

RULE ANALYSIS

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

Short Title: Pharmacies Compounding Sterile Preparations

Rule Numbers: §291.133

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

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

Purpose: The amendments, if adopted, update the sterile compounding rules to be consistent with updated changes to USP 797.

1 **TITLE 22 EXAMINING BOARDS**
2 **PART 15 TEXAS STATE BOARD OF PHARMACY**
3 **CHAPTER 291 PHARMACIES**
4

5 **§291.133 Pharmacies Compounding Sterile Preparations**
6

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

10 (1) compounding of sterile preparations pursuant to a prescription or medication order for a patient
11 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 office for
14 office use by the practitioner;

15 (3) compounding and distribution of compounded sterile preparations by a Class A-S pharmacy for a
16 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 ownership.
19

20 (b) Definitions. In addition to the definitions for specific license classifications, the following words and
21 terms, when used in this section, shall have the following meanings, unless the context clearly indicates
22 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 Organization of
26 Standardization (ISO) Classification Air Cleanliness (ISO 14644-1). For example:

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

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

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

36 (3) Ancillary supplies--Supplies necessary for the preparation and administration of compounded
37 sterile preparations.

38 (4) Ante-area--An ISO Class 8 or better area where personnel may perform hand hygiene and garbing
39 procedures, staging of components, order entry, labeling, and other high-particulate generating
40 activities. It is also a transition area that:

41 (A) provides assurance that pressure relationships are constantly maintained so that air flows from
42 clean to dirty areas; and

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

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

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

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

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

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

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

65 (11) Buffer Area--An ISO Class 7 area where the primary engineering control area is physically
66 located. Activities that occur in this area include the preparation and staging of components and
67 supplies used when compounding sterile preparations.

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

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

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

83 (15) Compounding Aseptic Isolator--A form of barrier isolator specifically designed for compounding
84 pharmaceutical ingredients or preparations. It is designed to maintain an aseptic compounding
85 environment within the isolator throughout the compounding and material transfer processes. Air
86 exchange into the isolator from the surrounding environment shall not occur unless it has first passed
87 through a microbial retentive filter (HEPA minimum).

88 (16) Compounding Aseptic Containment Isolator--A compounding aseptic isolator designed to provide
89 worker protection from exposure to undesirable levels of airborne drug throughout the compounding
90 and material transfer processes and to provide an aseptic environment for compounding sterile
91 preparations. Air exchange with the surrounding environment should not occur unless the air is first
92 passed through a microbial retentive filter (HEPA minimum) system capable of containing airborne
93 concentrations of the physical size and state of the drug being compounded. Where volatile hazardous
94 drugs are prepared, the exhaust air from the isolator should be appropriately removed by properly
95 designed building ventilation.

96 **(17) Compounding Personnel – A pharmacist, pharmacy technician, or pharmacy technician**
97 **trainee who performs the actual compounding; a pharmacist who supervises pharmacy**
98 **technicians or pharmacy technician trainees compounding sterile preparations, and a**
99 **pharmacist who performs an intermediate or final verification of a compounded sterile**
100 **preparation.**

101 ~~(17)~~ **(18)** Critical Area--An ISO Class 5 environment.

102 ~~(18)~~ **(19)** Critical Sites--A location that includes any component or fluid pathway surfaces (e.g., vial
103 septa, injection ports, beakers) or openings (e.g., opened ampuls, needle hubs) exposed and at risk of
104 direct contact with air (e.g., ambient room or HEPA filtered), moisture (e.g., oral and mucosal
105 secretions), or touch contamination. Risk of microbial particulate contamination of the critical site
106 increases with the size of the openings and exposure time.

107 ~~(19)~~ **(20)** Device--An instrument, apparatus, implement, machine, contrivance, implant, in-vitro
108 reagent, or other similar or related article, including any component part or accessory, that is required
109 under federal or state law to be ordered or prescribed by a practitioner.

110 ~~(20)~~ **(21)** Direct Compounding Area--A critical area within the ISO Class 5 primary engineering control
111 where critical sites are exposed to unidirectional HEPA-filtered air, also known as first air.

112 ~~(21)~~ **(22)** Disinfectant--An agent that frees from infection, usually a chemical agent but sometimes a
113 physical one, and that destroys disease-causing pathogens or other harmful microorganisms but may
114 not kill bacterial and fungal spores. It refers to substances applied to inanimate objects.

115 ~~(22)~~ **(23)** First Air--The air exiting the HEPA filter in a unidirectional air stream that is essentially
116 particle free.

117 ~~(23)~~ **(24)** Hazardous Drugs--Drugs that, studies in animals or humans indicate exposure to the drugs,
118 have a potential for causing cancer, development or reproductive toxicity, or harm to organs.

119 ~~(24)~~ **(25)** Hot water--The temperature of water from the pharmacy's sink maintained at a minimum of
120 105 degrees F (41 degrees C).

121 ~~(25)~~ **(26)** HVAC--Heating, ventilation, and air conditioning.

122 ~~(26)~~ **(27)** Immediate use--A sterile preparation that is not prepared according to USP 797 standards
123 (i.e., outside the pharmacy and most likely not by pharmacy personnel) which shall be stored for no
124 longer than one hour after completion of the preparation.

125 ~~(27)~~ **(28)** IPA--Isopropyl alcohol (2-propanol).

126 ~~(28)~~ **(29)** Labeling--All labels and other written, printed, or graphic matter on an immediate container of
127 an article or preparation or on, or in, any package or wrapper in which it is enclosed, except any outer
128 shipping container. The term "label" designates that part of the labeling on the immediate container.

129 ~~(29)~~ **(30)** Media-Fill Test--A test used to qualify aseptic technique of compounding personnel or
130 processes and to ensure that the processes used are able to produce sterile preparation without
131 microbial contamination. During this test, a microbiological growth medium such as Soybean-Casein
132 Digest Medium is substituted for the actual drug preparation to simulate admixture compounding. The
133 issues to consider in the development of a media-fill test are the following: media-fill procedures, media
134 selection, fill volume, incubation, time and temperature, inspection of filled units, documentation,
135 interpretation of results, and possible corrective actions required.

136 ~~(30)~~ **(31)** Multiple-Dose Container--A multiple-unit container for articles or preparations intended for
137 potential administration only and usually contains antimicrobial preservatives. The beyond-use date for
138 an opened or entered (e.g., needle-punctured) multiple-dose container with antimicrobial preservatives
139 is 28 days, unless otherwise specified by the manufacturer.

140 ~~(31)~~ **(32)** Negative Pressure Room--A room that is at a lower pressure compared to adjacent spaces
141 and, therefore, the net flow of air is into the room.

142 ~~(32)~~ **(33)** Office use--The administration of a compounded drug to a patient by a practitioner in the
143 practitioner's office or by the practitioner in a health care facility or treatment setting, including a
144 hospital, ambulatory surgical center, or pharmacy in accordance with Chapter 562 of the Act, or for
145 administration or provision by a veterinarian in accordance with §563.054 of the Act.

146 ~~(33)~~ **(34)** Pharmacy Bulk Package--A container of a sterile preparation for potential use that contains
147 many single doses. The contents are intended for use in a pharmacy admixture program and are
148 restricted to the preparation of admixtures for infusion or, through a sterile transfer device, for the filling
149 of empty sterile syringes. The closure shall be penetrated only one time after constitution with a suitable
150 sterile transfer device or dispensing set, which allows measured dispensing of the contents. The
151 pharmacy bulk package is to be used only in a suitable work area such as a laminar flow hood (or an
152 equivalent clean air compounding area).

153 ~~(34)~~ **(35)** Prepackaging--The act of repackaging and relabeling quantities of drug products from a
154 manufacturer's original container into unit dose packaging or a multiple dose container for distribution
155 within a facility licensed as a Class C pharmacy or to other pharmacies under common ownership for
156 distribution within those facilities. The term as defined does not prohibit the prepackaging of drug
157 products for use within other pharmacy classes.

158 ~~(35)~~ **(36)** Preparation or Compounded Sterile Preparation--A sterile admixture compounded in a
159 licensed pharmacy or other healthcare-related facility pursuant to the order of a licensed prescriber.
160 The components of the preparation may or may not be sterile products.

161 ~~(36)~~ **(37)** Primary Engineering Control--A device or room that provides an ISO Class 5 environment for
162 the exposure of critical sites when compounding sterile preparations. Such devices include, but may not
163 be limited to, laminar airflow workbenches, biological safety cabinets, compounding aseptic isolators,
164 and compounding aseptic containment isolators.

165 ~~(37)~~ **(38)** Product--A commercially manufactured sterile drug or nutrient that has been evaluated for
166 safety and efficacy by the U.S. Food and Drug Administration (FDA). Products are accompanied by full
167 prescribing information, which is commonly known as the FDA-approved manufacturer's labeling or
168 product package insert.

169 ~~(38)~~ **(39)** Positive Control--A quality assurance sample prepared to test positive for microbial growth.

170 ~~(39)~~ **(40)** Positive Pressure Room--A room that is at a higher pressure compared to adjacent spaces
171 and, therefore, the net airflow is out of the room.

172 ~~(40)~~ **(41)** Quality assurance--The set of activities used to ensure that the process used in the
173 preparation of sterile drug preparations lead to preparations that meet predetermined standards of
174 quality.

175 ~~(41)~~ **(42)** Quality control--The set of testing activities used to determine that the ingredients,
176 components (e.g., containers), and final compounded sterile preparations prepared meet
177 predetermined requirements with respect to identity, purity, non-pyrogenicity, and sterility.

178 ~~(42)~~ **(43)** Reasonable quantity--An amount of a compounded drug that:

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

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

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

187 ~~(43)~~ **(44)** Segregated Compounding Area--A designated space, either a demarcated area or room,
188 that is restricted to preparing low-risk level compounded sterile preparations with 12-hour or less

189 beyond-use date. Such area shall contain a device that provides unidirectional airflow of ISO Class 5
190 air quality for preparation of compounded sterile preparations and shall be void of activities and
191 materials that are extraneous to sterile compounding.

192 ~~(44)~~ **(45)** Single-dose container--A single-unit container for articles or preparations intended for
193 parenteral administration only. It is intended for a single use. A single-dose container is labeled as
194 such. Examples of single-dose containers include pre-filled syringes, cartridges, fusion-sealed
195 containers, and closure-sealed containers when so labeled.

196 ~~(45)~~ **(46)** SOPs--Standard operating procedures.

197 ~~(46)~~ **(47)** Sterilizing Grade Membranes--Membranes that are documented to retain 100% of a culture
198 of 107 microorganisms of a strain of *Brevundimonas* (*Pseudomonas*) *diminuta* per square centimeter of
199 membrane surface under a pressure of not less than 30 psi (2.0 bar). Such filter membranes are
200 nominally at 0.22-**micrometer** [μm] or 0.2-**micrometer** [μm] nominal pore size, depending on the
201 manufacturer's practice.

202 ~~(47)~~ **(48)** Sterilization by Filtration--Passage of a fluid or solution through a sterilizing grade membrane
203 to produce a sterile effluent.

204 ~~(48)~~ **(49)** Terminal Sterilization--The application of a lethal process, e.g., steam under pressure or
205 autoclaving, to sealed final preparation containers for the purpose of achieving a predetermined sterility
206 assurance level of usually less than 10^{-6} or a probability of less than one in one million of a non-sterile
207 unit.

208 ~~(49)~~ **(50)** Unidirectional Flow--An airflow moving in a single direction in a robust and uniform manner
209 and at sufficient speed to reproducibly sweep particles away from the critical processing or testing area.

210 ~~(50)~~ **(51)** USP/NF--The current edition of the United States Pharmacopeia/National Formulary.

211

212 (c) Personnel.

213 (1) Pharmacist-in-charge.

214 (A) General. The pharmacy shall have a pharmacist-in-charge in compliance with the specific license
215 classification of the pharmacy.

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

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

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

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

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

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

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

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

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

234 (2) Pharmacists.

235 (A) General.

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

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

241 (iii) A pharmacist shall review all compounding records for accuracy and conduct in-process and
242 final checks and verification of calculations to ensure that errors have not occurred in the compounding
243 process.

244 (iv) A pharmacist is responsible for ensuring the proper maintenance, cleanliness, and use of all
245 equipment used in the compounding process.

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

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

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

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

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

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

259 (II) possess knowledge about:

260 (-a-) aseptic processing;

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

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

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

265 (-e-) sterilization techniques.

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

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

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

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

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

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

282 (III) possess knowledge about:

283 (-a-) aseptic processing;

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

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

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

288 (-e-) sterilization techniques.

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

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

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

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

300 (3) Pharmacy technicians and pharmacy technician trainees.

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

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

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

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

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

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

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

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

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

324 (-c-) the supervising pharmacist conducts **periodic** in-process **checks as documented in the**
325 **pharmacy's policy and procedures** and **a** final **check** [~~checks~~].

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

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

330 (i) Pharmacy technicians and pharmacy technician trainees may compound sterile preparations
331 provided the pharmacy technicians and/or pharmacy technician trainees are supervised by a
332 pharmacist who has completed the training specified in paragraph (2) of this subsection, conducts in-
333 process and final checks, and affixes his or her initials to the appropriate quality control records.

334 (ii) All pharmacy technicians and pharmacy technician trainees who compound sterile preparations
335 for administration to patients shall comply with the following:

336 (I) complete through completion of a single course, a minimum of 40 hours of instruction and
337 experience in the areas listed in paragraph (4)(D) of this subsection. Such training shall be obtained
338 through completion of a course sponsored by an ACPE accredited provider which provides 40 hours of
339 instruction and experience;

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

344 (III) possess knowledge about:

345 (-a-) aseptic processing;

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

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

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

350 (-e-) sterilization techniques.

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

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

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

357 (III) the supervising pharmacist conducts in-process and final checks.

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

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

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

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

369 (4) Evaluation and testing requirements.

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

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

377 (i) every 12 months for low- and medium-risk level compounding; and
378 (ii) every six months for high-risk level compounding.

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

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

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

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

387 (i) aseptic technique;

388 (ii) critical area contamination factors;

389 (iii) environmental monitoring;

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

391 (v) equipment and supplies;

392 (vi) sterile preparation calculations and terminology;

393 (vii) sterile preparation compounding documentation;

394 (viii) quality assurance procedures;

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

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

397 (xi) cleaning procedures; and

398 (xii) general conduct in the clean room.

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

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

410 (G) Media-fill tests procedures for assessing the preparation of specific types of sterile preparations
411 shall be representative of the most challenging or stressful conditions encountered by the pharmacy
412 personnel being evaluated [~~for each risk level~~] and, **if applicable**, for sterilizing high-risk level
413 compounded sterile preparations.

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

416 (I) Commercially available sterile fluid culture media, such as Soybean-Casein Digest Medium shall
417 be able to promote exponential colonization of bacteria that are most likely to be transmitted to
418 compounding sterile preparations from the compounding personnel and environment. Media-filled vials
419 are generally incubated at 20 to 25 or at 30 to 35 for a minimum of 14 days. If two temperatures are
420 used for incubation of media-filled samples, then these filled containers should be incubated for at least
421 7 days at each temperature. Failure is indicated by visible turbidity in the medium on or before 14 days.

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

- 425 (i) during orientation and training prior to the regular performance of those tasks;
- 426 (ii) whenever the quality assurance program yields an unacceptable result;
- 427 (iii) whenever unacceptable techniques are observed; and
- 428 (iv) at least on an annual basis for low- and medium-risk level compounding, and every six months
429 for high-risk level compounding.

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

- 433 (i) Sampling of compounding personnel glove fingertips shall be performed for all risk level
434 compounding.
- 435 (ii) All compounding personnel shall demonstrate competency in proper hand hygiene and garbing
436 procedures and in aseptic work practices (e.g., disinfection of component surfaces, routine disinfection
437 of gloved hands).
- 438 (iii) Sterile contact agar plates shall be used to sample the gloved fingertips of compounding
439 personnel after garbing in order to assess garbing competency and after completing the media-fill
440 preparation (without applying sterile 70% IPA).
- 441 (iv) The visual observation shall be documented and maintained to provide a permanent record and
442 long-term assessment of personnel competency.
- 443 (v) All compounding personnel shall successfully complete an initial competency **evaluation** and
444 gloved fingertip/thumb sampling procedure no less than three times before initially being allowed to
445 compound sterile preparations for patient use. Immediately after the compounding personnel completes
446 the hand hygiene and garbing procedure (**i.e., after donning of sterile gloves and before any**
447 **disinfecting** [e.g., donning of sterile gloves prior to any disinfection] with sterile 70% IPA), the
448 evaluator will collect a gloved fingertip and thumb sample from both hands ~~from~~ **of** the compounding
449 personnel onto agar plates **by having the individual** lightly **touching** [pressing] each fingertip **onto**
450 **[into]** the agar. The **test** plates will be incubated for the appropriate incubation period and at the
451 appropriate temperature. **Results of the initial gloved fingertip evaluations shall indicate zero**
452 **colony-forming units (0 CFU) growth on the agar plates, or the test shall be considered a failure.**
453 **In the event of a failed gloved fingertip test, the evaluation shall be repeated until the individual**
454 **can successful don sterile gloves and pass the gloved fingertip evaluation, defined as zero**
455 **CFUs growth. No preparation intended for patient use shall be compounded by an individual**
456 **until the results of the initial gloved fingertip evaluation indicate that the individual can**
457 **competently perform aseptic procedures except that a pharmacist may temporarily supervise**
458 **pharmacy technicians compounding sterile preparations while waiting for the results of the**
459 **evaluation for no more than three days.** [~~Re-evaluation of all compounding personnel shall occur at~~
460 ~~least annually for compounding personnel who compound low and medium risk level preparations and~~
461 ~~every six months for compounding personnel who compound high risk level preparations.~~]

462
463 **(iv) Re-evaluation of all compounding personnel shall occur at least annually for compounding**
464 **personnel who compound low and medium risk level preparations and every six months for**
465 **compounding personnel who compound high risk level preparations. Results of gloved fingertip**
466 **tests conducted immediately after compounding personnel complete a compounding procedure**
467 **shall indicate no more than 3 CFUs growth, or the test shall be considered a failure, in which**

468 **case, the evaluation shall be repeated until an acceptable test can be achieved (i.e., the results**
469 **indicated no more than 3 CFUs growth).**

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

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

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

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

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

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

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

487

488 (d) Operational Standards.

489 (1) General Requirements.

490 (A) Sterile preparations may be compounded:

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

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

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

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

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

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

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

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

508 (II) facility's lot number;

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

511 (IV) quantity or amount in the container;

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

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

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

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

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

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

523 (D) A pharmacy may not compound preparations that are essentially copies of commercially
524 available products (e.g., the preparation is dispensed in a strength that is only slightly different from a
525 commercially available product) unless the prescribing practitioner specifically orders the strength or
526 dosage form and specifies why the patient needs the particular strength or dosage form of the
527 preparation or why the preparation for office use is needed in the particular strength or dosage form of
528 the preparation. The prescribing practitioner shall provide documentation of a patient specific medical
529 need and the preparation produces a clinically significant therapeutic response (e.g., the physician
530 requests an alternate preparation due to hypersensitivity to excipients or preservative in the FDA-
531 approved product, or the physician requests an effective alternate dosage form) or if the drug product is
532 not commercially available. The unavailability of such drug product must be documented prior to
533 compounding. The methodology for documenting unavailability includes maintaining a copy of the
534 wholesaler's notification showing back-ordered, discontinued, or out-of-stock items. This documentation
535 must be available in hard-copy or electronic format for inspection by the board.

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

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

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

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

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

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

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

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

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

561 (IV) For a low-risk preparation, in the absence of direct sterility testing results or appropriate
562 information sources that justify different limits, the storage periods may not exceed the following
563 periods: before administration the compounded sterile preparation is stored properly and are exposed
564 for not more than 48 hours at controlled room temperature, for not more than 14 days if stored at a cold
565 temperature, and for 45 days if stored in a frozen state between minus 25 degrees Celsius and minus
566 10 degrees Celsius. For delayed activation device systems, the storage period begins when the device
567 is activated.

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

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

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

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

578 (i) The compounded sterile preparations are compounded in compounding aseptic isolator or
579 compounding aseptic containment isolator that does not meet the requirements described in paragraph
580 **(7)(C) or (D) of this subsection (relating to Primary Engineering Control Device)** [~~(6)(A)(ii)(II) of~~
581 ~~this subsection relating to Low and Medium Risk Preparations~~] or the compounded sterile preparations
582 are compounded in laminar airflow workbench or a biological safety cabinet that cannot be located
583 within an ISO Class 7 buffer area.

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

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

590 (iv) For a low-risk preparation compounded as described in clauses (i) - (iii) of this subparagraph,
591 administration of such compounded sterile preparations must commence within 12 hours of preparation
592 or as recommended in the manufacturers' package insert, whichever is less.

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

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

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

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

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

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

606 (V) For a medium-risk preparation, in the absence of direct sterility testing results the beyond use
607 dates may not exceed the following time periods: before administration, the compounded sterile

608 preparations are properly stored and are exposed for not more than 30 hours at controlled room
609 temperature, for not more than 9 days at a cold temperature, and for 45 days in solid frozen state
610 between minus 25 degrees Celsius and minus 10 degrees Celsius.

611 (ii) Examples of medium-risk compounding. Examples of medium-risk compounding include the
612 following.

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

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

618 (III) Filling of reservoirs of injection and infusion devices with volumes of sterile drug solutions that
619 will be administered over several days at ambient temperatures between 25 and 40 degrees Celsius
620 (77 and 104 degrees Fahrenheit).

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

674 (C) During preparation, aseptic technique is followed and, if not immediately administered, the
675 finished compounded sterile preparation is under continuous supervision to minimize the potential for
676 contact with non-sterile surfaces, introduction of particulate matter of biological fluids, mix-ups with
677 other compounded sterile preparations, and direct contact of outside surfaces.

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

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

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

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

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

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

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

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

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

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

701 (A) a reference text on injectable drug preparations, such as Handbook on Injectable Drug Products;
702 (B) a specialty reference text appropriate for the scope of pharmacy services provided by the
703 pharmacy, e.g., if the pharmacy prepares hazardous drugs, a reference text on the preparation of
704 hazardous drugs; and

705 (C) the United States Pharmacopeia/National Formulary containing USP Chapter 71, Sterility Tests,
706 USP Chapter 85, Bacterial Endotoxins Test, Pharmaceutical Compounding—Non-sterile Preparations,
707 USP Chapter 795, USP Chapter 797, Pharmaceutical Compounding--Sterile Preparations, and USP
708 Chapter 1163, Quality Assurance in Pharmaceutical Compounding.

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

711 (A) Low and Medium Risk Preparations.

712 ~~(i)~~ A pharmacy that prepares low- and medium-risk preparations shall have a clean room for the
713 compounding of sterile preparations that is constructed to minimize the opportunities for particulate and
714 microbial contamination. The clean room shall:

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

716 ~~(ii)~~ ~~(ii)~~ be maintained at a comfortable temperature (e.g., 20 degrees Celsius or cooler) allowing
717 compounding personnel to perform flawlessly when attired in the required aseptic compounding garb;

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

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

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

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

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

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

728 ~~(ix)~~ ~~(ix)~~ have drugs and supplies stored on shelving areas above the floor to permit adequate
729 floor cleaning;

730 ~~(x)~~ ~~(x)~~ contain only the appropriate compounding supplies and not be used for bulk storage for
731 supplies and materials. Objects that shed particles shall not be brought into the clean room;

732 ~~(xi)~~ ~~(xi)~~ contain an ante-area that provides at least an ISO class 8 air quality and contains a sink
733 with hot and cold running water that enables hands-free use with a closed system of soap dispensing to
734 minimize the risk of extrinsic contamination; and

735 ~~(xii)~~ ~~(xii)~~ contain a buffer area designed to maintain at least ISO Class 7 conditions for 0.5-
736 **micrometer** ~~[µm]~~ and larger particles under dynamic working conditions. The following is applicable for
737 the buffer area.

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

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

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

747 ~~(IV)~~ ~~(IV)~~ The buffer area shall not contain sources of water (i.e., sinks) or floor drains.

748 ~~[(ii) The pharmacy shall prepare sterile preparations in a primary engineering control device, such as a laminar air flow hood, biological safety cabinet, compounding aseptic isolator, compounding aseptic containment isolator which is capable of maintaining at least ISO Class 5 conditions for 0.5-µm particles while compounding sterile preparations.]~~

751 ~~—[(I) The primary engineering control shall:~~

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

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

761 ~~— (c) have pre-filters inspected periodically and replaced as needed, in accordance with written policies and procedures and the manufacturer's specification, and the inspection and/or replacement date documented; and~~

762 ~~— (d) be located in a buffer area that has a minimum differential positive pressure of 0.02 to 0.05 inches water column.~~

763 ~~—(II) The compounding aseptic isolator or compounding aseptic containment isolator must be placed in an ISO Class 7 buffer area unless the isolator meets all of the following conditions.~~

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

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

766 ~~— (c) The pharmacy shall maintain documentation from the manufacturer that the isolator meets this standard when located in worse than ISO Class 7 environments.]~~

767 (B) High-risk Preparations.

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

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

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

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

784 (i) ~~[General.]~~

785 ~~[(4)] Hazardous drugs shall be prepared only under conditions that protect personnel during preparation and storage.~~

786 ~~[(ii) [(4)] Hazardous drugs shall be stored separately from other inventory in a manner to prevent contamination and personnel exposure.~~

787 ~~[(iii) [(4)] All personnel involved in the compounding of hazardous drugs shall wear appropriate protective apparel, such as gowns, face masks, eye protection, hair covers, shoe covers or dedicated~~

795 shoes, and appropriate gloving at all times when handling hazardous drugs, including receiving,
796 distribution, stocking, inventorying, preparation, for administration and disposal.

797 **(iv)** ~~[(IV)]~~ Appropriate safety and containment techniques for compounding hazardous drugs shall
798 be used in conjunction with aseptic techniques required for preparing sterile preparations.

799 **(v)** ~~[(V)]~~ Disposal of hazardous waste shall comply with all applicable local, state, and federal
800 requirements.

801 **(vi)** ~~[(VI)]~~ Prepared doses of hazardous drugs must be dispensed, labeled with proper precautions
802 inside and outside, and distributed in a manner to minimize patient contact with hazardous agents.

803 ~~[(ii) Primary engineering control device. Hazardous drugs shall be prepared in a Class II or III
804 vertical flow biological safety cabinet or compounding aseptic containment isolator located in an ISO
805 Class 7 area that is physically separated from other preparation areas. The area for preparation of
806 sterile chemotherapeutic preparations shall:~~

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

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

810 ~~— (iii) Facilities that prepare a low volume of hazardous drugs. Pharmacies that prepare a low volume
811 of hazardous drugs, are not required to comply with the provisions of clause (ii) of this subparagraph if
812 the pharmacy uses a device that provides two tiers of containment (e.g., closed-system vial transfer
813 device within a BSC or CACI that is located in a non-negative pressure room).]~~

814 (E) Cleaning and disinfecting the sterile compounding areas. The following cleaning and disinfecting
815 practices and frequencies apply to direct and contiguous compounding areas, which include ISO Class
816 5 compounding areas for exposure of critical sites as well as buffer areas, ante-areas, and segregated
817 compounding areas.

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

820 (ii) These procedures shall be conducted at the beginning of each work shift, before each batch
821 preparation is started, **when there are spills, and when surface contamination is known or**
822 **suspected resulting from procedural breaches, and** every 30 minutes during continuous
823 compounding of individual compounded sterile preparations, **unless a particular compounding**
824 **procedure requires more than 30 minutes to complete, in which case, the direct compounding**
825 **area is to be cleaned immediately after the compounding activity is completed.** ~~[when there are
826 spills, and when surface contamination is known or suspected from procedural breaches.]~~

827 (iii) Before compounding is performed, all items shall be removed from the direct and contiguous
828 compounding areas and all surfaces are cleaned by removing loose material and residue from spills,
829 followed by an application of a residue-free disinfecting agent (e.g., IPA), which is allowed to dry before
830 compounding begins.

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

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

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

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

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

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

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

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

861 (I) date and time of cleaning;

862 (II) type of cleaning performed; and

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

864 (F) Security requirements. The pharmacist-in-charge may authorize personnel to gain access to that
865 area of the pharmacy containing dispensed sterile preparations, in the absence of the pharmacist, for
866 the purpose of retrieving dispensed prescriptions to deliver to patients. If the pharmacy allows such
867 after-hours access, the area containing the dispensed sterile preparations shall be an enclosed and
868 lockable area separate from the area containing undispensed prescription drugs. A list of the authorized
869 personnel having such access shall be in the pharmacy's policy and procedure manual.

870 (G) Storage requirements and beyond-use dating.

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

873 (ii) Beyond-use dating.

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

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

880 ~~(III) Beyond-use dates for compounded sterile preparations that lack justification from either~~
881 ~~appropriate literature sources or by direct testing evidence shall be assigned as described in Chapter~~
882 ~~795, in Stability Criteria and Beyond-Use Dating under Pharmaceutical Compounding-Nonsterile~~
883 ~~Preparations of the USP/NF.~~

884 **(III)** ~~(IV)~~ When assigning a beyond-use date, compounding personnel shall consult and apply
885 drug-specific and general stability documentation and literature where available, and they should

886 consider the nature of the drug and its degradation mechanism, the container in which it is packaged,
887 the expected storage conditions, and the intended duration of therapy.

888 **(IV) [(V)]** The sterility and storage and stability beyond-use date for attached and activated
889 container pairs of drug products for intravascular administration shall be applied as indicated by the
890 manufacturer.

891 **(7) Primary engineering control device. The pharmacy shall prepare sterile preparations in a**
892 **primary engineering control device (PEC), such as a laminar air flow hood, biological safety**
893 **cabinet, compounding aseptic isolator (CAI), or compounding aseptic containment isolator**
894 **(CACI) which is capable of maintaining at least ISO Class 5 conditions for 0.5 micrometer**
895 **particles while compounding sterile preparations.** [Equipment and supplies]

896
897 **(A) Laminar air flow hood. If the pharmacy is using a laminar air flow hood as its PEC, the**
898 **laminar air flow hood shall:**

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

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

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

909 **(iv) be located in a buffer area that has a minimum differential positive pressure of 0.02 to**
910 **0.05 inches water column.**

911
912 **(B) Biological safety cabinet.**

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

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

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

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

925
926 **(iii) If the pharmacy is using a biological safety cabinet as its PEC for the preparation of non-**
927 **hazardous sterile compounded preparations, the biological safety cabinet shall:**

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

931 **(II) be certified by a qualified independent contractor according to the International**
932 **Organization of Standardization (ISO) Classification of Particulate Matter in Room Air (ISO**

933 14644-1) for operational efficiency at least every six months and whenever the device or room is
934 relocated or altered or major service to the facility is performed, in accordance with the
935 manufacturer's specifications and test procedures specified in the Institute of Environmental
936 Sciences and Technology (IEST) document IEST-RP-CC002.3;

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

940 (IV) be located in a buffer area that has a minimum differential positive pressure of 0.02 to
941 0.05 inches water column.

942
943 (C) Compounding aseptic isolator.

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

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

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

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

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

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

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

962 (II) be maintained at a comfortable temperature (e.g., 20 degrees Celsius or cooler)
963 allowing compounding personnel to perform flawlessly when attired in the required
964 aseptic compounding garb;

965 (III) be used only for the compounding of low- and medium-risk, non-hazardous sterile
966 preparations;

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

970 (V) have non-porous and washable floors or floor covering to enable regular
971 disinfection; and

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

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

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(D) Compounding aseptic containment isolator.

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

(I) be vented to the outside of the building in which the pharmacy is located;

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

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

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

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

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

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

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

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

(II) be maintained at a comfortable temperature (e.g., 20 degrees Celsius or cooler) allowing compounding personnel to perform flawlessly when attired in the required aseptic compounding garb;

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

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

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

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

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

- 1027 (A) a calibrated system or device (i.e., thermometer) to monitor the temperature to ensure that proper
1028 storage requirements are met, if sterile preparations are stored in the refrigerator;
- 1029 (B) a calibrated system or device to monitor the temperature where bulk chemicals are stored;
- 1030 (C) a temperature-sensing mechanism suitably placed in the controlled temperature storage space to
1031 reflect accurately the true temperature;
- 1032 (D) if applicable, a Class A prescription balance, or analytical balance and weights. Such balance
1033 shall be properly maintained and subject to periodic inspection by the Texas State Board of Pharmacy;
- 1034 (E) equipment and utensils necessary for the proper compounding of sterile preparations. Such
1035 equipment and utensils used in the compounding process shall be:
- 1036 (i) of appropriate design, appropriate capacity, and be operated within designed operational limits;
- 1037 (ii) of suitable composition so that surfaces that contact components, in-process material, or drug
1038 products shall not be reactive, additive, or absorptive so as to alter the safety, identity, strength, quality,
1039 or purity of the drug preparation beyond the desired result;
- 1040 (iii) cleaned and sanitized immediately prior to and after each use; and
- 1041 (iv) routinely inspected, calibrated(if necessary), or checked to ensure proper performance;
- 1042 (F) appropriate disposal containers for used needles, syringes, etc., and if applicable, hazardous
1043 waste from the preparation of hazardous drugs and/or biohazardous waste;
- 1044 (G) appropriate packaging or delivery containers to maintain proper storage conditions for sterile
1045 preparations;
- 1046 (H) infusion devices, if applicable; and
- 1047 (I) all necessary supplies, including:
- 1048 (i) disposable needles, syringes, and other supplies for aseptic mixing;
- 1049 (ii) disinfectant cleaning solutions;
- 1050 **(iii) sterile isopropyl alcohol;**
- 1051 **(iv) sterile gloves, both for hazardous and non-hazardous drug compounding;**
- 1052 **(v) sterile IPA-based surgical scrub;**
- 1053 **(vi) [~~(iii)~~] hand washing agents with bactericidal action;**
- 1054 **(vii) [~~(iv)~~] disposable, lint free towels or wipes;**
- 1055 **(viii) [~~(v)~~] appropriate filters and filtration equipment;**
- 1056 **(ix) [~~(vi)~~] hazardous spill kits, if applicable; and**
- 1057 **(x) [~~(vii)~~] masks, caps, coveralls or gowns with tight cuffs, shoe covers, and gloves, as applicable.**
- 1058
- 1059 **(9) [~~(8)~~] Labeling.**
- 1060 (A) Prescription drug or medication orders. In addition to the labeling requirements for the
1061 pharmacy's specific license classification, the label dispensed or distributed pursuant to a prescription
1062 drug or medication order shall contain the following:
- 1063 (i) the generic name(s) or the official name(s) of the principal active ingredient(s) of the
1064 compounded sterile preparation;
- 1065 (ii) for outpatient prescription orders only, a statement that the compounded sterile preparation has
1066 been compounded by the pharmacy. (An auxiliary label may be used on the container to meet this
1067 requirement);
- 1068 (iii) a beyond-use date. The beyond-use date shall be determined as outlined in Chapter 797,
1069 Pharmacy Compounding--Sterile Preparations of the USP/NF, and paragraph (7)(G) of this subsection;
- 1070 (B) Batch. If the sterile preparation is compounded in a batch, the following shall also be included on
1071 the batch label:
- 1072 (i) unique lot number assigned to the batch;
- 1073 (ii) quantity;

1074 (iii) appropriate ancillary instructions, such as storage instructions or cautionary statements,
1075 including hazardous drug warning labels where appropriate; and
1076 (iv) device-specific instructions, where appropriate.
1077 (C) Pharmacy bulk package. The label of a pharmacy bulk package shall:
1078 (i) state prominently "Pharmacy Bulk Package--Not for Direct Infusion;"
1079 (ii) contain or refer to information on proper techniques to help ensure safe use of the preparation;
1080 and
1081 (iii) bear a statement limiting the time frame in which the container may be used once it has been
1082 entered, provided it is held under the labeled storage conditions.
1083

1084 **(10)** ~~[(9)]~~ Written drug information for prescription drug orders only. Written information about the
1085 compounded preparation or its major active ingredient(s) shall be given to the patient at the time of
1086 dispensing a prescription drug order. A statement which indicates that the preparation was
1087 compounded by the pharmacy must be included in this written information. If there is no written
1088 information available, the patient shall be advised that the drug has been compounded and how to
1089 contact a pharmacist, and if appropriate, the prescriber, concerning the drug.
1090

1091 **(11)** ~~[(40)]~~ Pharmaceutical Care Services. In addition to the pharmaceutical care requirements for the
1092 pharmacy's specific license classification, the following requirements for sterile preparations
1093 compounded pursuant to prescription drug orders must be met.

1094 (A) Primary provider. There shall be a designated physician primarily responsible for the patient's
1095 medical care. There shall be a clear understanding between the physician, the patient, and the
1096 pharmacy of the responsibilities of each in the areas of the delivery of care, and the monitoring of the
1097 patient. This shall be documented in the patient medication record (PMR).

1098 (B) Patient training. The pharmacist-in-charge shall develop policies to ensure that the patient and/or
1099 patient's caregiver receives information regarding drugs and their safe and appropriate use, including
1100 instruction when applicable, regarding:

1101 (i) appropriate disposition of hazardous solutions and ancillary supplies;
1102 (ii) proper disposition of controlled substances in the home;
1103 (iii) self-administration of drugs, where appropriate;
1104 (iv) emergency procedures, including how to contact an appropriate individual in the event of
1105 problems or emergencies related to drug therapy; and
1106 (v) if the patient or patient's caregiver prepares sterile preparations in the home, the following
1107 additional information shall be provided:

1108 (I) safeguards against microbial contamination, including aseptic techniques for compounding
1109 intravenous admixtures and aseptic techniques for injecting additives to premixed intravenous
1110 solutions;

1111 (II) appropriate storage methods, including storage durations for sterile pharmaceuticals and
1112 expirations of self-mixed solutions;

1113 (III) handling and disposition of premixed and self-mixed intravenous admixtures; and

1114 (IV) proper disposition of intravenous admixture compounding supplies such as syringes, vials,
1115 ampules, and intravenous solution containers.

1116 (C) Pharmacist-patient relationship. It is imperative that a pharmacist-patient relationship be
1117 established and maintained throughout the patient's course of therapy. This shall be documented in the
1118 patient's medication record (PMR).

1119 (D) Patient monitoring. The pharmacist-in-charge shall develop policies to ensure that:

- 1120 (i) the patient's response to drug therapy is monitored and conveyed to the appropriate health care
1121 provider;
- 1122 (ii) the first dose of any new drug therapy is administered in the presence of an individual qualified
1123 to monitor for and respond to adverse drug reactions; and
- 1124 (iii) reports of adverse events with a compounded sterile preparation are reviewed promptly and
1125 thoroughly to correct and prevent future occurrences.

1126

1127 **(12)** ~~[(11)]~~ Drugs, components, and materials used in sterile compounding.

1128 (A) Drugs used in sterile compounding shall be a USP/NF grade substances manufactured in an
1129 FDA-registered facility.

1130 (B) If USP/NF grade substances are not available shall be of a chemical grade in one of the following
1131 categories:

- 1132 (i) Chemically Pure (CP);
1133 (ii) Analytical Reagent (AR);
1134 (iii) American Chemical Society (ACS); or
1135 (iv) Food Chemical Codex.

1136 (C) If a drug, component or material is not purchased from a FDA-registered facility, the pharmacist
1137 shall establish purity and stability by obtaining a Certificate of Analysis from the supplier and the
1138 pharmacist shall compare the monograph of drugs in a similar class to the Certificate of Analysis.

1139 (D) All components shall:

- 1140 (i) be manufactured in an FDA-registered facility; or
1141 (ii) in the professional judgment of the pharmacist, be of high quality and obtained from acceptable
1142 and reliable alternative sources; and
1143 (iii) stored in properly labeled containers in a clean, dry area, under proper temperatures.

1144 (E) Drug preparation containers and closures shall not be reactive, additive, or absorptive so as to
1145 alter the safety, identity, strength, quality, or purity of the compounded drug preparation beyond the
1146 desired result.

1147 (F) Components, drug preparation containers, and closures shall be rotated so that the oldest stock
1148 is used first.

1149 (G) Container closure systems shall provide adequate protection against foreseeable external factors
1150 in storage and use that can cause deterioration or contamination of the compounded drug preparation.

1151 (H) A pharmacy may not compound a preparation that contains ingredients appearing on a federal
1152 Food and Drug Administration list of drug products withdrawn or removed from the market for safety
1153 reasons.

1154

1155 **(13)** ~~[(12)]~~ Compounding process.

1156 (A) Standard operating procedures (SOPs). All significant procedures performed in the compounding
1157 area shall be covered by written SOPs designed to ensure accountability, accuracy, quality, safety, and
1158 uniformity in the compounding process. At a minimum, SOPs shall be developed and implemented for:

- 1159 (i) the facility;
1160 (ii) equipment;
1161 (iii) personnel;
1162 (iv) preparation evaluation;
1163 (v) quality assurance;
1164 (vi) preparation recall;
1165 (vii) packaging; and
1166 (viii) storage of compounded sterile preparations.

1167 (B) USP/NF. Any compounded formulation with an official monograph in the USP/NF shall be
1168 compounded, labeled, and packaged in conformity with the USP/NF monograph for the drug.

1169 (C) Personnel Cleansing and Garbing.

1170 (i) Any person with an apparent illness or open lesion, including rashes, sunburn, weeping sores,
1171 conjunctivitis, and active respiratory infection, that may adversely affect the safety or quality of a drug
1172 preparation being compounded shall be excluded from working in ISO Class 5 and ISO Class 7
1173 compounding areas until the condition is remedied.

1174 (ii) Before entering the buffer area, compounding personnel must remove the following:

1175 (I) personal outer garments (e.g., bandanas, coats, hats, jackets, scarves, sweaters, vests);

1176 (II) all cosmetics, because they shed flakes and particles; and

1177 (III) all hand, wrist, and other body jewelry or piercings (e.g., earrings, lip or eyebrow piercings)
1178 that can interfere with the effectiveness of personal protective equipment (e.g., fit of gloves and cuffs of
1179 sleeves).

1180 (iii) The wearing of artificial nails or extenders is prohibited while working in the sterile compounding
1181 environment. Natural nails shall be kept neat and trimmed.

1182 (iv) Personnel shall don personal protective equipment and perform hand hygiene in an order that
1183 proceeds from the dirtiest to the cleanest activities as follows:

1184 (I) Activities considered the dirtiest include donning of dedicated shoes or shoe covers, head and
1185 facial hair covers (e.g., beard covers in addition to face masks), and face mask/eye shield. Eye shields
1186 are optional unless working with irritants like germicidal disinfecting agents or when preparing
1187 hazardous drugs.

1188 (II) After donning dedicated shoes or shoe covers, head and facial hair covers, and face masks,
1189 personnel shall perform a hand hygiene procedure by removing debris from underneath fingernails
1190 using a nail cleaner under running warm water followed by vigorous hand washing. Personnel shall
1191 begin washing arms at the hands and continue washing to elbows for at least 30 seconds with either a
1192 plain (non-antimicrobial) soap, or antimicrobial soap, and water while in the ante-area. Hands and
1193 forearms to the elbows shall be completely dried using lint-free disposable towels. [~~an electronic hands-
1194 free hand dryer, or a HEPA filtered hands dryer.~~]

1195 (III) After completion of hand washing, personnel shall don clean non-shedding gowns with
1196 sleeves that fit snugly around the wrists and enclosed at the neck.

1197 (IV) Once inside the buffer area or segregated compounding area, and prior to donning sterile
1198 powder-free gloves, antiseptic hand cleansing shall be performed using a **sterile IPA 70%** [~~waterless
1199 alcohol~~]-based surgical hand scrub with persistent activity following manufacturers' recommendations.
1200 Hands shall be allowed to dry thoroughly before donning sterile gloves.

1201 (V) Sterile gloves that form a continuous barrier with the gown shall be the last item donned before
1202 compounding begins. **Sterile gloves shall be donned using proper technique to ensure the
1203 sterility of the glove is not compromised while donning. The cuff of the sterile glove shall cover
1204 the cuff of the gown at the wrist. When preparing hazardous preparations, the compounder
1205 shall double glove ensuring that the outer gloves are sterile powder-free chemotherapy-rated
1206 gloves.** Routine application of sterile 70% IPA shall occur throughout the compounding day and
1207 whenever non-sterile surfaces are touched.

1208 (v) When compounding personnel shall temporarily exit the ISO Class 7 environment during a work
1209 shift, the exterior gown, if not visibly soiled, may be removed and retained in the ISO Class 8 ante-area,
1210 to be re-donned during that same work shift only. However, shoe covers, hair and facial hair covers,
1211 face mask/eye shield, and gloves shall be replaced with new ones before re-entering the ISO Class 7
1212 clean environment along with performing proper hand hygiene.

1213 (vi) During high-risk compounding activities that precede terminal sterilization, such as weighing
1214 and mixing of non-sterile ingredients, compounding personnel shall be garbed and gloved the same as
1215 when performing compounding in an ISO Class 5 environment. Properly garbed and gloved
1216 compounding personnel who are exposed to air quality that is either known or suspected to be worse
1217 than ISO Class 7 shall re-garb personal protective equipment along with washing their hands properly,
1218 performing antiseptic hand cleansing with a **sterile IPA 70% [waterless alcohol]** based surgical hand
1219 scrub, and donning sterile gloves upon re-entering the ISO Class 7 buffer area.

1220 (vii) When compounding aseptic isolators or compounding aseptic containment isolators are the
1221 source of the ISO Class 5 environment, **at the start of each new compounding procedure, a new**
1222 **pair of sterile gloves shall be donned within the CAI or CACI. In addition,** the compounding
1223 personnel should follow the requirements as specified in this subparagraph, unless the isolator
1224 manufacturer can provide written documentation based on validated environmental testing that any
1225 components of personal protective equipment or cleansing are not required.

1226
1227 **(14)** [(13)] Quality Assurance.
1228 (A) Initial Formula Validation. Prior to routine compounding of a sterile preparation, a pharmacy shall
1229 conduct an evaluation that shows that the pharmacy is capable of compounding a preparation that is
1230 sterile and that contains the stated amount of active ingredient(s).

1231 (i) Low risk preparations.

1232 (I) Quality assurance practices include, but are not limited to the following:

1233 (-a-) Routine disinfection and air quality testing of the direct compounding environment to
1234 minimize microbial surface contamination and maintain ISO Class 5 air quality.

1235 (-b-) Visual confirmation that compounding personnel are properly donning and wearing
1236 appropriate items and types of protective garments and goggles.

1237 (-c-) Review of all orders and packages of ingredients to ensure that the correct identity and
1238 amounts of ingredients were compounded.

1239 (-d-) Visual inspection of compounded sterile preparations to ensure the absence of particulate
1240 matter in solutions, the absence of leakage from vials and bags, and the accuracy and thoroughness of
1241 labeling.

1242 (II) Example of a Media-Fill Test Procedure. This, or an equivalent test, is performed at least
1243 annually by each person authorized to compound in a low-risk level under conditions that closely
1244 simulate the most challenging or stressful conditions encountered during compounding of low-risk level
1245 sterile preparations. Once begun, this test is completed without interruption within an ISO Class 5 air
1246 quality environment. Three sets of four 5-milliliter aliquots of sterile Soybean-Casein Digest Medium are
1247 transferred with the same sterile 10-milliliter syringe and vented needle combination into separate
1248 sealed, empty, sterile 30-milliliter clear vials (i.e., four 5-milliliter aliquots into each of three 30-milliliter
1249 vials). Sterile adhesive seals are aseptically affixed to the rubber closures on the three filled vials. The
1250 vials are incubated within a range of 20 - 35 degrees Celsius for a minimum of 14 days. Failure is
1251 indicated by visible turbidity in the medium on or before 14 days. The media-fill test must include a
1252 positive-control sample.

1253 (ii) Medium risk preparations.

1254 (I) Quality assurance procedures for medium-risk level compounded sterile preparations include all
1255 those for low-risk level compounded sterile preparations, as well as a more challenging media-fill test
1256 passed annually, or more frequently.

1257 (II) Example of a Media-Fill Test Procedure. This, or an equivalent test, is performed at least
1258 annually under conditions that closely simulate the most challenging or stressful conditions
1259 encountered during compounding. This test is completed without interruption within an ISO Class 5 air

1260 quality environment. Six 100-milliliter aliquots of sterile Soybean-Casein Digest Medium are aseptically
1261 transferred by gravity through separate tubing sets into separate evacuated sterile containers. The six
1262 containers are then arranged as three pairs, and a sterile 10-milliliter syringe and 18-gauge needle
1263 combination is used to exchange two 5-milliliter aliquots of medium from one container to the other
1264 container in the pair. For example, after a 5-milliliter aliquot from the first container is added to the
1265 second container in the pair, the second container is agitated for 10 seconds, then a 5-milliliter aliquot
1266 is removed and returned to the first container in the pair. The first container is then agitated for 10
1267 seconds, and the next 5-milliliter aliquot is transferred from it back to the second container in the pair.
1268 Following the two 5-milliliter aliquot exchanges in each pair of containers, a 5-milliliter aliquot of medium
1269 from each container is aseptically injected into a sealed, empty, sterile 10-milliliter clear vial, using a
1270 sterile 10-milliliter syringe and vented needle. Sterile adhesive seals are aseptically affixed to the
1271 rubber closures on the three filled vials. The vials are incubated within a range of 20 - 35 degrees
1272 Celsius for a minimum of 14 days. Failure is indicated by visible turbidity in the medium on or before 14
1273 days. The media-fill test must include a positive-control sample.

1274 (iii) High risk preparations.

1275 (I) Procedures for high-risk level compounded sterile preparations include all those for low-risk
1276 level compounded sterile preparations. In addition, a media-fill test that represents high-risk level
1277 compounding is performed twice a year by each person authorized to compound high-risk level
1278 compounded sterile preparations.

1279 (II) Example of a Media-Fill Test Procedure Compounded Sterile Preparations Sterilized by
1280 Filtration. This test, or an equivalent test, is performed under conditions that closely simulate the most
1281 challenging or stressful conditions encountered when compounding high-risk level compounded sterile
1282 preparations. Note: Sterility tests for autoclaved compounded sterile preparations are not required
1283 unless they are prepared in batches of more than 25 units. This test is completed without interruption in
1284 the following sequence:

1285 (-a-) Dissolve 3 grams of non-sterile commercially available Soybean-Casein Digest Medium in
1286 100 milliliters of non-bacteriostatic water to make a 3% non-sterile solution.

1287 (-b-) Draw 25 milliliters of the medium into each of three 30-milliliter sterile syringes. Transfer 5
1288 milliliters from each syringe into separate sterile 10-milliliter vials. These vials are the positive controls
1289 to generate exponential microbial growth, which is indicated by visible turbidity upon incubation.

1290 (-c-) Under aseptic conditions and using aseptic techniques, affix a sterile 0.2-micron porosity
1291 filter unit and a 20-gauge needle to each syringe. Inject the next 10 milliliters from each syringe into
1292 three separate 10-milliliter sterile vials. Repeat the process for three more vials. Label all vials, affix
1293 sterile adhesive seals to the closure of the nine vials, and incubate them at 20 to 35 degrees Celsius for
1294 a minimum of 14 days. Inspect for microbial growth over 14 days as described in Chapter 797
1295 Pharmaceutical Compounding--Sterile Preparations, of the USP/NF.

1296 **(III) Bubble Point Testing. Bubble point testing is an evaluation of the integrity of the**
1297 **filter(s) used to sterilize high-risk preparations. Bubble point testing is not a replacement**
1298 **sterility testing and shall not be interpreted as such. A bubble point test shall be performed**
1299 **after a sterilization procedure on all filters used to sterilize each high-risk preparation or batch**
1300 **preparation and the results documented. The results should be compared with the filter**
1301 **manufacturers bubble point pressure for the specific filter used (typically between 50 and 54**
1302 **psig). If a filter fails the bubble point test, the preparation or batch must be sterilized again**
1303 **using new unused filters.**

1304 (B) Finished preparation release checks and tests.

1305 (i) All high-risk level compounded sterile preparations that are prepared in groups of more than 25
1306 identical individual single-dose packages (such as ampuls, bags, syringes, and vials), or in multiple

1307 dose vials for administration to multiple patients, or are exposed longer than 12 hours at 2 - 8 degrees
1308 Celsius and longer than six hours at warmer than 8 degrees Celsius before they are sterilized shall be
1309 tested to ensure they are sterile and do not contain excessive bacterial endotoxins as specified in
1310 Chapter 71, Sterility Tests of the USP/NF before being dispensed or administered.

1311 (ii) All compounded sterile preparations that are intended to be solutions must be visually examined
1312 for the presence of particulate matter and not administered or dispensed when such matter is observed.

1313 (iii) The prescription drug and medication orders, written compounding procedure, preparation
1314 records, and expended materials used to make compounded sterile preparations at all contamination
1315 risk levels shall be inspected for accuracy of correct identities and amounts of ingredients, aseptic
1316 mixing and sterilization, packaging, labeling, and expected physical appearance before they are
1317 dispensed or administered.

1318 **(iv) Written procedures for double-checking compounding accuracy shall be followed for**
1319 **every compounded sterile preparation during preparation and immediately prior to release,**
1320 **including label accuracy and the accuracy of the addition of all drug products or ingredients**
1321 **used to prepare the finished preparation and their volumes or quantities. A pharmacist shall**
1322 **ensure that components used in compounding are accurately weighed, measured, or**
1323 **subdivided as appropriate to conform to the formula being prepared.**

1324 **(C) Environmental Testing**

1325 (i) ~~(C)~~ Viable and nonviable environmental sampling testing. Environmental sampling shall occur,
1326 at a minimum, every six months as part of a comprehensive quality management program and under
1327 any of the following conditions:

1328 (I) ~~(i)~~ as part of the commissioning and certification of new facilities and equipment;

1329 (II) ~~(ii)~~ following any servicing of facilities and equipment;

1330 (III) ~~(iii)~~ as part of the re-certification of facilities and equipment;

1331 (IV) ~~(iv)~~ in response to identified problems with end products or staff technique; or

1332 (V) ~~(v)~~ in response to issues with compounded sterile preparations, observed compounding
1333 personnel work practices, or patient-related infections (where the compounded sterile preparation is
1334 being considered as a potential source of the infection).

1335 (ii) ~~(D)~~ Total particle counts. Certification that each ISO classified area (e.g., ISO Class 5, 7, and
1336 8), is within established guidelines shall be performed no less than every six months and whenever the
1337 equipment is relocated or the physical structure of the buffer area or ante-area has been altered. All
1338 certification records shall be maintained and reviewed to ensure that the controlled environments
1339 comply with the proper air cleanliness, room pressures, and air changes per hour. Testing shall be
1340 performed by qualified operators using current, state-of-the-art equipment, with results of the following:

1341 (I) ~~(i)~~ ISO Class 5 - not more than 3520 particles 0.5 **micrometer** [μm] and larger size per cubic
1342 meter of air;

1343 (II) ~~(ii)~~ ISO Class 7 - not more than 352,000 particles of 0.5 **micrometer** [μm] and larger size per
1344 cubic meter of air for any buffer area; and

1345 (III) ~~(iii)~~ ISO Class 8 - not more than 3,520,000 particles of 0.5 **micrometer** [μm] and larger size per
1346 cubic meter of air for any ante-area.

1347 (iii) ~~(E)~~ Pressure differential monitoring. A pressure gauge or velocity meter shall be installed to
1348 monitor the pressure differential or airflow between the buffer area and the ante-area and between the
1349 ante-area and the general environment outside the compounding area. The results shall be reviewed
1350 and documented on a log at least every work shift (minimum frequency shall be at least daily) or by a
1351 continuous recording device. The pressure between the ISO Class 7 and the general pharmacy area
1352 shall not be less than 0.02 inch water column.

1353 **(iv)** ~~(F)~~ Sampling plan. An appropriate environmental sampling plan shall be developed for airborne
1354 viable particles based on a risk assessment of compounding activities performed. Selected sampling
1355 sites shall include locations within each ISO Class 5 environment and in the ISO Class 7 and 8 areas
1356 and in the segregated compounding areas at greatest risk of contamination. The plan shall include
1357 sample location, method of collection, frequency of sampling, volume of air sampled, and time of day as
1358 related to activity in the compounding area and action levels.

1359 **(v)** ~~(G)~~ Viable air sampling. Evaluation of airborne microorganisms using volumetric collection
1360 methods in the controlled air environments shall be performed by properly trained individuals for all
1361 compounding risk levels. For low-, medium-, and high-risk level compounding, air sampling shall be
1362 performed at locations that are prone to contamination during compounding activities and during other
1363 activities such as staging, labeling, gowning, and cleaning. Locations shall include zones of air
1364 backwash turbulence within the laminar airflow workbench and other areas where air backwash
1365 turbulence may enter the compounding area. For low-risk level compounded sterile preparations within
1366 12-hour or less beyond-use-date prepared in a primary engineering control that maintains an ISO Class
1367 5, air sampling shall be performed at locations inside the ISO Class 5 environment and other areas that
1368 are in close proximity to the ISO Class 5 environment during the certification of the primary engineering
1369 control.

1370 **(vi)** ~~(H)~~ Air sampling frequency and process. Air sampling shall be performed at least every 6
1371 months as a part of the re-certification of facilities and equipment. A sufficient volume of air shall be
1372 sampled and the manufacturer's guidelines for use of the electronic air sampling equipment followed. At
1373 the end of the designated sampling or exposure period for air sampling activities, the microbial growth
1374 media plates are recovered and their covers secured and they are inverted and incubated at a
1375 temperature and for a time period conducive to multiplication of microorganisms. Sampling data shall
1376 be collected and reviewed on a periodic basis as a means of evaluating the overall control of the
1377 compounding environment. If an activity consistently shows elevated levels of microbial growth,
1378 competent microbiology personnel shall be consulted.

1379 **(vii)** ~~(I)~~ Compounding accuracy checks. Written procedures for double-checking compounding
1380 accuracy shall be followed for every compounded sterile preparation during preparation and
1381 immediately prior to release, including label accuracy and the accuracy of the addition of all drug
1382 products or ingredients used to prepare the finished preparation and their volumes or quantities. At
1383 each step of the compounding process, the pharmacist shall ensure that components used in
1384 compounding are accurately weighed, measured, or subdivided as appropriate to conform to the
1385 formula being prepared.

1386
1387 **(15)** ~~(14)~~ Quality control.
1388 (A) Quality control procedures. The pharmacy shall follow established quality control procedures to
1389 monitor the compounding environment and quality of compounded drug preparations for conformity
1390 with the quality indicators established for the preparation. When developing these procedures,
1391 pharmacy personnel shall consider the provisions of USP Chapter 71, Sterility Tests, USP Chapter 85,
1392 Bacterial Endotoxins Test, Pharmaceutical Compounding-Non-sterile Preparations, USP Chapter 795,
1393 USP Chapter 797, Pharmaceutical Compounding--Sterile Preparations, Chapter 1075, Good
1394 Compounding Practices, and Chapter 1160, Pharmaceutical Calculations in Prescription Compounding,
1395 and USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding of the current USP/NF.
1396 Such procedures shall be documented and be available for inspection.

1397 (B) Verification of compounding accuracy and sterility.
1398 (i) The accuracy of identities, concentrations, amounts, and purities of ingredients in compounded
1399 sterile preparations shall be confirmed by reviewing labels on packages, observing and documenting

1400 correct measurements with approved and correctly standardized devices, and reviewing information in
1401 labeling and certificates of analysis provided by suppliers.

1402 (ii) If the correct identity, purity, strength, and sterility of ingredients and components of
1403 compounded sterile preparations cannot be confirmed such ingredients and components shall be
1404 discarded immediately. **Any compounded sterile preparation that fails sterility testing following**
1405 **sterilization by one method (e.g., filtration) is to be discarded and not subjected to a second**
1406 **method of sterilization.**

1407 (iii) If individual ingredients, such as bulk drug substances, are not labeled with expiration dates,
1408 when the drug substances are stable indefinitely in their commercial packages under labeled storage
1409 conditions, such ingredients may gain or lose moisture during storage and use and shall require testing
1410 to determine the correct amount to weigh for accurate content of active chemical moieties in
1411 compounded sterile preparations.

1412
1413 (e) Records. Any testing, cleaning, procedures, or other activities required in this subsection shall be
1414 documented and such documentation shall be maintained by the pharmacy.

1415 (1) Maintenance of records. Every record required under this section must be:

1416 (A) kept by the pharmacy and be available, for at least two years for inspecting and copying by the
1417 board or its representative and to other authorized local, state, or federal law enforcement agencies;
1418 and

1419 (B) supplied by the pharmacy within 72 hours, if requested by an authorized agent of the Texas State
1420 Board of Pharmacy. If the pharmacy maintains the records in an electronic format, the requested
1421 records must be provided in an electronic format. Failure to provide the records set out in this section,
1422 either on site or within 72 hours, constitutes prima facie evidence of failure to keep and maintain
1423 records in violation of the Act.

1424 (2) Compounding records.

1425 (A) Compounding pursuant to patient specific prescription drug orders. Compounding records for all
1426 compounded preparations shall be maintained by the pharmacy electronically or manually as part of the
1427 prescription drug or medication order, formula record, formula book, or compounding log and shall
1428 include:

1429 (i) the date of preparation;

1430 (ii) a complete formula, including methodology and necessary equipment which includes the brand
1431 name(s) of the raw materials, or if no brand name, the generic name(s) or official name and name(s) of
1432 the manufacturer(s) or distributor of the raw materials and the quantities of each;

1433 (iii) signature or initials of the pharmacist or pharmacy technician or pharmacy technician trainee
1434 performing the compounding;

1435 (iv) signature or initials of the pharmacist responsible for supervising pharmacy technicians or
1436 pharmacy technician trainees and conducting in-process and finals checks of compounded
1437 pharmaceuticals if pharmacy technicians or pharmacy technician trainees perform the compounding
1438 function;

1439 (v) the quantity in units of finished preparation or amount of raw materials;

1440 (vi) the container used and the number of units prepared; and

1441 (vii) a reference to the location of the following documentation which may be maintained with other
1442 records, such as quality control records:

1443 (I) the criteria used to determine the beyond-use date; and

1444 (II) documentation of performance of quality control procedures.

1445 (B) Compounding records when batch compounding or compounding in anticipation of future
1446 prescription drug or medication orders.

1447 (i) Master work sheet. A master work sheet shall be developed and approved by a pharmacist for
1448 preparations prepared in batch. Once approved, a duplicate of the master work sheet shall be used as
1449 the preparation work sheet from which each batch is prepared and on which all documentation for that
1450 batch occurs. The master work sheet shall contain at a minimum:

- 1451 (I) the formula;
- 1452 (II) the components;
- 1453 (III) the compounding directions;
- 1454 (IV) a sample label;
- 1455 (V) evaluation and testing requirements;
- 1456 (VI) specific equipment used during preparation; and
- 1457 (VII) storage requirements.

1458 (ii) Preparation work sheet. The preparation work sheet for each batch of preparations shall
1459 document the following:

- 1460 (I) identity of all solutions and ingredients and their corresponding amounts, concentrations, or
1461 volumes;
- 1462 (II) lot number for each component;
- 1463 (III) component manufacturer/distributor or suitable identifying number;
- 1464 (IV) container specifications (e.g., syringe, pump cassette);
- 1465 (V) unique lot or control number assigned to batch;
- 1466 (VI) expiration date of batch-prepared preparations;
- 1467 (VII) date of preparation;
- 1468 (VIII) name, initials, or electronic signature of the person(s) involved in the preparation;
- 1469 (IX) name, initials, or electronic signature of the responsible pharmacist;
- 1470 (X) finished preparation evaluation and testing specifications, if applicable; and
- 1471 (XI) comparison of actual yield to anticipated or theoretical yield, when appropriate.

1472

1473 (f) Office Use Compounding and Distribution of Sterile Compounded Preparations

1474 (1) General.

1475 (A) A pharmacy may compound, dispense, deliver, and distribute a compounded sterile preparation
1476 as specified in Subchapter D, Texas Pharmacy Act Chapter 562.

1477 (B) A Class A-S pharmacy is not required to register or be licensed under Chapter 431, Health and
1478 Safety Code, to distribute sterile compounded preparations to a Class C or Class C-S pharmacy.

1479 (C) A Class C-S pharmacy is not required to register or be licensed under Chapter 431, Health and
1480 Safety Code, to distribute sterile compounded preparations that the Class C-S pharmacy has
1481 compounded for other Class C or Class C-S pharmacies under common ownership.

1482 (D) To compound and deliver a compounded preparation under this subsection, a pharmacy must:

- 1483 (i) verify the source of the raw materials to be used in a compounded drug;
- 1484 (ii) comply with applicable United States Pharmacopoeia guidelines, including the testing
1485 requirements, and the Health Insurance Portability and Accountability Act of 1996 (Pub. L. No. 104-
1486 191);
- 1487 (iii) enter into a written agreement with a practitioner for the practitioner's office use of a
1488 compounded preparation;
- 1489 (iv) comply with all applicable competency and accrediting standards as determined by the board;
1490 and
- 1491 (v) comply with the provisions of this subsection.

1492 (2) Written Agreement. A pharmacy that provides sterile compounded preparations to practitioners for
1493 office use or to another pharmacy shall enter into a written agreement with the practitioner or
1494 pharmacy. The written agreement shall:

1495 (A) address acceptable standards of practice for a compounding pharmacy and a practitioner and
1496 receiving pharmacy that enter into the agreement including a statement that the compounded drugs
1497 may only be administered to the patient and may not be dispensed to the patient or sold to any other
1498 person or entity except to a veterinarian as authorized by §563.054 of the Act;

1499 (B) require the practitioner or receiving pharmacy to include on a patient's chart, medication order or
1500 medication administration record the lot number and beyond-use date of a compounded preparation
1501 administered to a patient;

1502 (C) describe the scope of services to be performed by the pharmacy and practitioner or receiving
1503 pharmacy, including a statement of the process for:

1504 (i) a patient to report an adverse reaction or submit a complaint; and
1505 (ii) the pharmacy to recall batches of compounded preparations.

1506 (3) Recordkeeping.

1507 (A) Maintenance of Records.

1508 (i) Records of orders and distribution of sterile compounded preparations to a practitioner for office
1509 use or to an institutional pharmacy for administration to a patient shall:

1510 (I) be kept by the pharmacy and be available, for at least two years from the date of the record, for
1511 inspecting and copying by the board or its representative and to other authorized local, state, or federal
1512 law enforcement agencies;

1513 (II) maintained separately from the records of preparations dispensed pursuant to a prescription or
1514 medication order; and

1515 (III) supplied by the pharmacy within 72 hours, if requested by an authorized agent of the Texas
1516 State Board of Pharmacy or its representative. If the pharmacy maintains the records in an electronic
1517 format, the requested records must be provided in an electronic format. Failure to provide the records
1518 set out in this subsection, either on site or within 72 hours for whatever reason, constitutes prima facie
1519 evidence of failure to keep and maintain records.

1520 (ii) Records may be maintained in an alternative data retention system, such as a data processing
1521 system or direct imaging system provided the data processing system is capable of producing a hard
1522 copy of the record upon the request of the board, its representative, or other authorized local, state, or
1523 federal law enforcement or regulatory agencies.

1524 (B) Orders. The pharmacy shall maintain a record of all sterile compounded preparations ordered by
1525 a practitioner for office use or by an institutional pharmacy for administration to a patient. The record
1526 shall include the following information:

1527 (i) date of the order;

1528 (ii) name, address, and phone number of the practitioner who ordered the preparation and if
1529 applicable, the name, address and phone number of the institutional pharmacy ordering the
1530 preparation; and

1531 (iii) name, strength, and quantity of the preparation ordered.

1532 (C) Distributions. The pharmacy shall maintain a record of all sterile compounded preparations
1533 distributed pursuant to an order to a practitioner for office use or by an institutional pharmacy for
1534 administration to a patient. The record shall include the following information:

1535 (i) date the preparation was compounded;

1536 (ii) date the preparation was distributed;

1537 (iii) name, strength and quantity in each container of the preparation;

1538 (iv) pharmacy's lot number;

1539 (v) quantity of containers shipped; and
1540 (vi) name, address, and phone number of the practitioner or institutional pharmacy to whom the
1541 preparation is distributed.

1542 (D) Audit Trail.

1543 (i) The pharmacy shall store the order and distribution records of preparations for all sterile
1544 compounded preparations ordered by and or distributed to a practitioner for office use or by a
1545 pharmacy licensed to compound sterile preparations for administration to a patient in such a manner as
1546 to be able to provide an audit trail for all orders and distributions of any of the following during a
1547 specified time period:

1548 (I) any strength and dosage form of a preparation (by either brand or generic name or both);
1549 (II) any ingredient;
1550 (III) any lot number;
1551 (IV) any practitioner;
1552 (V) any facility; and
1553 (VI) any pharmacy, if applicable.

1554 (ii) The audit trail shall contain the following information:

1555 (I) date of order and date of the distribution;
1556 (II) practitioner's name, address, and name of the institutional pharmacy, if applicable;
1557 (III) name, strength and quantity of the preparation in each container of the preparation;
1558 (IV) name and quantity of each active ingredient;
1559 (V) quantity of containers distributed; and
1560 (VI) pharmacy's lot number.

1561 (4) Labeling. The pharmacy shall affix a label to the preparation containing the following information:

1562 (A) name, address, and phone number of the compounding pharmacy;
1563 (B) the statement: "For Institutional or Office Use Only--Not for Resale"; or if the preparation is
1564 distributed to a veterinarian the statement: "Compounded Preparation";
1565 (C) name and strength of the preparation or list of the active ingredients and strengths;
1566 (D) pharmacy's lot number;
1567 (E) beyond-use date as determined by the pharmacist using appropriate documented criteria;
1568 (F) quantity or amount in the container;
1569 (G) appropriate ancillary instructions, such as storage instructions or cautionary statements,
1570 including hazardous drug warning labels where appropriate; and
1571 (H) device-specific instructions, where appropriate.

1572 (g) Recall Procedures.

1573 (1) The pharmacy shall have written procedures for the recall of any compounded sterile preparation
1574 provided to a patient, to a practitioner for office use, or a pharmacy for administration. Written
1575 procedures shall include, but not be limited to the requirements as specified in paragraph (3) of this
1576 subsection.

1577 (2) The pharmacy shall immediately initiate a recall of any sterile preparation compounded by the
1578 pharmacy upon identification of a potential or confirmed harm to a patient.

1579 (3) In the event of a recall, the pharmacist-in-charge shall ensure that:

1580 (A) each practitioner, facility, and/or pharmacy to which the preparation was distributed is notified, in
1581 writing, of the recall;
1582 (B) each patient to whom the preparation was dispensed is notified, in writing, of the recall;
1583 (C) the board is notified of the recall, in writing, not later than 24 hours after the recall is issued;
1584 (D) if the preparation is distributed for office use, the Texas Department of State Health Services,
1585 Drugs and Medical Devices Group, is notified of the recall, in writing;

1586 (E) the preparation is quarantined; and

1587 (F) the pharmacy keeps a written record of the recall including all actions taken to notify all parties
1588 and steps taken to ensure corrective measures.

1589 (4) If a pharmacy fails to initiate a recall, the board may require a pharmacy to initiate a recall if there
1590 is potential for or confirmed harm to a patient.

1591 (5) A pharmacy that compounds sterile preparations shall notify the board immediately of any adverse
1592 effects reported to the pharmacy or that are known by the pharmacy to be potentially attributable to a
1593 sterile preparation compounded by the pharmacy.

1594