are out-of-date; update the requirements for sterility testing; clarify the requirements for temperature and humidity; and clarify the requirements for blood labeling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

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 10⁷ 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 10⁻⁶ 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 Pharmacopeia/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)] **Initial** [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)] **Initial** [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 challenge testing,
435 and such evaluation documented. Compounding personnel shall not evaluate their own
436 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 **unless the pharmacies are under common ownership and control;**
439 **provided the media-fill testing uses process that are equivalent (e.g., similar equipment**
440 **and most challenging or stressful conditions); and the pharmacy maintains**
441 **documentation of the media-fill tests.** No preparation intended for patient use shall be
442 compounded by an individual until the on-site media-fill tests indicate that the individual can
443 competently perform aseptic procedures, except that a pharmacist may temporarily
444 compound sterile preparations and supervise pharmacy technicians compounding sterile
445 preparations without media-fill tests provided the pharmacist completes the on-site media-fill
446 tests within seven days of commencing work at the pharmacy.

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

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

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

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

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

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

466 (iii) whenever unacceptable techniques are observed; and

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

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

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

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

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

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

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

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

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

510 (5) Documentation of Training. The pharmacy shall maintain a record of the training and

511 continuing education on each person who compounds sterile preparations. The record shall
512 contain, at a minimum, a written record of initial and in-service training, education, and the
513 results of written and practical testing and media-fill testing of pharmacy personnel. The
514 record shall be maintained and available for inspection by the board and contain the
515 following information:

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

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

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

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

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

525 (d) Operational Standards.

526 (1) General Requirements.

527 (A) Sterile preparations may be compounded:

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

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

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

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

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

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

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

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

- 545 (II) facility's lot number;
- 546 (III) beyond-use date as determined by the pharmacist using appropriate documented criteria
547 as outlined in paragraph (6)(G) of this subsection;
- 548 (IV) quantity or amount in the container;
- 549 (V) appropriate ancillary instructions, such as storage instructions or cautionary statements,
550 including hazardous drug warning labels where appropriate; and
- 551 (VI) device-specific instructions, where appropriate.
- 552 (C) Commercially available products may be compounded for dispensing to individual
553 patients or for office use provided the following conditions are met:
- 554 (i) the commercial product is not reasonably available from normal distribution channels in a
555 timely manner to meet individual patient's needs;
- 556 (ii) the pharmacy maintains documentation that the product is not reasonably available due to
557 a drug shortage or unavailability from the manufacturer; and
- 558 (iii) the prescribing practitioner has requested that the drug be compounded as described in
559 subparagraph (D) of this paragraph.
- 560 (D) A pharmacy may not compound preparations that are essentially copies of commercially
561 available products (e.g., the preparation is dispensed in a strength that is only slightly
562 different from a commercially available product) unless the prescribing practitioner
563 specifically orders the strength or dosage form and specifies why the individual patient needs
564 the particular strength or dosage form of the preparation or why the preparation for office use
565 is needed in the particular strength or dosage form of the preparation. The prescribing
566 practitioner shall provide documentation of a patient specific medical need and the
567 preparation produces a clinically significant therapeutic response (e.g., the physician requests
568 an alternate preparation due to hypersensitivity to excipients or preservative in the FDA-
569 approved product, or the physician requests an effective alternate dosage form) or if the drug
570 product is not commercially available. The unavailability of such drug product must be
571 documented prior to compounding. The methodology for documenting unavailability
572 includes maintaining a copy of the wholesaler's notification showing back-ordered,
573 discontinued, or out-of-stock items. This documentation must be available in hard-copy or
574 electronic format for inspection by the board.
- 575 (E) A pharmacy may enter into an agreement to compound and dispense
576 prescription/medication orders for another pharmacy provided the pharmacy complies with
577 the provisions of §291.125 of this title (relating to Centralized Prescription Dispensing).
- 578 (F) Compounding pharmacies/pharmacists may advertise and promote the fact that they
579 provide sterile prescription compounding services, which may include specific drug
580 preparations and classes of drugs.
- 581 (G) A pharmacy may not compound veterinary preparations for use in food producing
582 animals except in accordance with federal guidelines.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

661 (ii) Examples of medium-risk compounding. Examples of medium-risk compounding include
662 the following.

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

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

669 (III) Filling of reservoirs of injection and infusion devices with volumes of sterile drug
670 solutions that will be administered over several days at ambient temperatures between 25 and
671 40 degrees Celsius (77 and 104 degrees Fahrenheit).

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

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

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

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

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

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

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

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

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

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

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

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

696 hours at controlled room temperature, for not more than 3 days at a cold temperature, and for
697 45 days in solid frozen state between minus 25 degrees Celsius and minus 10 degrees Celsius.

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

706 (ii) Examples of high-risk compounding. Examples of high-risk compounding include the
707 following.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

- 810 (xii) contain a buffer area. The following is applicable for the buffer area.
- 811 (I) There shall be some demarcation designation that delineates the ante-area from the buffer
812 area. The demarcation shall be such that it does not create conditions that could adversely
813 affect the cleanliness of the area.
- 814 (II) The buffer area shall be segregated from surrounding, unclassified spaces to reduce the
815 risk of contaminants being blown, dragged, or otherwise introduced into the filtered
816 unidirectional airflow environment, and this segregation should be continuously monitored.
- 817 (III) A buffer area that is not physically separated from the ante-area shall employ the
818 principle of displacement airflow as defined in Chapter 797, Pharmaceutical Compounding--
819 Sterile Preparations, of the USP/NF, with limited access to personnel.
- 820 (IV) The buffer area shall not contain sources of water (i.e., sinks) or floor drains other than
821 distilled or sterile water introduced for facilitating the use of heat block wells for
822 radiopharmaceuticals.
- 823 (B) High-risk Preparations.
- 824 (i) In addition to the requirements in subparagraph (A) of this paragraph, when high-risk
825 preparations are compounded, the primary engineering control shall be located in a buffer
826 area that provides a physical separation, through the use of walls, doors and pass-throughs
827 and has a minimum differential positive pressure of 0.02 to 0.05 inches water column.
- 828 (ii) Presterilization procedures for high-risk level compounded sterile preparations, such as
829 weighing and mixing, shall be completed in no worse than an ISO Class 8 environment.
- 830 (C) Automated compounding device.
- 831 (i) General. If automated compounding devices are used, the pharmacy shall have a method
832 to calibrate and verify the accuracy of automated compounding devices used in aseptic
833 processing and document the calibration and verification on a daily basis, based on the
834 manufacturer's recommendations, and review the results at least weekly.
- 835 (ii) Loading bulk drugs into automated compounding devices.
- 836 (I) Automated compounding device may be loaded with bulk drugs only by a pharmacist or
837 by pharmacy technicians or pharmacy technician trainees under the direction and direct
838 supervision of a pharmacist.
- 839 (II) The label of an automated compounding device container shall indicate the brand name
840 and strength of the drug; or if no brand name, then the generic name, strength, and name of
841 the manufacturer or distributor.
- 842 (III) Records of loading bulk drugs into an automated compounding device shall be
843 maintained to show:
- 844 (-a-) name of the drug, strength, and dosage form;

845 (-b-) manufacturer or distributor;

846 (-c-) manufacturer's lot number;

847 (-d-) manufacturer's expiration date;

848 (-e-) quantity added to the automated compounding device;

849 (-f-) date of loading;

850 (-g-) name, initials, or electronic signature of the person loading the automated compounding
851 device; and

852 (-h-) name, initials, or electronic signature of the responsible pharmacist.

853 (IV) The automated compounding device shall not be used until a pharmacist verifies that the
854 system is properly loaded and affixes his or her signature or electronic signature to the record
855 specified in subclause (III) of this clause.

856 (D) Hazardous drugs. If the preparation is hazardous, the following is also applicable.

857 (i) Hazardous drugs shall be prepared only under conditions that protect personnel during
858 preparation and storage.

859 (ii) Hazardous drugs shall be stored separately from other inventory in a manner to prevent
860 contamination and personnel exposure.

861 (iii) All personnel involved in the compounding of hazardous drugs shall wear appropriate
862 protective apparel, such as gowns, face masks, eye protection, hair covers, shoe covers or
863 dedicated shoes, and appropriate gloving at all times when handling hazardous drugs,
864 including receiving, distribution, stocking, inventorying, preparation, for administration and
865 disposal.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

930 (I) date and time of cleaning;

931 (II) type of cleaning performed; and

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

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

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

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

943 (ii) Beyond-use dating.

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

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

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

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

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

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

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

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

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

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

978 (B) Biological safety cabinet.

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

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

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

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

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

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

- 995 doors, personnel traffic, or air streams from the heating, ventilating and air condition system;
- 996 (II) be certified by a qualified independent contractor according to the International
997 Organization of Standardization (ISO) Classification of Particulate Matter in Room Air (ISO
998 14644-1) for operational efficiency at least every six months and whenever the device or
999 room is relocated or altered or major service to the facility is performed, in accordance with
1000 the manufacturer's specifications and test procedures specified in the Institute of
1001 Environmental Sciences and Technology (IEST) document IEST-RP-CC002.3;
- 1002 (III) have pre-filters inspected periodically and replaced as needed, in accordance with
1003 written policies and procedures and the manufacturer's specification, and the inspection
1004 and/or replacement date documented; and
- 1005 (IV) be located in a buffer area that has a minimum differential positive pressure of 0.02 to
1006 0.05 inches water column.
- 1007 (C) Compounding aseptic isolator.
- 1008 (i) If the pharmacy is using a compounding aseptic isolator (CAI) as its PEC, the CAI shall
1009 provide unidirectional airflow within the main processing and antechambers, and be placed in
1010 an ISO Class 7 buffer area unless the isolator meets all of the following conditions:
- 1011 (I) The isolator must provide isolation from the room and maintain ISO Class 5 during
1012 dynamic operating conditions including transferring ingredients, components, and devices
1013 into and out of the isolator and during preparation of compounded sterile preparations.
- 1014 (II) Particle counts sampled approximately 6 to 12 inches upstream of the critical exposure
1015 site must maintain ISO Class 5 levels during compounding operations.
- 1016 (III) The CAI must be validated according to CETA CAG-002-2006 standards.
- 1017 (IV) The pharmacy shall maintain documentation from the manufacturer that the isolator
1018 meets this standard when located in worse than ISO Class 7 environments.
- 1019 (ii) If the isolator meets the requirements in clause (i) of this subparagraph, the CAI may be
1020 placed in a non-ISO classified area of the pharmacy; however, the area shall be segregated
1021 from other areas of the pharmacy and shall:
- 1022 (I) be clean, well lit, and of sufficient size;
- 1023 (II) be used only for the compounding of low- and medium-risk, non-hazardous sterile
1024 preparations;
- 1025 (III) be located in an area of the pharmacy with non-porous and washable floors or floor
1026 covering to enable regular disinfection; and
- 1027 (IV) be an area in which the CAI is placed in a manner as to avoid conditions that could
1028 adversely affect its operation.
- 1029 (iii) In addition to the requirements specified in clauses (i) and (ii) of this subparagraph, if the

1030 CAI is used in the compounding of high-risk non-hazardous preparations, the CAI shall be
1031 placed in an area or room with at least ISO 8 quality air so that high-risk powders weighed in
1032 at least ISO-8 air quality conditions, compounding utensils for measuring and other
1033 compounding equipment are not exposed to lesser air quality prior to the completion of
1034 compounding and packaging of the high-risk preparation.

1035 (D) Compounding aseptic containment isolator.

1036 (i) If the pharmacy is using a compounding aseptic containment isolator as its PEC for the
1037 preparation of low- and medium-risk hazardous drugs, the CACI shall be located in a
1038 separate room away from other areas of the pharmacy and shall:

1039 (I) provide at least 0.01 inches water column negative pressure compared to the other areas of
1040 the pharmacy;

1041 (II) provide unidirectional airflow within the main processing and antechambers, and be
1042 placed in an ISO Class 7 buffer area, unless the CACI meets all of the following conditions.

1043 (-a-) The isolator must provide isolation from the room and maintain ISO Class 5 during
1044 dynamic operating conditions including transferring ingredients, components, and devices
1045 into and out of the isolator and during preparation of compounded sterile preparations.

1046 (-b-) Particle counts sampled approximately 6 to 12 inches upstream of the critical exposure
1047 site must maintain ISO Class 5 levels during compounding operations.

1048 (-c-) The CACI must be validated according to CETA CAG-002-2006 standards.

1049 (-d-) The pharmacy shall maintain documentation from the manufacturer that the isolator
1050 meets this standard when located in worse than ISO Class 7 environments.

1051 (ii) If the CACI meets all conditions specified in clause (i) of this subparagraph, the CACI
1052 shall not be located in the same room as a CAI, but shall be located in a separate room in the
1053 pharmacy, that is not required to maintain ISO classified air. The room in which the CACI is
1054 located shall provide a minimum of 0.01 inches water column negative pressure compared
1055 with the other areas of the pharmacy and shall meet the following requirements:

1056 (I) be clean, well lit, and of sufficient size;

1057 (II) be maintained at a **temperature of 20 degrees Celsius or cooler and a humidity below**
1058 **60%**~~[comfortable temperature (e.g., 20 degrees Celsius or cooler) allowing compounding~~
1059 ~~personnel to perform flawlessly when attired in the required aseptic compounding garb];~~

1060 (III) be used only for the compounding of hazardous sterile preparations;

1061 (IV) be located in an area of the pharmacy with walls, ceilings, floors, fixtures, shelving,
1062 counters, and cabinets that are smooth, impervious, free from cracks and crevices, non-
1063 shedding and resistant to damage by disinfectant agents; and

1064 (V) have non-porous and washable floors or floor covering to enable regular disinfection.

1065 (iii) If the CACI is used in the compounding of high-risk hazardous preparations, the CACI
1066 shall be placed in an area or room with at least ISO 8 quality air so that high-risk powders,
1067 weighed in at least ISO-8 air quality conditions, are not exposed to lesser air quality prior to
1068 the completion of compounding and packaging of the high-risk preparation.

1069 (8) Additional Equipment and Supplies. Pharmacies compounding sterile preparations shall
1070 have the following equipment and supplies:

1071 (A) a calibrated system or device (i.e., thermometer) to monitor the temperature to ensure that
1072 proper storage requirements are met, if sterile preparations are stored in the refrigerator;

1073 (B) a calibrated system or device to monitor the temperature where bulk chemicals are stored;

1074 (C) a temperature-sensing mechanism suitably placed in the controlled temperature storage
1075 space to reflect accurately the true temperature;

1076 (D) if applicable, a Class A prescription balance, or analytical balance and weights. Such
1077 balance shall be properly maintained and subject to periodic inspection by the Texas State
1078 Board of Pharmacy;

1079 (E) equipment and utensils necessary for the proper compounding of sterile preparations.
1080 Such equipment and utensils used in the compounding process shall be:

1081 (i) of appropriate design, appropriate capacity, and be operated within designed operational
1082 limits;

1083 (ii) of suitable composition so that surfaces that contact components, in-process material, or
1084 drug products shall not be reactive, additive, or absorptive so as to alter the safety, identity,
1085 strength, quality, or purity of the drug preparation beyond the desired result;

1086 (iii) cleaned and sanitized immediately prior to and after each use; and

1087 (iv) routinely inspected, calibrated (if necessary), or checked to ensure proper performance;

1088 (F) appropriate disposal containers for used needles, syringes, etc., and if applicable,
1089 hazardous waste from the preparation of hazardous drugs and/or biohazardous waste;

1090 (G) appropriate packaging or delivery containers to maintain proper storage conditions for
1091 sterile preparations;

1092 (H) infusion devices, if applicable; and

1093 (I) all necessary supplies, including:

1094 (i) disposable needles, syringes, and other supplies for aseptic mixing;

1095 (ii) disinfectant cleaning solutions;

1096 (iii) sterile 70% isopropyl alcohol;

- 1097 (iv) sterile gloves, both for hazardous and non-hazardous drug compounding;
- 1098 (v) sterile alcohol-based or water-less alcohol based surgical scrub;
- 1099 (vi) hand washing agents with bactericidal action;
- 1100 (vii) disposable, lint free towels or wipes;
- 1101 (viii) appropriate filters and filtration equipment;
- 1102 (ix) hazardous spill kits, if applicable; and
- 1103 (x) masks, caps, coveralls or gowns with tight cuffs, shoe covers, and gloves, as applicable.
- 1104 (9) Labeling.
- 1105 (A) Prescription drug or medication orders. In addition to the labeling requirements for the
1106 pharmacy's specific license classification, the label dispensed or distributed pursuant to a
1107 prescription drug or medication order shall contain the following:
- 1108 (i) the generic name(s) or the official name(s) of the principal active ingredient(s) of the
1109 compounded sterile preparation;
- 1110 (ii) for outpatient prescription orders other than sterile radiopharmaceuticals, a statement that
1111 the compounded sterile preparation has been compounded by the pharmacy. (An auxiliary
1112 label may be used on the container to meet this requirement);
- 1113 (iii) a beyond-use date. The beyond-use date shall be determined as outlined in Chapter 797,
1114 Pharmacy Compounding--Sterile Preparations of the USP/NF, and paragraph (7)(G) of this
1115 subsection;
- 1116 (B) Batch. If the sterile preparation is compounded in a batch, the following shall also be
1117 included on the batch label:
- 1118 (i) unique lot number assigned to the batch;
- 1119 (ii) quantity;
- 1120 (iii) appropriate ancillary instructions, such as storage instructions or cautionary statements,
1121 including hazardous drug warning labels where appropriate; and
- 1122 (iv) device-specific instructions, where appropriate.
- 1123 (C) Pharmacy bulk package. The label of a pharmacy bulk package shall:
- 1124 (i) state prominently "Pharmacy Bulk Package--Not for Direct Infusion;"
- 1125 (ii) contain or refer to information on proper techniques to help ensure safe use of the
1126 preparation; and

- 1127 (iii) bear a statement limiting the time frame in which the container may be used once it has
1128 been entered, provided it is held under the labeled storage conditions.
- 1129 (10) Written drug information for prescription drug orders only. Written information about
1130 the compounded preparation or its major active ingredient(s) shall be given to the patient at
1131 the time of dispensing a prescription drug order. A statement which indicates that the
1132 preparation was compounded by the pharmacy must be included in this written information.
1133 If there is no written information available, the patient shall be advised that the drug has been
1134 compounded and how to contact a pharmacist, and if appropriate, the prescriber, concerning
1135 the drug. This paragraph does not apply to the preparation of radiopharmaceuticals.
- 1136 (11) Pharmaceutical Care Services. In addition to the pharmaceutical care requirements for
1137 the pharmacy's specific license classification, the following requirements for sterile
1138 preparations compounded pursuant to prescription drug orders must be met. This paragraph
1139 does not apply to the preparation of radiopharmaceuticals.
- 1140 (A) Primary provider. There shall be a designated physician primarily responsible for the
1141 patient's medical care. There shall be a clear understanding between the physician, the
1142 patient, and the pharmacy of the responsibilities of each in the areas of the delivery of care,
1143 and the monitoring of the patient. This shall be documented in the patient medication record
1144 (PMR).
- 1145 (B) Patient training. The pharmacist-in-charge shall develop policies to ensure that the patient
1146 and/or patient's caregiver receives information regarding drugs and their safe and appropriate
1147 use, including instruction when applicable, regarding:
- 1148 (i) appropriate disposition of hazardous solutions and ancillary supplies;
- 1149 (ii) proper disposition of controlled substances in the home;
- 1150 (iii) self-administration of drugs, where appropriate;
- 1151 (iv) emergency procedures, including how to contact an appropriate individual in the event of
1152 problems or emergencies related to drug therapy; and
- 1153 (v) if the patient or patient's caregiver prepares sterile preparations in the home, the following
1154 additional information shall be provided:
- 1155 (I) safeguards against microbial contamination, including aseptic techniques for
1156 compounding intravenous admixtures and aseptic techniques for injecting additives to
1157 premixed intravenous solutions;
- 1158 (II) appropriate storage methods, including storage durations for sterile pharmaceuticals and
1159 expirations of self-mixed solutions;
- 1160 (III) handling and disposition of premixed and self-mixed intravenous admixtures; and
- 1161 (IV) proper disposition of intravenous admixture compounding supplies such as syringes,
1162 vials, ampules, and intravenous solution containers.

- 1163 (C) Pharmacist-patient relationship. It is imperative that a pharmacist-patient relationship be
1164 established and maintained throughout the patient's course of therapy. This shall be
1165 documented in the patient's medication record (PMR).
- 1166 (D) Patient monitoring. The pharmacist-in-charge shall develop policies to ensure that:
- 1167 (i) the patient's response to drug therapy is monitored and conveyed to the appropriate health
1168 care provider;
- 1169 (ii) the first dose of any new drug therapy is administered in the presence of an individual
1170 qualified to monitor for and respond to adverse drug reactions; and
- 1171 (iii) reports of adverse events with a compounded sterile preparation are reviewed promptly
1172 and thoroughly to correct and prevent future occurrences.
- 1173 (12) Drugs, components, and materials used in sterile compounding.
- 1174 (A) Drugs used in sterile compounding shall be a USP/NF grade substances manufactured in
1175 an FDA-registered facility.
- 1176 (B) If USP/NF grade substances are not available shall be of a chemical grade in one of the
1177 following categories:
- 1178 (i) Chemically Pure (CP);
- 1179 (ii) Analytical Reagent (AR);
- 1180 (iii) American Chemical Society (ACS); or
- 1181 (iv) Food Chemical Codex.
- 1182 (C) If a drug, component or material is not purchased from a FDA-registered facility, the
1183 pharmacist shall establish purity and stability by obtaining a Certificate of Analysis from the
1184 supplier and the pharmacist shall compare the monograph of drugs in a similar class to the
1185 Certificate of Analysis.
- 1186 (D) All components shall:
- 1187 (i) be manufactured in an FDA-registered facility; or
- 1188 (ii) in the professional judgment of the pharmacist, be of high quality and obtained from
1189 acceptable and reliable alternative sources; and
- 1190 (iii) stored in properly labeled containers in a clean, dry area, under proper temperatures.
- 1191 (E) Drug preparation containers and closures shall not be reactive, additive, or absorptive so
1192 as to alter the safety, identity, strength, quality, or purity of the compounded drug preparation
1193 beyond the desired result.
- 1194 (F) Components, drug preparation containers, and closures shall be rotated so that the oldest

- 1195 stock is used first.
- 1196 (G) Container closure systems shall provide adequate protection against foreseeable external
1197 factors in storage and use that can cause deterioration or contamination of the compounded
1198 drug preparation.
- 1199 (H) A pharmacy may not compound a preparation that contains ingredients appearing on a
1200 federal Food and Drug Administration list of drug products withdrawn or removed from the
1201 market for safety reasons.
- 1202 (13) Compounding process.
- 1203 (A) Standard operating procedures (SOPs). All significant procedures performed in the
1204 compounding area shall be covered by written SOPs designed to ensure accountability,
1205 accuracy, quality, safety, and uniformity in the compounding process. At a minimum, SOPs
1206 shall be developed and implemented for:
- 1207 (i) the facility;
- 1208 (ii) equipment;
- 1209 (iii) personnel;
- 1210 (iv) preparation evaluation;
- 1211 (v) quality assurance;
- 1212 (vi) preparation recall;
- 1213 (vii) packaging; and
- 1214 (viii) storage of compounded sterile preparations.
- 1215 (B) USP/NF. Any compounded formulation with an official monograph in the USP/NF shall
1216 be compounded, labeled, and packaged in conformity with the USP/NF monograph for the
1217 drug.
- 1218 (C) Personnel Cleansing and Garbing.
- 1219 (i) Any person with an apparent illness or open lesion, including rashes, sunburn, weeping
1220 sores, conjunctivitis, and active respiratory infection, that may adversely affect the safety or
1221 quality of a drug preparation being compounded shall be excluded from working in ISO Class
1222 5, ISO Class 7, and ISO Class 8 compounding areas until the condition is remedied.
- 1223 (ii) Before entering the buffer area, compounding personnel must remove the following:
- 1224 (I) personal outer garments (e.g., bandanas, coats, hats, jackets, scarves, sweaters, vests);
- 1225 (II) all cosmetics, because they shed flakes and particles; and

- 1226 (III) all hand, wrist, and other body jewelry or piercings (e.g., earrings, lip or eyebrow
1227 piercings) that can interfere with the effectiveness of personal protective equipment (e.g., fit
1228 of gloves and cuffs of sleeves).
- 1229 (iii) The wearing of artificial nails or extenders is prohibited while working in the sterile
1230 compounding environment. Natural nails shall be kept neat and trimmed.
- 1231 (iv) Personnel shall don personal protective equipment and perform hand hygiene in an order
1232 that proceeds from the dirtiest to the cleanest activities as follows:
- 1233 (I) Activities considered the dirtiest include donning of dedicated shoes or shoe covers, head
1234 and facial hair covers (e.g., beard covers in addition to face masks), and face mask/eye shield.
1235 Eye shields are optional unless working with irritants like germicidal disinfecting agents or
1236 when preparing hazardous drugs.
- 1237 (II) After donning dedicated shoes or shoe covers, head and facial hair covers, and face
1238 masks, personnel shall perform a hand hygiene procedure by removing debris from
1239 underneath fingernails using a nail cleaner under running warm water followed by vigorous
1240 hand washing. Personnel shall begin washing arms at the hands and continue washing to
1241 elbows for at least 30 seconds with either a plain (non-antimicrobial) soap, or antimicrobial
1242 soap, and water while in the ante-area. Hands and forearms to the elbows shall be completely
1243 dried using lint-free disposable towels, an electronic hands-free hand dryer, or a HEPA
1244 filtered hand dryer.
- 1245 (III) After completion of hand washing, personnel shall don clean non-shedding gowns with
1246 sleeves that fit snugly around the wrists and enclosed at the neck.
- 1247 (IV) Once inside the buffer area or segregated compounding area, and prior to donning sterile
1248 powder-free gloves, antiseptic hand cleansing shall be performed using a waterless alcohol-
1249 based surgical hand scrub with persistent activity following manufacturers' recommendations.
1250 Hands shall be allowed to dry thoroughly before donning sterile gloves.
- 1251 (V) Sterile gloves that form a continuous barrier with the gown shall be the last item donned
1252 before compounding begins. Sterile gloves shall be donned using proper technique to ensure
1253 the sterility of the glove is not compromised while donning. The cuff of the sterile glove shall
1254 cover the cuff of the gown at the wrist. When preparing hazardous preparations, the
1255 compounder shall double glove or shall use single gloves ensuring that the gloves are sterile
1256 powder-free chemotherapy-rated gloves. Routine application of sterile 70% IPA shall occur
1257 throughout the compounding day and whenever non-sterile surfaces are touched.
- 1258 (v) When compounding personnel shall temporarily exit the buffer area during a work shift,
1259 the exterior gown, if not visibly soiled, may be removed and retained in the ante-area, to be
1260 re-donned during that same work shift only. However, shoe covers, hair and facial hair
1261 covers, face mask/eye shield, and gloves shall be replaced with new ones before re-entering
1262 the buffer area along with performing proper hand hygiene.
- 1263 (vi) During high-risk compounding activities that precede terminal sterilization, such as
1264 weighing and mixing of non-sterile ingredients, compounding personnel shall be garbed and
1265 gloved the same as when performing compounding in an ISO Class 5 environment. Properly
1266 garbed and gloved compounding personnel who are exposed to air quality that is either

1267 known or suspected to be worse than ISO Class 7 shall re-garb personal protective equipment
1268 along with washing their hands properly, performing antiseptic hand cleansing with a sterile
1269 70% IPA-based or another suitable sterile alcohol-based surgical hand scrub, and donning
1270 sterile gloves upon re-entering the ISO Class 7 buffer area.

1271 (vii) When compounding aseptic isolators or compounding aseptic containment isolators are
1272 the source of the ISO Class 5 environment, at the start of each new compounding procedure,
1273 a new pair of sterile gloves shall be donned within the CAI or CACI. In addition, the
1274 compounding personnel should follow the requirements as specified in this subparagraph,
1275 unless the isolator manufacturer can provide written documentation based on validated
1276 environmental testing that any components of personal protective equipment or cleansing are
1277 not required.

1278 (14) Quality Assurance.

1279 (A) Initial Formula Validation. Prior to routine compounding of a sterile preparation, a
1280 pharmacy shall conduct an evaluation that shows that the pharmacy is capable of
1281 compounding a preparation that is sterile and that contains the stated amount of active
1282 ingredient(s).

1283 (i) Low risk preparations.

1284 (I) Quality assurance practices include, but are not limited to the following:

1285 (-a-) Routine disinfection and air quality testing of the direct compounding environment to
1286 minimize microbial surface contamination and maintain ISO Class 5 air quality.

1287 (-b-) Visual confirmation that compounding personnel are properly donning and wearing
1288 appropriate items and types of protective garments and goggles.

1289 (-c-) Review of all orders and packages of ingredients to ensure that the correct identity and
1290 amounts of ingredients were compounded.

1291 (-d-) Visual inspection of compounded sterile preparations, except for sterile
1292 radiopharmaceuticals, to ensure the absence of particulate matter in solutions, the absence of
1293 leakage from vials and bags, and the accuracy and thoroughness of labeling.

1294 (II) Example of a Media-Fill Test Procedure. This, or an equivalent test, is performed at least
1295 annually by each person authorized to compound in a low-risk level under conditions that
1296 closely simulate the most challenging or stressful conditions encountered during
1297 compounding of low-risk level sterile preparations. Once begun, this test is completed
1298 without interruption within an ISO Class 5 air quality environment. Three sets of four 5-
1299 milliliter aliquots of sterile Soybean-Casein Digest Medium are transferred with the same
1300 sterile 10-milliliter syringe and vented needle combination into separate sealed, empty, sterile
1301 30-milliliter clear vials (i.e., four 5-milliliter aliquots into each of three 30-milliliter vials).
1302 Sterile adhesive seals are aseptically affixed to the rubber closures on the three filled vials.
1303 The vials are incubated within a range of 20 - 35 degrees Celsius for a minimum of 14 days.
1304 Failure is indicated by visible turbidity in the medium on or before 14 days. The media-fill
1305 test must include a positive-control sample.

1306 (ii) Medium risk preparations.

1307 (I) Quality assurance procedures for medium-risk level compounded sterile preparations
1308 include all those for low-risk level compounded sterile preparations, as well as a more
1309 challenging media-fill test passed annually, or more frequently.

1310 (II) Example of a Media-Fill Test Procedure. This, or an equivalent test, is performed at least
1311 annually under conditions that closely simulate the most challenging or stressful conditions
1312 encountered during compounding. This test is completed without interruption within an ISO
1313 Class 5 air quality environment. Six 100-milliliter aliquots of sterile Soybean-Casein Digest
1314 Medium are aseptically transferred by gravity through separate tubing sets into separate
1315 evacuated sterile containers. The six containers are then arranged as three pairs, and a sterile
1316 10-milliliter syringe and 18-gauge needle combination is used to exchange two 5-milliliter
1317 aliquots of medium from one container to the other container in the pair. For example, after a
1318 5-milliliter aliquot from the first container is added to the second container in the pair, the
1319 second container is agitated for 10 seconds, then a 5-milliliter aliquot is removed and
1320 returned to the first container in the pair. The first container is then agitated for 10 seconds,
1321 and the next 5-milliliter aliquot is transferred from it back to the second container in the pair.
1322 Following the two 5-milliliter aliquot exchanges in each pair of containers, a 5-milliliter
1323 aliquot of medium from each container is aseptically injected into a sealed, empty, sterile 10-
1324 milliliter clear vial, using a sterile 10-milliliter syringe and vented needle. Sterile adhesive
1325 seals are aseptically affixed to the rubber closures on the three filled vials. The vials are
1326 incubated within a range of 20 - 35 degrees Celsius for a minimum of 14 days. Failure is
1327 indicated by visible turbidity in the medium on or before 14 days. The media-fill test must
1328 include a positive-control sample.

1329 (iii) High risk preparations.

1330 (I) Procedures for high-risk level compounded sterile preparations include all those for low-
1331 risk level compounded sterile preparations. In addition, a media-fill test that represents high-
1332 risk level compounding is performed twice a year by each person authorized to compound
1333 high-risk level compounded sterile preparations.

1334 (II) Example of a Media-Fill Test Procedure Compounded Sterile Preparations Sterilized by
1335 Filtration. This test, or an equivalent test, is performed under conditions that closely simulate
1336 the most challenging or stressful conditions encountered when compounding high-risk level
1337 compounded sterile preparations. Note: Sterility tests for autoclaved compounded sterile
1338 preparations are not required unless they are prepared in batches of more than 25 units. This
1339 test is completed without interruption in the following sequence:

1340 (-a-) Dissolve 3 grams of non-sterile commercially available Soybean-Casein Digest Medium
1341 in 100 milliliters of non-bacteriostatic water to make a 3% non-sterile solution.

1342 (-b-) Draw 25 milliliters of the medium into each of three 30-milliliter sterile syringes.
1343 Transfer 5 milliliters from each syringe into separate sterile 10-milliliter vials. These vials are
1344 the positive controls to generate exponential microbial growth, which is indicated by visible
1345 turbidity upon incubation.

1346 (-c-) Under aseptic conditions and using aseptic techniques, affix a sterile 0.2-micron porosity
1347 filter unit and a 20-gauge needle to each syringe. Inject the next 10 milliliters from each

1348 syringe into three separate 10-milliliter sterile vials. Repeat the process for three more vials.
1349 Label all vials, affix sterile adhesive seals to the closure of the nine vials, and incubate them
1350 at 20 to 35 degrees Celsius for a minimum of 14 days. Inspect for microbial growth over 14
1351 days as described in Chapter 797 Pharmaceutical Compounding--Sterile Preparations, of the
1352 USP/NF.

1353 (III) Filter Integrity Testing. Filters need to undergo testing to evaluate the integrity of filters
1354 used to sterilize high-risk preparations, such as Bubble Point Testing or comparable filter
1355 integrity testing. Such testing is not a replacement for sterility testing and shall not be
1356 interpreted as such. Such test shall be performed after a sterilization procedure on all filters
1357 used to sterilize each high-risk preparation or batch preparation and the results documented.
1358 The results should be compared with the filter manufacturer's specification for the specific
1359 filter used. If a filter fails the integrity test, the preparation or batch must be sterilized again
1360 using new unused filters.

1361 (B) Finished preparation release checks and tests.

1362 (i) All high-risk level compounded sterile preparations that are prepared in groups of more
1363 than 25 identical individual single-dose packages (such as ampuls, bags, syringes, and vials),
1364 or in multiple dose vials for administration to multiple patients, or are exposed longer than 12
1365 hours at 2 - 8 degrees Celsius and longer than six hours at warmer than 8 degrees Celsius
1366 before they are sterilized shall be tested to ensure they are sterile and do not contain excessive
1367 bacterial endotoxins as specified in Chapter 71, Sterility Tests of the USP/NF before being
1368 dispensed or administered.

1369 (ii) All compounded sterile preparations, except for sterile radiopharmaceuticals, that are
1370 intended to be solutions must be visually examined for the presence of particulate matter and
1371 not administered or dispensed when such matter is observed.

1372 (iii) The prescription drug and medication orders, written compounding procedure,
1373 preparation records, and expended materials used to make compounded sterile preparations at
1374 all contamination risk levels shall be inspected for accuracy of correct identities and amounts
1375 of ingredients, aseptic mixing and sterilization, packaging, labeling, and expected physical
1376 appearance before they are dispensed or administered.

1377 (iv) Written procedures for checking compounding accuracy shall be followed for every
1378 compounded sterile preparation during preparation, in accordance with pharmacy's policies
1379 and procedures, and immediately prior to release, including label accuracy and the accuracy
1380 of the addition of all drug products or ingredients used to prepare the finished preparation and
1381 their volumes or quantities. A pharmacist shall ensure that components used in compounding
1382 are accurately weighed, measured, or subdivided as appropriate to conform to the formula
1383 being prepared.

1384 (C) Environmental Testing.

1385 (i) Viable and nonviable environmental sampling testing. Environmental sampling shall
1386 occur, at a minimum, every six months as part of a comprehensive quality management
1387 program and under any of the following conditions:

1388 (I) as part of the commissioning and certification of new facilities and equipment;

- 1389 (II) following any servicing of facilities and equipment;
- 1390 (III) as part of the re-certification of facilities and equipment;
- 1391 (IV) in response to identified problems with end products or staff technique; or
- 1392 (V) in response to issues with compounded sterile preparations, observed compounding
1393 personnel work practices, or patient-related infections (where the compounded sterile
1394 preparation is being considered as a potential source of the infection).
- 1395 (ii) Total particle counts. Certification that each ISO classified area (e.g., ISO Class 5, 7, and
1396 8), is within established guidelines shall be performed no less than every six months and
1397 whenever the equipment is relocated or the physical structure of the buffer area or ante-area
1398 has been altered. All certification records shall be maintained and reviewed to ensure that the
1399 controlled environments comply with the proper air cleanliness, room pressures, and air
1400 changes per hour. Testing shall be performed by qualified operators using current, state-of-
1401 the-art equipment, with results of the following:
- 1402 (I) ISO Class 5 - not more than 3520 particles 0.5 micrometer and larger size per cubic meter
1403 of air;
- 1404 (II) ISO Class 7 - not more than 352,000 particles of 0.5 micrometer and larger size per cubic
1405 meter of air for any buffer area; and
- 1406 (III) ISO Class 8 - not more than 3,520,000 particles of 0.5 micrometer and larger size per
1407 cubic meter of air for any ante-area.
- 1408 (iii) Pressure differential monitoring. A pressure gauge or velocity meter shall be installed to
1409 monitor the pressure differential or airflow between the buffer area and the ante-area and
1410 between the ante-area and the general environment outside the compounding area. The results
1411 shall be reviewed and documented on a log at least every work shift (minimum frequency
1412 shall be at least daily) or by a continuous recording device. The pressure between the ISO
1413 Class 7 or ISO Class 8 and the general pharmacy area shall not be less than 0.02 inch water
1414 column.
- 1415 (iv) Sampling plan. An appropriate environmental sampling plan shall be developed for
1416 airborne viable particles based on a risk assessment of compounding activities performed.
1417 Selected sampling sites shall include locations within each ISO Class 5 environment and in
1418 the ISO Class 7 and 8 areas and in the segregated compounding areas at greatest risk of
1419 contamination. The plan shall include sample location, method of collection, frequency of
1420 sampling, volume of air sampled, and time of day as related to activity in the compounding
1421 area and action levels.
- 1422 (v) Viable air sampling. Evaluation of airborne microorganisms using volumetric collection
1423 methods in the controlled air environments shall be performed by properly trained individuals
1424 for all compounding risk levels. For low-, medium-, and high-risk level compounding, air
1425 sampling shall be performed at locations that are prone to contamination during compounding
1426 activities and during other activities such as staging, labeling, gowning, and cleaning.
1427 Locations shall include zones of air backwash turbulence within the laminar airflow
1428 workbench and other areas where air backwash turbulence may enter the compounding area.

1429 For low-risk level compounded sterile preparations within 12-hour or less beyond-use-date
1430 prepared in a primary engineering control that maintains an ISO Class 5, air sampling shall be
1431 performed at locations inside the ISO Class 5 environment and other areas that are in close
1432 proximity to the ISO Class 5 environment during the certification of the primary engineering
1433 control.

1434 (vi) Air sampling frequency and process. Air sampling shall be performed at least every 6
1435 months as a part of the re-certification of facilities and equipment. A sufficient volume of air
1436 shall be sampled and the manufacturer's guidelines for use of the electronic air sampling
1437 equipment followed. At the end of the designated sampling or exposure period for air
1438 sampling activities, the microbial growth media plates are recovered and their covers secured
1439 and they are inverted and incubated at a temperature and for a time period conducive to
1440 multiplication of microorganisms. Sampling data shall be collected and reviewed on a
1441 periodic basis as a means of evaluating the overall control of the compounding environment.
1442 If an activity consistently shows elevated levels of microbial growth, competent microbiology
1443 personnel shall be consulted.

1444 (vii) Compounding accuracy checks. Written procedures for checking compounding accuracy
1445 shall be followed for every compounded sterile preparation during preparation and
1446 immediately prior to release, including label accuracy and the accuracy of the addition of all
1447 drug products or ingredients used to prepare the finished preparation and their volumes or
1448 quantities. At each step of the compounding process, the pharmacist shall ensure that
1449 components used in compounding are accurately weighed, measured, or subdivided as
1450 appropriate to conform to the formula being prepared.

1451 (15) Quality control.

1452 (A) Quality control procedures. The pharmacy shall follow established quality control
1453 procedures to monitor the compounding environment and quality of compounded drug
1454 preparations for conformity with the quality indicators established for the preparation. When
1455 developing these procedures, pharmacy personnel shall consider the provisions of USP
1456 Chapter 71, Sterility Tests, USP Chapter 85, Bacterial Endotoxins Test, Pharmaceutical
1457 Compounding--Non-sterile Preparations, USP Chapter 795, USP Chapter 797, Pharmaceutical
1458 Compounding--Sterile Preparations, USP Chapter 800, Hazardous Drugs--Handling in
1459 Healthcare Settings, USP Chapter 823, Positron Emission Tomography Drugs for
1460 Compounding, Investigational, and Research Uses, USP Chapter 1160, Pharmaceutical
1461 Calculations in Prescription Compounding, and USP Chapter 1163, Quality Assurance in
1462 Pharmaceutical Compounding of the current USP/NF. Such procedures shall be documented
1463 and be available for inspection.

1464 (B) Verification of compounding accuracy and sterility.

1465 (i) The accuracy of identities, concentrations, amounts, and purities of ingredients in
1466 compounded sterile preparations shall be confirmed by reviewing labels on packages,
1467 observing and documenting correct measurements with approved and correctly standardized
1468 devices, and reviewing information in labeling and certificates of analysis provided by
1469 suppliers.

1470 (ii) If the correct identity, purity, strength, and sterility of ingredients and components of
1471 compounded sterile preparations cannot be confirmed such ingredients and components shall

1472 be discarded immediately. Any compounded sterile preparation that fails sterility testing
1473 following sterilization by one method (e.g., filtration) is to be discarded and not subjected to a
1474 second method of sterilization.

1475 (iii) If individual ingredients, such as bulk drug substances, are not labeled with expiration
1476 dates, when the drug substances are stable indefinitely in their commercial packages under
1477 labeled storage conditions, such ingredients may gain or lose moisture during storage and use
1478 and shall require testing to determine the correct amount to weigh for accurate content of
1479 active chemical moieties in compounded sterile preparations.

1480 (e) Records. Any testing, cleaning, procedures, or other activities required in this subsection
1481 shall be documented and such documentation shall be maintained by the pharmacy.

1482 (1) Maintenance of records. Every record required under this section must be:

1483 (A) kept by the pharmacy and be available, for at least two years for inspecting and copying
1484 by the board or its representative and to other authorized local, state, or federal law
1485 enforcement agencies; and

1486 (B) supplied by the pharmacy within 72 hours, if requested by an authorized agent of the
1487 Texas State Board of Pharmacy. If the pharmacy maintains the records in an electronic
1488 format, the requested records must be provided in an electronic format. Failure to provide the
1489 records set out in this section, either on site or within 72 hours, constitutes prima facie
1490 evidence of failure to keep and maintain records in violation of the Act.

1491 (2) Compounding records.

1492 (A) Compounding pursuant to patient specific prescription drug orders. Compounding
1493 records for all compounded preparations shall be maintained by the pharmacy electronically
1494 or manually as part of the prescription drug or medication order, formula record, formula
1495 book, or compounding log and shall include:

1496 (i) the date **and time** of preparation;

1497 (ii) a complete formula, including methodology and necessary equipment which includes the
1498 brand name(s) of the raw materials, or if no brand name, the generic name(s) or official name
1499 and name(s) of the manufacturer(s) or distributor of the raw materials and the quantities of
1500 each;

1501 (iii) **written or electronic** signature or initials of the pharmacist or pharmacy technician or
1502 pharmacy technician trainee performing the compounding;

1503 (iv) **written or electronic** signature or initials of the pharmacist responsible for supervising
1504 pharmacy technicians or pharmacy technician trainees and conducting final checks of
1505 compounded pharmaceuticals if pharmacy technicians or pharmacy technician trainees
1506 perform the compounding function;

1507 (v) the quantity in units of finished preparation or amount of raw materials;

1508 (vi) the container used and the number of units prepared; and

- 1509 (vii) a reference to the location of the following documentation which may be maintained
1510 with other records, such as quality control records:
- 1511 (I) the criteria used to determine the beyond-use date; and
- 1512 (II) documentation of performance of quality control procedures.
- 1513 (B) Compounding records when batch compounding or compounding in anticipation of
1514 future prescription drug or medication orders.
- 1515 (i) Master work sheet. A master work sheet shall be developed and approved by a pharmacist
1516 for preparations prepared in batch. Once approved, a duplicate of the master work sheet shall
1517 be used as the preparation work sheet from which each batch is prepared and on which all
1518 documentation for that batch occurs. The master work sheet shall contain at a minimum:
- 1519 (I) the formula;
- 1520 (II) the components;
- 1521 (III) the compounding directions;
- 1522 (IV) a sample label;
- 1523 (V) evaluation and testing requirements;
- 1524 (VI) specific equipment used during preparation; and
- 1525 (VII) storage requirements.
- 1526 (ii) Preparation work sheet. The preparation work sheet for each batch of preparations shall
1527 document the following:
- 1528 (I) identity of all solutions and ingredients and their corresponding amounts, concentrations,
1529 or volumes;
- 1530 (II) lot number for each component;
- 1531 (III) component manufacturer/distributor or suitable identifying number;
- 1532 (IV) container specifications (e.g., syringe, pump cassette);
- 1533 (V) unique lot or control number assigned to batch;
- 1534 (VI) expiration date of batch-prepared preparations;
- 1535 (VII) date of preparation;
- 1536 (VIII) name, initials, or electronic signature of the person(s) involved in the preparation;
- 1537 (IX) name, initials, or electronic signature of the responsible pharmacist;

- 1538 (X) finished preparation evaluation and testing specifications, if applicable; and
- 1539 (XI) comparison of actual yield to anticipated or theoretical yield, when appropriate.
- 1540 (f) Office Use Compounding and Distribution of Sterile Compounded Preparations
- 1541 (1) General.
- 1542 (A) A pharmacy may compound, dispense, deliver, and distribute a compounded sterile
1543 preparation as specified in Subchapter D, Texas Pharmacy Act Chapter 562.
- 1544 (B) A Class A-S pharmacy is not required to register or be licensed under Chapter 431,
1545 Health and Safety Code, to distribute sterile compounded preparations to a Class C or Class
1546 C-S pharmacy.
- 1547 (C) A Class C-S pharmacy is not required to register or be licensed under Chapter 431,
1548 Health and Safety Code, to distribute sterile compounded preparations that the Class C-S
1549 pharmacy has compounded for other Class C or Class C-S pharmacies under common
1550 ownership.
- 1551 (D) To compound and deliver a compounded preparation under this subsection, a pharmacy
1552 must:
- 1553 (i) verify the source of the raw materials to be used in a compounded drug;
- 1554 (ii) comply with applicable United States Pharmacopoeia guidelines, including the testing
1555 requirements, and the Health Insurance Portability and Accountability Act of 1996 (Pub. L.
1556 No. 104-191);
- 1557 (iii) enter into a written agreement with a practitioner for the practitioner's office use of a
1558 compounded preparation;
- 1559 (iv) comply with all applicable competency and accrediting standards as determined by the
1560 board; and
- 1561 (v) comply with the provisions of this subsection.
- 1562 (E) This subsection does not apply to Class B pharmacies compounding sterile
1563 radiopharmaceuticals that are furnished for departmental or physicians' use if such authorized
1564 users maintain a Texas radioactive materials license.
- 1565 (2) Written Agreement. A pharmacy that provides sterile compounded preparations to
1566 practitioners for office use or to another pharmacy shall enter into a written agreement with
1567 the practitioner or pharmacy. The written agreement shall:
- 1568 (A) address acceptable standards of practice for a compounding pharmacy and a practitioner
1569 and receiving pharmacy that enter into the agreement including a statement that the
1570 compounded drugs may only be administered to the patient and may not be dispensed to the
1571 patient or sold to any other person or entity except to a veterinarian as authorized by
1572 §563.054 of the Act;

1573 (B) require the practitioner or receiving pharmacy to include on a patient's chart, medication
1574 order or medication administration record the lot number and beyond-use date of a
1575 compounded preparation administered to a patient;

1576 (C) describe the scope of services to be performed by the pharmacy and practitioner or
1577 receiving pharmacy, including a statement of the process for:

1578 (i) a patient to report an adverse reaction or submit a complaint; and

1579 (ii) the pharmacy to recall batches of compounded preparations.

1580 (3) Recordkeeping.

1581 (A) Maintenance of Records.

1582 (i) Records of orders and distribution of sterile compounded preparations to a practitioner for
1583 office use or to an institutional pharmacy for administration to a patient shall:

1584 (I) be kept by the pharmacy and be available, for at least two years from the date of the
1585 record, for inspecting and copying by the board or its representative and to other authorized
1586 local, state, or federal law enforcement agencies;

1587 (II) maintained separately from the records of preparations dispensed pursuant to a
1588 prescription or medication order; and

1589 (III) supplied by the pharmacy within 72 hours, if requested by an authorized agent of the
1590 Texas State Board of Pharmacy or its representative. If the pharmacy maintains the records in
1591 an electronic format, the requested records must be provided in an electronic format. Failure
1592 to provide the records set out in this subsection, either on site or within 72 hours for whatever
1593 reason, constitutes prima facie evidence of failure to keep and maintain records.

1594 (ii) Records may be maintained in an alternative data retention system, such as a data
1595 processing system or direct imaging system provided the data processing system is capable of
1596 producing a hard copy of the record upon the request of the board, its representative, or other
1597 authorized local, state, or federal law enforcement or regulatory agencies.

1598 (B) Orders. The pharmacy shall maintain a record of all sterile compounded preparations
1599 ordered by a practitioner for office use or by an institutional pharmacy for administration to a
1600 patient. The record shall include the following information:

1601 (i) date of the order;

1602 (ii) name, address, and phone number of the practitioner who ordered the preparation and if
1603 applicable, the name, address and phone number of the institutional pharmacy ordering the
1604 preparation; and

1605 (iii) name, strength, and quantity of the preparation ordered.

1606 (C) Distributions. The pharmacy shall maintain a record of all sterile compounded
1607 preparations distributed pursuant to an order to a practitioner for office use or by an

1608 institutional pharmacy for administration to a patient. The record shall include the following
1609 information:

1610 (i) date the preparation was compounded;

1611 (ii) date the preparation was distributed;

1612 (iii) name, strength and quantity in each container of the preparation;

1613 (iv) pharmacy's lot number;

1614 (v) quantity of containers shipped; and

1615 (vi) name, address, and phone number of the practitioner or institutional pharmacy to whom
1616 the preparation is distributed.

1617 (D) Audit Trail.

1618 (i) The pharmacy shall store the order and distribution records of preparations for all sterile
1619 compounded preparations ordered by and or distributed to a practitioner for office use or by a
1620 pharmacy licensed to compound sterile preparations for administration to a patient in such a
1621 manner as to be able to provide an audit trail for all orders and distributions of any of the
1622 following during a specified time period:

1623 (I) any strength and dosage form of a preparation (by either brand or generic name or both);

1624 (II) any ingredient;

1625 (III) any lot number;

1626 (IV) any practitioner;

1627 (V) any facility; and

1628 (VI) any pharmacy, if applicable.

1629 (ii) The audit trail shall contain the following information:

1630 (I) date of order and date of the distribution;

1631 (II) practitioner's name, address, and name of the institutional pharmacy, if applicable;

1632 (III) name, strength and quantity of the preparation in each container of the preparation;

1633 (IV) name and quantity of each active ingredient;

1634 (V) quantity of containers distributed; and

1635 (VI) pharmacy's lot number.

- 1636 (4) Labeling. The pharmacy shall affix a label to the preparation containing the following
1637 information:
- 1638 (A) name, address, and phone number of the compounding pharmacy;
- 1639 (B) the statement: "For Institutional or Office Use Only--Not for Resale"; or if the
1640 preparation is distributed to a veterinarian the statement: "Compounded Preparation";
- 1641 (C) name and strength of the preparation or list of the active ingredients and strengths;
- 1642 (D) pharmacy's lot number;
- 1643 (E) beyond-use date as determined by the pharmacist using appropriate documented criteria;
- 1644 (F) quantity or amount in the container;
- 1645 (G) appropriate ancillary instructions, such as storage instructions or cautionary statements,
1646 including hazardous drug warning labels where appropriate; and
- 1647 (H) device-specific instructions, where appropriate.
- 1648 (g) Recall Procedures.
- 1649 (1) The pharmacy shall have written procedures for the recall of any compounded sterile
1650 preparation provided to a patient, to a practitioner for office use, or a pharmacy for
1651 administration. Written procedures shall include, but not be limited to the requirements as
1652 specified in paragraph (3) of this subsection.
- 1653 (2) The pharmacy shall immediately initiate a recall of any sterile preparation compounded
1654 by the pharmacy upon identification of a potential or confirmed harm to a patient.
- 1655 (3) In the event of a recall, the pharmacist-in-charge shall ensure that:
- 1656 (A) each practitioner, facility, and/or pharmacy to which the preparation was distributed is
1657 notified, in writing, of the recall;
- 1658 (B) each patient to whom the preparation was dispensed is notified, in writing, of the recall;
- 1659 (C) the board is notified of the recall, in writing, not later than 24 hours after the recall is
1660 issued;
- 1661 (D) if the preparation is distributed for office use, the Texas Department of State Health
1662 Services, Drugs and Medical Devices Group, is notified of the recall, in writing;
- 1663 (E) the preparation is quarantined; and
- 1664 (F) the pharmacy keeps a written record of the recall including all actions taken to notify all
1665 parties and steps taken to ensure corrective measures.
- 1666 (4) If a pharmacy fails to initiate a recall, the board may require a pharmacy to initiate a recall

1667 if there is potential for or confirmed harm to a patient.

1668 (5) A pharmacy that compounds sterile preparations shall notify the board immediately of
1669 any adverse effects reported to the pharmacy or that are known by the pharmacy to be
1670 potentially attributable to a sterile preparation compounded by the pharmacy.

From: Sidney Phillips
Sent: Wednesday, January 13, 2016 6:14 PM
To: Gay Dodson;
Subject: TSHP input on 291.133

Gay,

I am following up on our meeting in December with Brad Shields, myself, and Brian Cohen about possible changes to the patient specific record keeping and IV training documentation in 291.133. You ask us to put together a document detailing our request and send to you for discussion at the next TSBP meeting.

We have worked through multiple TSHP groups representing hospital pharmacies across the state of Texas.

Attached is the updated request for amendments to the two rules we discussed.

Myself, Brian Cohen, and several others from TSHP plan to be at the next board meeting to answer questions or present our position if requested.

Please let me know if you need any additional information.

Thank you for your time and help on this important issue.

Sid

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 formula, including methodology and necessary equipment which includes the brand name(s) 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 quantities of each;
- (iii) signature or initials of the pharmacist, or pharmacy technician, or pharmacy technician trainee performing the compounding;
- (iv) 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 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.

Board intent of the rule as described by Gay Dodson is to be able to track how the admixture was performed, products used, by whom it was performed, and who checked the admixture in the event of a recall or questionable event.

Health-systems are challenged meeting the rule as currently stated, since it does not allow the flexibility to use current and future systems that would contain the required information in multiple formats and locations. Recommended language would allow flexibility for health-systems to track patient specific IV compounded data through a variety of electronic systems and/or manual processes.

Proposed Rules:

(2) Compounding records.

(A) Compounding pursuant to patient specific prescription drug orders. Compounding records for compounded preparations shall be maintained by the pharmacy. The pharmacy will maintain the following for each preparation:

- (i) the date and time of preparation;
- (ii) individual ingredients, including the quantity and concentration of each additive and the volume of any diluents used.
- (iii) written or electronic signature or initials of the pharmacist, 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, if pharmacy technicians or pharmacy technician trainees perform the compounding function;
- (v) a reference to the following documentation which may be maintained with other records, such as quality control records:
 - (I) beyond use date and the criteria used to determine the beyond-use date
 - (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.

TSHP recommends the highlighted language to be added that would allow media-fill documentation for technicians and pharmacists that work at pharmacies under common ownership be shared across pharmacies. These pharmacies would perform admixtures under a consistent risk level and the PIC would ensure they maintain this documentation.