

RULE ANALYSIS

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

Short Title: Nuclear Pharmacies Preparing Sterile Radiopharmaceuticals

Rule Numbers: §§291.51 – 291.54, 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 rules for nuclear pharmacies compounding sterile radiopharmaceuticals.

1 **TITLE 22 EXAMINING BOARDS**
2 **PART 15 TEXAS STATE BOARD OF PHARMACY**
3 **CHAPTER 291 PHARMACIES**
4 **SUBCHAPTER C NUCLEAR PHARMACY (CLASS B)**

5
6 **§291.51 Purpose**
7

8 The purpose of this subchapter is to provide standards for the preparation, labeling, and
9 distribution of [~~compounded~~] radiopharmaceuticals by licensed nuclear pharmacies, pursuant to
10 a radioactive prescription drug order. The intent of this subchapter is to establish a minimum
11 acceptable level of pharmaceutical care to the patient so that the patient's health is protected
12 while contributing to positive patient outcomes. The board has determined that this subchapter
13 is necessary to protect the health and welfare of the citizens of this state.
14

15 **§291.52 Definitions**
16

17 The following words and terms, when used in this subchapter, shall have the following
18 meanings, unless the context clearly indicates otherwise. Any term not defined in this section
19 shall have the definition set forth in the Act, §551.003.
20

21 (1) Act--The Texas Pharmacy Act, Chapters 551 [~~566 and 568~~] - 569, Occupations Code, as
22 amended.
23

24 (2) Accurately as prescribed--Dispensing, delivering, and/or distributing a prescription drug
25 order or radioactive prescription drug order:
26

27 (A) to the correct patient (or agent of the patient) for whom the drug or device was prescribed;
28

29 (B) with the correct drug in the correct strength, quantity, and dosage form ordered by the
30 practitioner; and
31

32 (C) with correct labeling (including directions for use) as ordered by the practitioner. Provided,
33 however, that nothing herein shall prohibit pharmacist substitution if substitution is conducted in
34 strict accordance with applicable laws and rules, including Subchapter A, Chapter 562 of the
35 Act.
36

37 (3) ACPE--Accreditation Council for Pharmacy Education.
38

39 (4) Administer--The direct application of a prescription drug and/or radiopharmaceutical, by
40 injection, inhalation, ingestion, or any other means to the body of a patient by:
41

42 (A) a practitioner, an authorized agent under his supervision, or other person authorized by
43 law; or
44

45 (B) the patient at the direction of a practitioner.
46

47 (5) [~~Airborne particulate cleanliness class--The level of cleanliness specified by the maximum~~
48 ~~allowable number of particles per cubic meter of air as specified in the International~~
49 ~~Organization of Standardization (ISO) Classification Air Cleanliness (ISO 14644-1). For~~
50 ~~example:~~
51

52 ~~—(A) ISO Class 5 (formerly Class 100) is an atmospheric environment that contains less than~~
53 ~~3,520 particles 0.5 microns in diameter per cubic meter of air (formerly stated as 100 particles~~
54 ~~0.5 microns in diameter per cubic foot of air);~~

55
56 ~~—(B) ISO Class 7 (formerly Class 10,000) is an atmospheric environment that contains less~~
57 ~~than 352,000 particles 0.5 microns in diameter per cubic meter of air (formerly stated as 10,000~~
58 ~~particles 0.5 microns in diameter per cubic foot of air); and~~

59
60 ~~—(C) ISO Class 8 (formerly Class 100,000) is an atmospheric environment that contains less~~
61 ~~than 3,520,000 particles 0.5 microns in diameter per cubic meter of air (formerly stated as~~
62 ~~100,000 particles 0.5 microns in diameter per cubic foot of air).]~~

63
64 ~~[(6) Ancillary supplies--Supplies necessary for the administration of compounded sterile~~
65 ~~radiopharmaceuticals.]~~

66
67 ~~[(7) Aseptic processing--The technique involving procedures designed to preclude~~
68 ~~contamination of drugs, packaging, equipment, or supplies by microorganisms during~~
69 ~~processing.]~~

70
71 ~~[(8)] Authentication of product history--Identifying the purchasing source, the intermediate~~
72 ~~handling, and the ultimate disposition of any component of a radioactive drug.~~

73
74 **(6)** ~~[(9)]~~ Authorized nuclear pharmacist--A pharmacist who:

75
76 (A) has completed the specialized training requirements specified by this subchapter for the
77 preparation and distribution of radiopharmaceuticals; and

78
79 (B) is named on a Texas radioactive material license, issued by the Texas Department of
80 State Health Services, Radiation Control Program.

81
82 **(7)** ~~[(10)]~~ Authorized user--Any individual named on a Texas radioactive material license,
83 issued by the Texas Department of State Health Services, Radiation Control Program.

84
85 ~~[(11) Automated compounding or drug dispensing device--An automated device that~~
86 ~~compounds, measures, counts, packages, and/or labels a specified quantity of dosage units for~~
87 ~~a designated drug product.]~~

88
89 ~~[(12) Biological Safety Cabinet, Class II--A ventilated cabinet for personnel, product, and~~
90 ~~environmental protection having an open front with inward airflow for personnel protection,~~
91 ~~downward HEPA filtered laminar airflow for product protection, and HEPA filtered exhausted air~~
92 ~~for environmental protection.]~~

93
94 **(8)** ~~[(13)]~~ Board--The Texas State Board of Pharmacy.

95
96 ~~[(14) Clean room or controlled area--A room in which the concentration of airborne particles is~~
97 ~~controlled to meet a specified airborne particulate cleanliness class. Microorganisms in the~~
98 ~~environment are monitored so that a microbial level for air, surface, and personnel gear are not~~
99 ~~exceeded for a specified cleanliness class.]~~

100
101 **(9)** ~~[(15)]~~ Component--Any ingredient intended for use in the compounding of a drug
102 preparation, including those that may not appear in such preparation.

103
104 **(10)** ~~[(16)]~~ Compounding--The preparation, mixing, assembling, packaging, or labeling of a drug
105 or device:

106
107 (A) as the result of a practitioner's prescription drug or medication order based on the
108 practitioner-patient-pharmacist relationship in the course of professional practice;

109
110 (B) for administration to a patient by a practitioner as the result of a practitioner's initiative
111 based on the practitioner-patient-pharmacist relationship in the course of professional practice;

112
113 (C) in anticipation of prescription drug or medication orders based on routine, regularly
114 observed prescribing patterns; or

115
116 (D) for or as an incident to research, teaching, or chemical analysis and not for sale or
117 dispensing, except as allowed under §562.154 or Chapter 563 of the Act.

118
119 **(11)** ~~[(17)]~~ Controlled substance--A drug, immediate precursor, or other substance listed in
120 Schedules I - V or Penalty Groups 1-4 of the Texas Controlled Substances Act, as amended, or
121 a drug, immediate precursor, or other substance included in Schedule I, II, III, IV, or V of the
122 Federal Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended (Public
123 Law 91-513).

124
125 ~~[(18) Critical site--Sterile ingredients of compounded sterile preparations and locations on
126 devices and components used to prepare, package, and transfer compounded sterile
127 preparations that provide opportunity for exposure to contamination.]~~

128
129 **(12)** ~~[(19)]~~ Dangerous drug--A drug or device that:

130
131 (A) is not included in Penalty Group 1, 2, 3, or 4, Chapter 481, Health and Safety Code, and
132 is unsafe for self-medication; or

133
134 (B) bears or is required to bear the legend:

135
136 (i) "Caution: federal law prohibits dispensing without prescription" or "Rx only" or another
137 legend that complies with federal law; or

138
139 (ii) "Caution: federal law restricts this drug to use by or on the order of a licensed
140 veterinarian."

141
142 **(13)** ~~[(20)]~~ Data communication device--An electronic device that receives electronic
143 information from one source and transmits or routes it to another (e.g., bridge, router, switch, or
144 gateway).

145
146 **(14)** ~~[(21)]~~ Deliver or delivery--The actual, constructive, or attempted transfer of a prescription
147 drug or device, radiopharmaceutical, or controlled substance from one person to another,
148 whether or not for a consideration.

149
150 **(15)** ~~[(22)]~~ Designated agent--

151
152 (A) an individual, including a licensed nurse, physician assistant, **nuclear medicine**
153 **technologist**, or pharmacist:

154
155 (i) who is designated by a practitioner and authorized to communicate a prescription drug
156 order to a pharmacist; and
157
158 (ii) for whom the practitioner assumes legal responsibility;
159
160 (B) a licensed nurse, physician assistant, or pharmacist employed in a health care facility to
161 whom a practitioner communicates a prescription drug order; or
162
163 (C) a registered nurse or physician assistant authorized by a practitioner to administer a
164 prescription drug order for a dangerous drug under Subchapter B, Chapter 157 (Occupations
165 Code).
166
167 **(16)** ~~[(23)]~~ Device--An instrument, apparatus, implement, machine, contrivance, implant, in vitro
168 reagent, or other similar or related articles, including any component parts or accessory that is
169 required under federal or state law to be ordered or prescribed by a practitioner.
170
171 **(17)** ~~[(24)]~~ Diagnostic prescription drug order--A radioactive prescription drug order issued for a
172 diagnostic purpose.
173
174 **(18)** ~~[(25)]~~ Dispense--Preparing, packaging, compounding, or labeling for delivery a
175 prescription drug or device, or a radiopharmaceutical in the course of professional practice to an
176 ultimate user or his agent by or pursuant to the lawful order of a practitioner.
177
178 **(19)** ~~[(26)]~~ Dispensing pharmacist--The authorized nuclear pharmacist responsible for the final
179 check of the dispensed prescription before delivery to the patient.
180
181 **(20)** ~~[(27)]~~ Distribute--The delivering of a prescription drug or device, or a radiopharmaceutical
182 other than by administering or dispensing.
183
184 **(21)** ~~[(28)]~~ Electronic radioactive prescription drug order--A radioactive prescription drug order
185 which is transmitted by an electronic device to the receiver (pharmacy).
186
187 ~~[(29) Internal test assessment--Validation of tests for quality control necessary to insure the
188 integrity of the test.]~~
189
190 **(22)** ~~[(30)]~~ Nuclear pharmacy technique--The mechanical ability required to perform the
191 nonjudgmental, technical aspects of preparing and dispensing radiopharmaceuticals.
192
193 **(23)** ~~[(34)]~~ Original prescription--The:
194
195 (A) original written radioactive prescription drug orders; or
196
197 (B) original verbal or electronic radioactive prescription drug orders maintained either
198 manually or electronically by the pharmacist.
199
200 **(24)** ~~[(32)]~~ Pharmacist-in-charge--The pharmacist designated on a pharmacy license as the
201 pharmacist who has the authority or responsibility for a pharmacy's compliance with laws and
202 rules pertaining to the practice of pharmacy.
203

204 **(25)** ~~[(33)]~~ Pharmacy technician--An individual whose responsibility in a pharmacy is to provide
205 technical services that do not require professional judgment regarding preparing and distributing
206 drugs and who works under the direct supervision of and is responsible to a pharmacist.

207
208 **(26)** ~~[(34)]~~ Pharmacy technician trainee--An individual who is registered with the board as a
209 pharmacy technician trainee and is authorized to participate in a pharmacy's technician training
210 program.

211
212 ~~[(35) Process validation--Documented evidence providing a high degree of assurance that a
213 specific process will consistently produce a product meeting its predetermined specifications
214 and quality attributes.]~~

215
216 ~~[(36) Quality assurance--The set of activities used to ensure that the process used in the
217 preparation of sterile radiopharmaceuticals lead to preparations that meet predetermined
218 standards of quality.]~~

219
220 **(27)** ~~[(37)]~~ Radiopharmaceutical--A prescription drug or device that exhibits spontaneous
221 disintegration of unstable nuclei with the emission of a nuclear particle(s) or photon(s), including
222 any nonradioactive reagent kit or nuclide generator that is intended to be used in preparation of
223 any such substance.

224
225 ~~[(38) Radioactive drug quality control--The set of testing activities used to determine that the
226 ingredients, components (e.g., containers), and final radiopharmaceutical prepared meets
227 predetermined requirements with respect to identity, purity, non-pyrogenicity, and sterility and
228 the interpretation of the resulting data in order to determine the feasibility for use in humans and
229 animals including internal test assessment, authentication of product history, and the keeping of
230 mandatory records.]~~

231
232 **(28)** ~~[(39)]~~ Radioactive drug service--The act of distributing radiopharmaceuticals; the
233 participation in radiopharmaceutical selection and the performance of radiopharmaceutical drug
234 reviews.

235
236 **(29)** ~~[(40)]~~ Radioactive prescription drug order--An order from a practitioner or a practitioner's
237 designated agent for a radiopharmaceutical to be dispensed.

238
239 **(30)** ~~[(41)]~~ Sterile radiopharmaceutical--A dosage form of a radiopharmaceutical free from
240 living micro-organisms.

241
242 **(31)** ~~[(42)]~~ Therapeutic prescription drug order--A radioactive prescription drug order issued for
243 a specific patient for a therapeutic purpose.

244
245 **(32)** ~~[(43)]~~ Ultimate user--A person who has obtained and possesses a prescription drug or
246 radiopharmaceutical for administration to a patient by a practitioner.

247
248

§291.53 Personnel

249
250
251 (a) Pharmacists-in-Charge.

252
253 (1) General.

254

255 (A) Every nuclear pharmacy shall have an authorized nuclear pharmacist designated on the
256 nuclear pharmacy license as the pharmacist-in-charge who shall be responsible for a nuclear
257 pharmacy's compliance with laws and regulations, both state and federal, pertaining to the
258 practice of nuclear pharmacy.

259
260 (B) The nuclear pharmacy pharmacist-in-charge shall see that directives from the board are
261 communicated to the owner(s), management, other pharmacists, and interns of the nuclear
262 pharmacy.

263
264 (C) Each Class B pharmacy shall have one pharmacist-in-charge who is employed on a full-
265 time basis, who may be the pharmacist-in-charge for only one such pharmacy; provided,
266 however, such pharmacist-in-charge may be the pharmacist-in-charge of:

267
268 (i) more than one Class B pharmacy, if the additional Class B pharmacies are not open to
269 provide pharmacy services simultaneously; or

270
271 (ii) during an emergency, up to two Class B pharmacies open simultaneously if the
272 pharmacist-in-charge works at least 10 hours per week in each pharmacy for no more than a
273 period of 30 consecutive days.

274
275 (2) Responsibilities. The pharmacist-in-charge shall have the responsibility for, at a minimum,
276 the following:

277
278 (A) ensuring that radiopharmaceuticals are dispensed and delivered safely and accurately as
279 prescribed;

280
281 (B) developing a system to assure that all pharmacy personnel responsible for compounding
282 and/or supervising the compounding of radiopharmaceuticals within the pharmacy receive
283 appropriate education and training and competency evaluation;

284
285 (C) determining that all pharmacists involved in compounding sterile radiopharmaceuticals
286 obtain continuing education appropriate for the type of compounding done by the pharmacist;

287
288 (D) supervising a system to assure appropriate procurement of drugs and devices and
289 storage of all pharmaceutical materials including radiopharmaceuticals, components used in the
290 compounding of radiopharmaceuticals, and drug delivery devices;

291
292 (E) assuring that the equipment used in compounding is properly maintained;

293
294 (F) developing a system for the disposal and distribution of drugs from the Class B pharmacy;

295
296 (G) developing a system for bulk compounding or batch preparation of radiopharmaceuticals;

297
298 (H) developing a system for the compounding, sterility assurance, and quality control of
299 sterile radiopharmaceuticals;

300
301 (I) maintaining records of all transactions of the Class B pharmacy necessary to maintain
302 accurate control over and accountability for all pharmaceutical materials including
303 radiopharmaceuticals, required by applicable state and federal laws and rules;

304

305 (J) developing a system to assure the maintenance of effective controls against the theft or
306 diversion of prescription drugs, and records for such drugs;

307
308 (K) assuring that the pharmacy has a system to dispose of radioactive and cytotoxic waste in
309 a manner so as not to endanger the public health; and

310
311 (L) legally operating the pharmacy, including meeting all inspection and other requirements of
312 all state and federal laws or rules governing the practice of pharmacy.

313
314 (b) Owner. The owner of a Class B pharmacy shall have responsibility for all administrative and
315 operational functions of the pharmacy. The pharmacist-in-charge may advise the owner on
316 administrative and operational concerns. The owner shall have responsibility for, at a minimum,
317 the following, and if the owner is not a Texas licensed pharmacist, the owner shall consult with
318 the pharmacist-in-charge or another Texas licensed pharmacist:

319
320 (1) establishing policies for procurement of prescription drugs and devices and other products
321 dispensed from the Class B pharmacy;

322
323 (2) establishing policies and procedures for the security of the prescription department
324 including the maintenance of effective controls against the theft or diversion of prescription
325 drugs;

326
327 (3) if the pharmacy uses an automated pharmacy dispensing system, reviewing and approving
328 all policies and procedures for system operation, safety, security, accuracy and access, patient
329 confidentiality, prevention of unauthorized access, and malfunction;

330
331 (4) providing the pharmacy with the necessary equipment and resources commensurate with
332 its level and type of practice; and

333
334 (5) establishing policies and procedures regarding maintenance, storage, and retrieval of
335 records in a data processing system such that the system is in compliance with state and
336 federal requirements.

337
338 (c) Authorized nuclear pharmacists.

339
340 (1) General.

341
342 (A) The pharmacist-in-charge shall be assisted by a sufficient number of additional authorized
343 nuclear pharmacists as may be required to operate the pharmacy competently, safely, and
344 adequately to meet the needs of the patients of the pharmacy.

345
346 (B) All personnel performing tasks in the preparation and distribution of radiopharmaceuticals
347 shall be under the direct supervision of an authorized nuclear pharmacist. General qualifications
348 for an authorized nuclear pharmacist are the following. A pharmacist shall:

349
350 (i) meet minimal standards of training and experience in the handling of radioactive
351 materials in accordance with the requirements of the Texas Regulations for Control of Radiation
352 of the Radiation Control Program, Texas Department of State Health Services;

353
354 (ii) be a pharmacist licensed by the board to practice pharmacy in Texas; and

355

356 (iii) submit to the board either:

357

358 (I) written certification that he or she has current board certification as a nuclear pharmacist
359 by the Board of Pharmaceutical Specialties; or

360

361 (II) written certification signed by a preceptor authorized nuclear pharmacist that he or she
362 has achieved a level of competency sufficient to independently operate as an authorized
363 nuclear pharmacist and has satisfactorily completed 700 hours in a structured educational
364 program consisting of both:

365

366 (-a-) 200 hours of didactic training in a program accepted by the Radiation Control
367 Program, Texas Department of State Health Services in the following areas:

368

369 (-1-) radiation physics and instrumentation;

370

371 (-2-) radiation protection;

372

373 (-3-) mathematics pertaining to the use and measurement of radioactivity;

374

375 (-4-) radiation biology; and

376

377 (-5-) chemistry of radioactive material for medical use; and

378

379 (-b-) 500 hours of supervised practical experience in a nuclear pharmacy involving the
380 following:

381

382 (-1-) shipping, receiving, and performing related radiation surveys;

383

384 (-2-) using and performing checks for proper operation of instruments used to determine
385 the activity of dosages, survey meters, and, if appropriate, instruments used to measure alpha-
386 or beta-emitting radionuclides;

387

388 (-3-) calculating, assaying, and safely preparing dosages for patients or human research
389 subjects;

390

391 (-4-) using administrative controls to avoid adverse medical events in the administration
392 of radioactive material; and

393

394 (-5-) using procedures to prevent or minimize contamination and using proper
395 decontamination procedures.

396

397 (C) ~~[The board may issue a letter of notification that the evidence submitted by the~~
398 ~~pharmacist meets the requirements of subparagraph (B)(i) – (iii) of this paragraph and has been~~
399 ~~accepted by the board and that, based thereon, the pharmacist is recognized as an authorized~~
400 ~~nuclear pharmacist.]~~

401

402 ~~[(D)]~~ Authorized nuclear pharmacists are solely responsible for the direct supervision of
403 pharmacy technicians and pharmacy technician trainees and for delegating nuclear pharmacy
404 techniques and additional duties, other than those listed in paragraph **(3)** ~~[(2)]~~ of this subsection,
405 to pharmacy technicians and pharmacy technician trainees. Each authorized nuclear pharmacist
406 shall:

407
408 (i) verify the accuracy of all acts, tasks, or functions performed by pharmacy technicians and
409 pharmacy technician trainees; and

410
411 (ii) be responsible for any delegated act performed by pharmacy technicians and pharmacy
412 technician trainees under his or her supervision.

413
414 (E) All authorized nuclear pharmacists while on duty, shall be responsible for complying with
415 all state and federal laws or rules governing the practice of pharmacy.

416
417 (F) The dispensing pharmacist shall ensure that the drug is dispensed and delivered safely
418 and accurately as prescribed.

419
420 (2) Special requirements for compounding.

421
422 (A) Non-sterile preparations. All pharmacists engaged in compounding non-sterile
423 **preparations, including radioactive preparations** [radiopharmaceuticals] shall meet the
424 training requirements specified in §291.131 of this title (relating to Pharmacies Compounding
425 Non-Sterile Preparations).

426
427 (B) Sterile Preparations. All pharmacists engaged in compounding sterile **preparations,**
428 **including radioactive preparations** [radiopharmaceuticals] shall meet the training
429 requirements specified in §291.133 of this title (relating to Pharmacies Compounding Sterile
430 Preparations).

431
432 (3) Duties. Duties which may only be performed by an authorized nuclear pharmacist are as
433 follows:

434
435 (A) receiving verbal therapeutic prescription drug orders and reducing these orders to writing,
436 either manually or electronically;

437
438 (B) receiving verbal, diagnostic prescription drug orders in instances where patient specificity
439 is required for patient safety (e.g., radiolabeled blood products, radiolabeled antibodies) and
440 reducing these orders to writing, either manually or electronically;

441
442 (C) interpreting and evaluating radioactive prescription drug orders;

443
444 (D) selecting drug products; and

445
446 (E) performing the final check of the dispensed prescription before delivery to the patient to
447 ensure that the radioactive prescription drug order has been dispensed accurately as
448 prescribed.

449
450 (d) Pharmacy Technicians and Pharmacy Technician Trainees.

451
452 (1) General. All pharmacy technicians and pharmacy technician trainees shall meet the training
453 requirements specified in §297.6 of this title (relating to Pharmacy Technician and Pharmacy
454 Technician Trainee Training).

455
456 (2) Special requirements for compounding.

457

458 (A) Non-sterile preparations. All pharmacy technicians and pharmacy technician trainees
459 engaged in compounding non-sterile **preparations, including radioactive preparations**
460 [~~radiopharmaceuticals~~] shall meet the training requirements specified in §291.131 of this title.
461

462 (B) Sterile Preparations. All pharmacy technicians and pharmacy technician trainees engaged
463 in compounding sterile **preparations, including radioactive preparations**
464 [~~radiopharmaceuticals~~] shall meet the training requirements specified in §291.133 of this title.
465

466 (3) Duties.

467 (A) Pharmacy technicians and pharmacy technician trainees may not perform any of the
468 duties listed in subsection (c)(3) of this section.
469

470 (B) An authorized nuclear pharmacist may delegate to pharmacy technicians and pharmacy
471 technician trainees any nuclear pharmacy technique which is associated with the preparation
472 and distribution of radiopharmaceuticals provided:
473

474 (i) an authorized nuclear pharmacist verifies the accuracy of all acts, tasks, and functions
475 performed by pharmacy technicians and pharmacy technician trainees; and
476

477 (ii) pharmacy technicians and pharmacy technician trainees are under the direct supervision
478 of and responsible to a pharmacist.
479

480 (4) Ratio of authorized nuclear pharmacist to pharmacy technicians and pharmacy technician
481 trainees.
482

483 (A) The ratio of authorized nuclear pharmacists to pharmacy technicians and pharmacy
484 technician trainees may be 1:4, provided at least one of the four is a pharmacy technician and is
485 trained in the handling of radioactive materials.
486

487 (B) The ratio of authorized nuclear pharmacists to pharmacy technician trainees may not
488 exceed 1:3.
489

490 ~~[(e) Special education, training, and evaluation requirements for pharmacy personnel
491 compounding or responsible for the direct supervision of pharmacy personnel compounding
492 sterile radiopharmaceuticals. All pharmacy personnel preparing sterile radiopharmaceuticals
493 shall meet the training requirements specified in §291.133 of this title.]~~
494
495

496 **§291.54 Operational Standards**

497 (a) Licensing requirements.

500 (1) It is unlawful for a person to provide radioactive drug services unless such provision is
501 performed by a person licensed to act as an authorized nuclear pharmacist, as defined by the
502 board, or is a person acting under the direct supervision of an authorized nuclear pharmacist
503 acting in accordance with the Act and its rules, and the regulations of the Texas Department of
504 State Health Services, Radiation Control Program. Subsection (a) of this section does not apply
505 to:
506
507

508 (A) a licensed practitioner or his or her designated agent for administration to his or her
509 patient, provided no person may receive, possess, use, transfer, own, acquire, or dispose of
510 radiopharmaceuticals except as authorized in a specific or a general license as provided in
511 accordance with the requirements of the Texas Department of State Health Services, Radiation
512 Control Program, Texas Administrative Code, Title 25, Part 1, Subchapter F, §289.252 relating
513 to Licensing of Radioactive Material, or the Act;

514
515 (B) institutions and/or facilities with nuclear medicine services operated by practitioners and
516 who are licensed by the Texas Department of State Health Services, Radiation Control
517 Program, to prescribe, administer, and dispense radioactive materials (drugs and/or devices).

518
519 (2) An applicant for a Class B pharmacy shall provide evidence to the board of the possession
520 of a Texas Department of State Health Services radioactive material license or proof of
521 application for a radioactive material license.

522
523 (3) A Class B pharmacy shall register with the board on a pharmacy license application
524 provided by the board, following the procedures specified in §291.1 of this title (relating to
525 Pharmacy License Application).

526
527 (4) A Class B pharmacy which changes ownership shall notify the board within ten days of the
528 change of ownership and apply for a new and separate license as specified in §291.3 of this title
529 (relating to Required Notifications).

530
531 (5) A Class B pharmacy which changes location and/or name shall notify the board within ten
532 days of the change and file for an amended license as specified in §291.3 of this title.

533
534 (6) A Class B pharmacy owned by a partnership or corporation which changes managing
535 officers shall notify the board in writing of the names of the new managing officers within ten
536 days of the change, following the procedures in §291.3 of this title.

537
538 (7) A Class B pharmacy shall notify the board in writing within ten days of closing, following the
539 procedures in §291.5 of this title (relating to Closing a Pharmacy).

540
541 (8) A separate license is required for each principal place of business and only one pharmacy
542 license may be issued to a specific location.

543
544 (9) A fee as specified in §291.6 of this title (relating to Pharmacy License Fees) will be charged
545 for the issuance and renewal of a license and the issuance of an amended license.

546
547 (10) A Class B pharmacy, licensed under the provisions of the Act, §560.051(a)(2), which also
548 operates another type of pharmacy which would otherwise be required to be licensed under the
549 Act, §560.051(a)(1), concerning community pharmacy (Class A), is not required to secure a
550 license for such other type of pharmacy; provided, however, such licensee is required to comply
551 with the provisions of §291.31 of this title (relating to Definitions); §291.32 of this title (relating to
552 Personnel); §291.33 of this title (relating to Operational Standards); §291.34 of this title (relating
553 to Records); and §291.35 of this title (relating to Official Prescription Requirements), to the
554 extent such rules are applicable to the operation of the pharmacy.

555
556 (11) A Class B [~~nuclear~~] pharmacy engaged in the compounding of non-sterile [~~non-~~
557 ~~radioactive~~] preparations, **including radioactive preparations**, shall comply with the provisions
558 of §291.131 of this title (relating to Pharmacies Compounding Non-Sterile Preparations).

559
560 (12) A Class B [~~nuclear~~] pharmacy engaged in the compounding of sterile [~~non-radioactive~~]
561 preparations, **including radioactive preparations**, shall comply with the provisions of
562 §291.133 of this title (relating to Pharmacies Compounding Sterile Preparations).

563
564 [~~(b) Risk levels for compounded sterile radiopharmaceuticals. Risk Levels for sterile~~
565 ~~compounded radiopharmaceuticals shall be as listed below.~~

566
567 ~~—(1) Low-risk level compounded sterile radiopharmaceuticals.~~

568
569 ~~—(A) Low-risk level compounded sterile radiopharmaceuticals are those compounded under all~~
570 ~~of the following conditions.~~

571
572 ~~—(i) The compounded sterile preparations are compounded with aseptic manipulations~~
573 ~~entirely within ISO Class 5 or better air quality using only sterile ingredients, products,~~
574 ~~components, and devices.~~

575
576 ~~—(ii) The compounding involves only transfer, measuring, and mixing manipulations with~~
577 ~~closed or sealed packaging systems that are performed promptly and attentively.~~

578
579 ~~—(iii) Manipulations are limited to aseptically opening ampuls, penetrating sterile stoppers on~~
580 ~~vials with sterile needles and syringes, and transferring sterile liquids in sterile syringes to sterile~~
581 ~~administration devices and packages of other sterile products.~~

582
583 ~~—(iv) For a low-risk preparation, in the absence of passing a sterility test, the storage periods~~
584 ~~cannot exceed the following periods: before administration, 48 hours at controlled room~~
585 ~~temperature, for not more than 14 days if stored in cold temperatures, and for 45 days if stored~~
586 ~~in a frozen state at minus 20 degrees Celsius or colder). For delayed activation device systems,~~
587 ~~the storage period begins when the device is activated.~~

588
589 ~~—(B) Examples of low-risk compounding include radiopharmaceuticals compounded from~~
590 ~~sterile components in closed sterile containers and with a volume of 100 mL or less for a single-~~
591 ~~dose injection or not more than 30 mL taken from a multidose container.~~

592
593 ~~—(2) Medium-risk level compounded sterile radiopharmaceuticals.~~

594
595 ~~—(A) Medium-risk level compounded sterile radiopharmaceuticals are those compounded~~
596 ~~aseptically under low-risk conditions and one or more of the of the following conditions exists.~~

597
598 ~~—(i) Multiple individual or small doses of sterile products are combined or pooled to prepare a~~
599 ~~compounded sterile radiopharmaceuticals that will be administered either to multiple patients or~~
600 ~~to one patient on multiple occasions.~~

601
602 ~~—(ii) The compounding process includes complex aseptic manipulations other than the single-~~
603 ~~volume transfer.~~

604
605 ~~—(iii) The compounding process requires unusually long duration, such as that required to~~
606 ~~complete the dissolution or homogenous mixing.~~

607
608 ~~—(iv) The sterile compounded radiopharmaceuticals do not contain broad-spectrum~~
609 ~~bacteriostatic substances, and they are administered over several days.~~

610
611 ~~—(v) For a medium-risk preparation, in the absence of passing sterility test, the storage~~
612 ~~periods cannot exceed the following time periods: before administration, the compounded sterile~~
613 ~~preparations are properly stored and are exposed for not more than 30 hours at controlled room~~
614 ~~temperature for not more than 7 days at a cold temperature, and for 45 days in solid frozen~~
615 ~~state at minus 20 degrees or colder.~~
616
617 ~~—(B) Examples of medium-risk compounding include the following.~~
618
619 ~~—(i) Compounding of total parenteral nutrition fluids using a manual or automated device~~
620 ~~during which there are multiple injections, detachments, and attachments of nutrient source~~
621 ~~products to the device or machine to deliver all nutritional components to a final sterile~~
622 ~~container.~~
623
624 ~~—(ii) Filling of reservoirs of injection and infusion devices with multiple sterile drug products~~
625 ~~and evacuations of air from these reservoirs before the filled device is dispensed.~~
626
627 ~~—(iii) Filling of reservoirs of injection and infusion devices with volumes of sterile drug~~
628 ~~solutions that will be administered over several days at ambient temperatures between 25 and~~
629 ~~40 degrees Celsius (77 and 104 degrees Fahrenheit).~~
630
631 ~~—(iv) Transfer of volumes from multiple ampuls or vials into a single, final sterile container or~~
632 ~~product.~~
633
634 ~~—(3) High-risk level compounded sterile radiopharmaceuticals.~~
635
636 ~~—(A) High-risk level compounded sterile radiopharmaceuticals are those compounded under~~
637 ~~any of the following conditions.~~
638
639 ~~—(i) Non-sterile ingredients, including manufactured products are incorporated, or a non-~~
640 ~~sterile device is employed before terminal sterilization.~~
641
642 ~~—(ii) Sterile ingredients, components, devices, and mixtures are exposed to air quality inferior~~
643 ~~to ISO Class 5. This includes storage in environments inferior to ISO Class 5 of opened or~~
644 ~~partially used packages of manufactured sterile products that lack antimicrobial preservatives.~~
645
646 ~~—(iii) Non-sterile preparations are exposed no more than 6 hours before being sterilized.~~
647
648 ~~—(iv) It is assumed, and not verified by examination of labeling and documentation from~~
649 ~~suppliers or by direct determination, that the chemical purity and content strength of ingredients~~
650 ~~meet their original or compendial specifications in unopened or in opened packages of bulk~~
651 ~~ingredients.~~
652
653 ~~—(v) For a high-risk preparation, in the absence of passing sterility test, the storage periods~~
654 ~~cannot exceed the following time periods: before administration, the compounded sterile~~
655 ~~preparations are properly stored and are exposed for not more than 24 hours at controlled room~~
656 ~~temperature for not more than 3 days at a cold temperature, and for 45 days in solid frozen~~
657 ~~state at minus 20 degrees or colder.~~
658
659 ~~—(B) Examples of high-risk compounding include the following.~~
660

661 ~~—(i) Dissolving non-sterile bulk drug and nutrient powders to make solutions, which will be~~
662 ~~terminally sterilized.~~
663
664 ~~—(ii) Sterile ingredients, components, devices, and mixtures are exposed to air quality inferior~~
665 ~~to ISO Class 5. This includes storage in environments inferior to ISO Class 5 of opened or~~
666 ~~partially used packages of manufactured sterile products that lack antimicrobial preservatives.~~
667
668 ~~—(iii) Measuring and mixing sterile ingredients in non-sterile devices before sterilization is~~
669 ~~performed.~~
670
671 ~~—(iv) Assuming, without appropriate evidence or direct determination, that packages of bulk~~
672 ~~ingredients contain at least 95% by weight of their active chemical moiety and have not been~~
673 ~~contaminated or adulterated between uses.]~~
674
675 ~~[(c) Environment.~~
676
677 ~~–(1) Special requirements for the compounding of sterile radiopharmaceuticals. When the~~
678 ~~pharmacy compounds sterile radiopharmaceuticals, the following is applicable.~~
679
680 ~~—(A) Low and Medium Risk Preparations.~~
681
682 ~~—(i) The pharmacy shall have a designated controlled area for the compounding of sterile~~
683 ~~radiopharmaceuticals that is functionally separate from areas for the preparation of non-sterile~~
684 ~~radiopharmaceuticals and is constructed to minimize the opportunities for particulate and~~
685 ~~microbial contamination. This controlled area for the preparation of sterile radiopharmaceuticals~~
686 ~~shall:~~
687
688 ~~—(I) have a controlled environment that is aseptic or contains an aseptic environmental~~
689 ~~control device(s). If the aseptic environmental control device is located within the controlled~~
690 ~~area, the controlled area must extend a minimum of six feet from the device and clearly marked~~
691 ~~to identify the separation between the controlled and non-controlled area;~~
692
693 ~~—(II) be clean, well lighted, and of sufficient size to support sterile compounding activities;~~
694
695 ~~—(III) be used only for the compounding of sterile radiopharmaceuticals;~~
696
697 ~~—(IV) be designed to avoid outside traffic and airflow;~~
698
699 ~~—(V) be designed such that hand sanitizing and gowning occurs outside the controlled area~~
700 ~~but accessible without use of the hands of the compounding personnel;~~
701
702 ~~—(VI) have non-porous and washable floors or floor covering to enable regular disinfection;~~
703
704 ~~—(VII) be ventilated in a manner not interfering with aseptic environmental control conditions;~~
705
706 ~~—(VIII) have walls, ceilings, and fixtures, shelving, counters, and cabinets that are smooth,~~
707 ~~impervious, free from cracks and crevices, and nonshedding (acoustical ceiling tiles that are~~
708 ~~coated with an acrylic paint are acceptable);~~
709
710 ~~—(IX) have drugs and supplies stored on shelving areas above the floor to permit adequate~~
711 ~~floor cleaning; and~~

712
713 ~~— (X) contain only the appropriate compounding supplies and not be used for bulk storage for~~
714 ~~supplies and materials. Objects that shed particles may not be brought into the controlled area.~~
715
716 ~~— (ii) The pharmacy shall prepare sterile radiopharmaceuticals in a primary engineering control~~
717 ~~device, such as a vertical air flow hood, which is capable of maintaining at least ISO Class 5~~
718 ~~conditions during normal activity.~~
719
720 ~~— (l) The primary engineering control shall:~~
721
722 ~~— (a) be located in the buffer area or room and placed in the buffer area in a manner as to~~
723 ~~avoid conditions that could adversely affect its operation such as strong air currents from~~
724 ~~opened doors, personnel traffic, or air streams from the heating, ventilating and air condition~~
725 ~~system;~~
726
727 ~~— (b) be certified by an independent contractor according to the International Organization~~
728 ~~of Standardization (ISO) Classification of Particulate Matter in Room Air (ISO 14644-1) for~~
729 ~~operational efficiency at least every six months and when it is relocated, in accordance with the~~
730 ~~manufacturer's specifications; and~~
731
732 ~~— (c) have pre-filters inspected periodically and replaced as needed, in accordance with~~
733 ~~written policies and procedures and the manufacturer's specification, and the inspection and/or~~
734 ~~replacement date documented.~~
735
736 ~~— (II) The compounding aseptic isolator or compounding aseptic containment isolator must~~
737 ~~be placed in an ISO Class 8 buffer area unless the isolator meets all of the following conditions.~~
738
739 ~~— (a) The isolator must provide isolation from the room and maintain ISO Class 5 during~~
740 ~~dynamic operating conditions including transferring ingredients, components, and devices into~~
741 ~~and out of the isolator and during preparation of compounded sterile preparations.~~
742
743 ~~— (b) Particle counts sampled approximately 6 to 12 inches upstream of the critical~~
744 ~~exposure site must maintain ISO Class 5 levels during compounding operations.~~
745
746 ~~— (c) The pharmacy shall maintain documentation from the manufacturer that the isolator~~
747 ~~meets this standard when located in worse than ISO Class 7 environments.~~
748
749 ~~— (B) High-risk Preparations. In addition to the requirements in subparagraph (A)(i)(l) of this~~
750 ~~paragraph, when high-risk preparations are compounded, the aseptic environment control~~
751 ~~device(s) shall be located in a controlled area that maintains at least an ISO Class 7~~
752 ~~environment.~~
753
754 ~~— (C) Automated compounding device(s). If automated compounding device(s) are used, the~~
755 ~~pharmacy shall have a method to calibrate and verify the accuracy of automated compounding~~
756 ~~devices used in aseptic processing and document the calibration and verification on a routine~~
757 ~~basis.]~~

758 **(b) Environment.**

759 **(1) General requirements.**

760
761
762

763 (A) The pharmacy shall be arranged in an orderly fashion and kept clean. All required
764 equipment shall be clean and in good operating condition.

765
766 (B) The pharmacy shall have a sink with hot and cold running water within the
767 pharmacy, exclusive of restroom facilities, available to all pharmacy personnel and
768 maintained in a sanitary condition.

769
770 (C) The pharmacy shall be properly lighted and ventilated.

771
772 (D) The temperature of the pharmacy shall be maintained within a range compatible
773 with the proper storage of drugs. The temperature of the refrigerator shall be maintained
774 within a range compatible with the proper storage of drugs requiring refrigeration.

775
776 (E) If the pharmacy has flammable materials, the pharmacy shall have a designated
777 area for the storage of flammable materials. Such area shall meet the requirements set by
778 local and state fire laws.

779
780 (2) Security requirements.

781
782 (A) All areas occupied by a pharmacy shall be capable of being locked by key, combination or
783 other mechanical or electronic means to prohibit unauthorized access, when a pharmacist is not
784 on-site except as provided in subparagraph (B) of this paragraph.

785
786 (B) The pharmacy may authorize personnel to gain access to that area of the pharmacy
787 containing dispensed [sterile] radiopharmaceuticals, in the absence of the pharmacist, for the
788 purpose of retrieving [dispensed prescriptions] the radiopharmaceuticals to be delivered
789 [deliver to patients]. If the pharmacy allows such after-hours access, the area containing the
790 dispensed [sterile] radiopharmaceuticals shall be an enclosed and lockable area separate from
791 the area containing undispensed prescription drugs. A list of the authorized personnel having
792 such access shall be in the pharmacy's policy and procedure manual.

793
794 (C) Each pharmacist while on duty shall be responsible for the security of the prescription
795 department, including provisions for effective control against theft or diversion of prescription
796 drugs, and records for such drugs

797
798 **(c)** ~~(d)~~ Prescription dispensing and delivery.

799
800 (1) Generic Substitution. A pharmacist may substitute on a prescription drug order issued for a
801 brand name product provided the substitution is authorized and performed in compliance with
802 Chapter 309 of this title (relating to Substitution of Drug Products).

803
804 (2) Prescription containers (immediate inner containers).

805
806 (A) A drug dispensed pursuant to a radioactive prescription drug order shall be dispensed in
807 an appropriate immediate inner container as follows.

808
809 (i) If a drug is susceptible to light, the drug shall be dispensed in a light-resistant container.

810
811 (ii) If a drug is susceptible to moisture, the drug shall be dispensed in a tight container.

812

813 (iii) The container should not interact physically or chemically with the drug product placed in
814 it so as to alter the strength, quality, or purity of the drug beyond the official requirements.

815
816 (B) Immediate inner prescription containers or closures shall not be re-used.

817
818 (3) Delivery containers (outer containers).

819
820 (A) Prescription containers may be placed in suitable containers for delivery which will
821 transport the radiopharmaceutical safely in compliance with all applicable laws and regulations.

822
823 (B) Delivery containers may be re-used provided they are maintained in a manner to prevent
824 cross contamination.

825
826 (4) Labeling.

827
828 (A) The immediate inner container of a radiopharmaceutical shall be labeled with:

829
830 (i) standard radiation symbol;

831
832 (ii) the words "caution-radioactive material" or "danger, radioactive material";

833
834 (iii) the name of the radiopharmaceutical or its abbreviation; and

835
836 (iv) the unique identification number of the prescription.

837
838 (B) The outer container of a radiopharmaceutical shall be labeled with:

839
840 (i) the name, address, and phone number of the pharmacy;

841
842 (ii) the date dispensed;

843
844 (iii) the directions for use, if applicable;

845
846 (iv) the unique identification number of the prescription;

847
848 (v) the name of the patient if known, or the statement, "for physician use" if the patient is
849 unknown;

850
851 (vi) the standard radiation symbol;

852
853 (vii) the words "caution-radioactive material" or "danger, radioactive material";

854
855 (viii) the name of the radiopharmaceutical or its abbreviation;

856
857 (ix) the amount of radioactive material contained in millicuries (mCi), microcuries (uCi), or
858 bequerels (Bq) and the corresponding time that applies to this activity, if different from the
859 requested calibration date and time;

860
861 (x) the initials or identification codes of the person preparing the product and the authorized
862 nuclear pharmacist who checked and released the final product unless recorded in the

863 pharmacy's data processing system. The record of the identity of these individuals shall not be
864 altered in the pharmacy's data processing system.

865
866 (xi) if a liquid, the volume in milliliters;

867
868 (xii) the requested calibration date and time; and

869
870 (xiii) the expiration date and/or time.

871
872 (C) The amount of radioactivity shall be determined by radiometric methods for each
873 individual preparation immediately at the time of dispensing and calculations shall be made to
874 determine the amount of activity that will be present at the requested calibration date and time,
875 due to radioactive decay in the intervening period, and this activity and time shall be placed on
876 the label per requirements set out in paragraph (4) of this subsection.

877
878 **(d)** ~~(e)~~ Equipment. The following minimum equipment is required in a nuclear pharmacy:

879
880 (1) vertical laminar flow hood;

881
882 (2) dose calibrator;

883
884 (3) a calibrated system or device (i.e., thermometer) to monitor the temperature to ensure that
885 proper storage requirements are met, if ~~[sterile]~~ preparations are stored in the refrigerator;

886
887 (4) if applicable, a Class A prescription balance, or analytical balance and weights. Such
888 balance shall be properly maintained and subject to periodic inspection by the board.

889
890 (5) scintillation analyzer;

891
892 (6) microscope and hemocytometer;

893
894 (7) equipment and utensils necessary for the proper compounding of prescription drug or
895 medication orders. Such equipment and utensils used in the compounding process shall be:

896
897 (A) of appropriate design, appropriate capacity, and be operated within designed operational
898 limits;

899
900 (B) of suitable composition so that surfaces that contact components, in-process material, or
901 drug products shall not be reactive, additive, or absorptive so as to alter the safety, identity,
902 strength, quality, or purity of the drug product beyond acceptable standards;

903
904 (C) cleaned and sanitized immediately prior to each use; and

905
906 (D) routinely inspected, calibrated (if necessary), or checked to ensure proper performance;

907
908 (8) appropriate disposal containers for used needles, syringes, etc., and if applicable, cytotoxic
909 waste from the preparation of chemotherapeutic agents, and/or biohazardous waste;

910
911 (9) all necessary supplies, including:

912
913 (A) disposable needles, syringes, and other aseptic mixing;

- 914
915 (B) disinfectant cleaning solutions;
916
917 (C) hand washing agents with bactericidal action;
918
919 (D) disposable, lint free towels or wipes;
920
921 (E) appropriate filters and filtration equipment;
922
923 (F) **radioactive** ~~cytotoxic~~ spill kits, if applicable; and
924
925 (G) masks, caps, coveralls or gowns with tight cuffs, shoe covers, and gloves, as applicable.
926
927 (10) adequate glassware, utensils, gloves, syringe shields and remote handling devices, and
928 adequate equipment for product quality control;
929
930 (11) adequate shielding material;
931
932 (12) data processing system including a printer or comparable equipment;
933
934 (13) radiation dosimeters for visitors and personnel and log entry book;
935
936 (14) exhaust/fume hood with monitor, for storage and handling of all volatile radioactive drugs
937 if applicable, to be determined by the Texas Department of State Health Services, Radiation
938 Control Program; and
939
940 (15) adequate radiation monitor(s).

941
942 **(e)** ~~(f)~~ Library. A nuclear pharmacy shall maintain a reference library which shall include the
943 following in hard copy or electronic format **current or updated copies of the following:**

944
945 (1) ~~current copies of the following:~~

946 ~~(A)~~ Texas Pharmacy Act and rules;

947
948 **(2)** ~~(B)~~ Texas Dangerous Drug Act and rules;

949
950 **(3)** ~~(C)~~ Texas Controlled Substances Act and rules; and

951
952 **(4)** ~~(D)~~ Federal Controlled Substances Act and rules (or official publication describing the
953 requirements of the Federal Controlled Substances Act and rules); **and**

954
955 ~~(2) a current or updated version of Chapter 797 of the USP/NF concerning Pharmacy
956 Compounding Sterile Preparations and other USP chapters applicable to the practice (e.g., USP
957 Chapter 823 Radiopharmaceuticals for Positron Emission Tomography – Compounding); and]~~

958
959 **(5)** ~~(3)~~ a minimum of one ~~current or updated~~ text dealing with nuclear medicine science.

960
961 **(f)** ~~(g)~~ Radiopharmaceuticals and/or radioactive materials.

962
963 (1) General requirements.
964

965
966 (A) Radiopharmaceuticals may only be dispensed pursuant to a radioactive prescription drug
967 order.

968
969 (B) An authorized nuclear pharmacist may distribute radiopharmaceuticals to authorized
970 users for patient use. A nuclear pharmacy may ~~[also]~~ furnish radiopharmaceuticals for
971 departmental or physicians' use if such authorized users maintain a Texas radioactive materials
972 license~~[-and the radiopharmaceutical is labeled "for physician use, provided such distribution is~~
973 ~~documented in the control system].~~

974
975 (C) An authorized nuclear pharmacist may transfer to authorized users radioactive materials
976 not intended for drug use in accordance with the requirements of the Texas Department of State
977 Health Services, Radiation Control Program, Texas Administrative Code, Title 25, Part 1,
978 Subchapter F, §289.252 relating to Licensing of Radioactive Material.

979
980 (D) The transportation of radioactive materials from the nuclear pharmacy must be in
981 accordance with current state and federal transportation regulations.

982
983 (2) Procurement and storage.

984
985 (A) The pharmacist-in-charge shall have the responsibility for the procurement and storage of
986 drugs, but may receive input from other appropriate staff relative to such responsibility.

987
988 (B) Prescription drugs and devices shall be stored within the prescription department or a
989 locked storage area.

990
991 (C) All drugs shall be stored at the proper temperature, as defined in the USP/NF and
992 §291.15 of this title (relating to Storage of Drugs).

993
994 **(D) The pharmacy's generator(s) shall be stored and eluted in an ISO Class 8 or**
995 **cleaner air environment.**

996
997 (3) Out-of-date and other unusable drugs or devices.

998
999 (A) Any drug or device bearing an expiration date shall not be dispensed beyond the
1000 expiration date of the drug or device.

1001
1002 (B) Outdated and other unusable drugs or devices shall be removed from dispensing stock
1003 and shall be quarantined together until such drugs or devices are disposed of properly.

1004
1005 ~~[(h) Loading bulk drugs into automated compounding devices.~~

1006
1007 ~~-(1) Automated compounding device may be loaded with bulk drugs only by an authorized~~
1008 ~~nuclear pharmacist or by supportive personnel under the direction and direct supervision of an~~
1009 ~~authorized pharmacist.~~

1010
1011 ~~-(2) The label of an automated compounding device container shall indicate the brand name~~
1012 ~~and strength of the drug; or if no brand name, then the generic name, strength, and name of the~~
1013 ~~manufacturer or distributor.~~

1014

1015 ~~—(3) Records of loading bulk drugs into an automated compounding device shall be maintained~~
1016 ~~to show:~~
1017
1018 ~~—(A) name of the drug, strength, and dosage form;~~
1019
1020 ~~—(B) manufacturer or distributor;~~
1021
1022 ~~—(C) manufacturer's lot number;~~
1023
1024 ~~—(D) expiration date;~~
1025
1026 ~~—(E) quantity added to the automated compounding device;~~
1027
1028 ~~—(F) date of loading;~~
1029
1030 ~~—(G) name, initials, or electronic signature of the person loading the automated compounding~~
1031 ~~device; and~~
1032
1033 ~~—(H) name, initials, or electronic signature of the responsible authorized nuclear pharmacist.~~
1034
1035 ~~—(4) The automated compounding device shall not be used until an authorized nuclear~~
1036 ~~pharmacist verifies that the system is properly loaded and affixes his or her signature or~~
1037 ~~electronic signature to the record specified in paragraph (3) of this subsection.]~~
1038
1039 ~~[(i) Sterile radiopharmaceuticals:~~
1040
1041 ~~—(1) Beyond-use date.~~
1042
1043 ~~—(A) The beyond-use date assigned shall be based on:~~
1044
1045 ~~—(i) established manufacturer's guidelines;~~
1046
1047 ~~—(ii) published literature; or~~
1048
1049 ~~—(iii) in-house or contracted stability studies.~~
1050
1051 ~~—(B) The method for establishing beyond-use dates shall be documented.~~
1052
1053 ~~—(2) Radioactive Drug Quality control. There shall be a documented, ongoing quality control~~
1054 ~~program that monitors and evaluates personnel performance, equipment and facilities.~~
1055 ~~Procedures shall be in place to assure that the pharmacy is capable of consistently preparing~~
1056 ~~radiopharmaceuticals which are sterile and stable. Quality control procedures shall include, but~~
1057 ~~are not limited to, the following:~~
1058
1059 ~~—(A) recall procedures;~~
1060
1061 ~~—(B) storage and dating;~~
1062
1063 ~~—(C) documentation of appropriate functioning of refrigerator, freezer, and other equipment;~~
1064

1065 —(D) documentation of aseptic environmental control device(s) certification at least every year
1066 and the regular replacement of pre-filters as necessary;

1067
1068 —(E) a process to evaluate and confirm the quality of the prepared radiopharmaceutical; and
1069

1070 —(F) documentation of facility maintenance such as cleaning and environmental testing.]
1071

1072

1073

1074

1075

1076

§291.133 Pharmacies Compounding Sterile Preparations

1077

1078 (a) Purpose. Pharmacies compounding sterile preparations, prepackaging pharmaceutical
1079 products, and distributing those products shall comply with all requirements for their specific
1080 license classification and this section. The purpose of this section is to provide standards for
1081 the:

1082

1083 (1) compounding of sterile preparations pursuant to a prescription or medication order for a
1084 patient from a practitioner in Class A-S, Class B, Class C-S, and Class E-S pharmacies;

1085

1086 (2) compounding, dispensing, and delivery of a reasonable quantity of a compounded sterile
1087 preparation in Class A-S, Class B, Class C-S, and Class E-S pharmacies to a practitioner's
1088 office for office use by the practitioner;

1089

1090 (3) compounding and distribution of compounded sterile preparations by a Class A-S
1091 pharmacy for a Class C-S pharmacy; and

1092

1093 (4) compounding of sterile preparations by a Class C-S pharmacy and the distribution of the
1094 compounded preparations to other Class C or Class C-S pharmacies under common ownership.

1095

1096 (b) Definitions. In addition to the definitions for specific license classifications, the following
1097 words and terms, when used in this section, shall have the following meanings, unless the
1098 context clearly indicates otherwise.

1099

1100 (1) ACPE--Accreditation Council for Pharmacy Education.

1101

1102 (2) Airborne particulate cleanliness class--The level of cleanliness specified by the maximum
1103 allowable number of particles per cubic meter of air as specified in the International
1104 Organization of Standardization (ISO) Classification Air Cleanliness (ISO 14644-1). For
1105 example:

1106

1107 (A) ISO Class 5 (formerly Class 100) is an atmospheric environment that contains less than
1108 3,520 particles 0.5 microns in diameter per cubic meter of air (formerly stated as 100 particles
1109 0.5 microns in diameter per cubic foot of air);

1110

1111 (B) ISO Class 7 (formerly Class 10,000) is an atmospheric environment that contains less
1112 than 352,000 particles 0.5 microns in diameter per cubic meter of air (formerly stated as 10,000
1113 particles 0.5 microns in diameter per cubic foot of air); and

1114

1115 (C) ISO Class 8 (formerly Class 100,000) is an atmospheric environment that contains less
1116 than 3,520,000 particles 0.5 microns in diameter per cubic meter of air (formerly stated as
1117 100,000 particles 0.5 microns in diameter per cubic foot of air).

1118

1119 (3) Ancillary supplies--Supplies necessary for the preparation and administration of
1120 compounded sterile preparations.

1121

1122 (4) Ante-area--An ISO Class 8 or better area where personnel may perform hand hygiene and
1123 garbing procedures, staging of components, order entry, labeling, and other high-particulate
1124 generating activities. It is also a transition area that:

1125

1126 (A) provides assurance that pressure relationships are constantly maintained so that air flows
1127 from clean to dirty areas; and

1128

1129 (B) reduces the need for the heating, ventilating and air conditioning (HVAC) control system
1130 to respond to large disturbances.

1131

1132 (5) Aseptic Processing--A mode of processing pharmaceutical and medical preparations that
1133 involves the separate sterilization of the preparation and of the package (containers-closures or
1134 packaging material for medical devices) and the transfer of the preparation into the container
1135 and its closure under at least ISO Class 5 conditions.

1136

1137 (6) Automated compounding device--An automated device that compounds, measures, and/or
1138 packages a specified quantity of individual components in a predetermined sequence for a
1139 designated sterile preparation.

1140

1141 (7) Batch--A specific quantity of a drug or other material that is intended to have uniform
1142 character and quality, within specified limits, and is produced during a single preparation cycle.

1143

1144 (8) Batch preparation compounding--Compounding of multiple sterile preparation units, in a
1145 single discrete process, by the same individual(s), carried out during one limited time period.
1146 Batch preparation/compounding does not include the preparation of multiple sterile preparation
1147 units pursuant to patient specific medication orders.

1148

1149 (9) Beyond-use date--The date or time after which the compounded sterile preparation shall
1150 not be stored or transported or begin to be administered to a patient. The beyond-use date is
1151 determined from the date or time the preparation is compounded.

1152

1153 (10) Biological Safety Cabinet, Class II--A ventilated cabinet for personnel, product or
1154 preparation, and environmental protection having an open front with inward airflow for personnel
1155 protection, downward HEPA filtered laminar airflow for product protection, and HEPA filtered
1156 exhausted air for environmental protection.

1157

1158 (11) Buffer Area--An ISO Class 7 **or, if a Class B pharmacy, ISO Class 8 or better,** area
1159 where the primary engineering control area is physically located. Activities that occur in this area
1160 include the preparation and staging of components and supplies used when compounding
1161 sterile preparations.

1162

1163 (12) Clean room--A room in which the concentration of airborne particles is controlled to meet
1164 a specified airborne particulate cleanliness class. Microorganisms in the environment are

1165 monitored so that a microbial level for air, surface, and personnel gear are not exceeded for a
1166 specified cleanliness class.

1167
1168 (13) Component--Any ingredient intended for use in the compounding of a drug preparation,
1169 including those that may not appear in such preparation.

1170
1171 (14) Compounding--The preparation, mixing, assembling, packaging, or labeling of a drug or
1172 device:

1173
1174 (A) as the result of a practitioner's prescription drug or medication order based on the
1175 practitioner-patient-pharmacist relationship in the course of professional practice;

1176
1177 (B) for administration to a patient by a practitioner as the result of a practitioner's initiative
1178 based on the practitioner-patient-pharmacist relationship in the course of professional practice;

1179
1180 (C) in anticipation of prescription drug or medication orders based on routine, regularly
1181 observed prescribing patterns; or

1182
1183 (D) for or as an incident to research, teaching, or chemical analysis and not for sale or
1184 dispensing, except as allowed under §562.154 or Chapter 563 of the Occupations Code.

1185
1186 (15) Compounding Aseptic Isolator--A form of barrier isolator specifically designed for
1187 compounding pharmaceutical ingredients or preparations. It is designed to maintain an aseptic
1188 compounding environment within the isolator throughout the compounding and material transfer
1189 processes. Air exchange into the isolator from the surrounding environment shall not occur
1190 unless it has first passed through a microbial retentive filter (HEPA minimum).

1191
1192 (16) Compounding Aseptic Containment Isolator--A compounding aseptic isolator designed to
1193 provide worker protection from exposure to undesirable levels of airborne drug throughout the
1194 compounding and material transfer processes and to provide an aseptic environment for
1195 compounding sterile preparations. Air exchange with the surrounding environment should not
1196 occur unless the air is first passed through a microbial retentive filter (HEPA minimum) system
1197 capable of containing airborne concentrations of the physical size and state of the drug being
1198 compounded. Where volatile hazardous drugs are prepared, the exhaust air from the isolator
1199 should be appropriately removed by properly designed building ventilation.

1200
1201 (17) Critical Area--An ISO Class 5 environment.

1202
1203 (18) Critical Sites--A location that includes any component or fluid pathway surfaces (e.g., vial
1204 septa, injection ports, beakers) or openings (e.g., opened ampuls, needle hubs) exposed and at
1205 risk of direct contact with air (e.g., ambient room or HEPA filtered), moisture (e.g., oral and
1206 mucosal secretions), or touch contamination. Risk of microbial particulate contamination of the
1207 critical site increases with the size of the openings and exposure time.

1208
1209 (19) Device--An instrument, apparatus, implement, machine, contrivance, implant, in-vitro
1210 reagent, or other similar or related article, including any component part or accessory, that is
1211 required under federal or state law to be ordered or prescribed by a practitioner.

1212
1213 (20) Direct Compounding Area--A critical area within the ISO Class 5 primary engineering
1214 control where critical sites are exposed to unidirectional HEPA-filtered air, also known as first
1215 air.

- 1216
1217 (21) Disinfectant--An agent that frees from infection, usually a chemical agent but sometimes a
1218 physical one, and that destroys disease-causing pathogens or other harmful microorganisms
1219 but may not kill bacterial and fungal spores. It refers to substances applied to inanimate objects.
1220
- 1221 (22) First Air--The air exiting the HEPA filter in a unidirectional air stream that is essentially
1222 particle free.
1223
- 1224 (23) Hazardous Drugs--Drugs that, studies in animals or humans indicate exposure to the
1225 drugs, have a potential for causing cancer, development or reproductive toxicity, or harm to
1226 organs. **For the purposes of this chapter, radiopharmaceuticals are not considered**
1227 **hazardous drugs.**
1228
- 1229 (24) Hot water--The temperature of water from the pharmacy's sink maintained at a minimum
1230 of 105 degrees F (41 degrees C).
1231
- 1232 (25) HVAC--Heating, ventilation, and air conditioning.
1233
- 1234 (26) Immediate use--A sterile preparation that is not prepared according to USP 797 standards
1235 (i.e., outside the pharmacy and most likely not by pharmacy personnel) which shall be stored for
1236 no longer than one hour after completion of the preparation.
1237
- 1238 (27) IPA--Isopropyl alcohol (2-propanol).
1239
- 1240 (28) Labeling--All labels and other written, printed, or graphic matter on an immediate
1241 container of an article or preparation or on, or in, any package or wrapper in which it is
1242 enclosed, except any outer shipping container. The term "label" designates that part of the
1243 labeling on the immediate container.
1244
- 1245 (29) Media-Fill Test--A test used to qualify aseptic technique of compounding personnel or
1246 processes and to ensure that the processes used are able to produce sterile preparation without
1247 microbial contamination. During this test, a microbiological growth medium such as Soybean-
1248 Casein Digest Medium is substituted for the actual drug preparation to simulate admixture
1249 compounding. The issues to consider in the development of a media-fill test are the following:
1250 media-fill procedures, media selection, fill volume, incubation, time and temperature, inspection
1251 of filled units, documentation, interpretation of results, and possible corrective actions required.
1252
- 1253 (30) Multiple-Dose Container--A multiple-unit container for articles or preparations intended for
1254 potential administration only and usually contains antimicrobial preservatives. The beyond-use
1255 date for an opened or entered (e.g., needle-punctured) multiple-dose container with
1256 antimicrobial preservatives is 28 days, unless otherwise specified by the manufacturer.
1257
- 1258 (31) Negative Pressure Room--A room that is at a lower pressure compared to adjacent
1259 spaces and, therefore, the net flow of air is into the room.
1260
- 1261 (32) Office use--The administration of a compounded drug to a patient by a practitioner in the
1262 practitioner's office or by the practitioner in a health care facility or treatment setting, including a
1263 hospital, ambulatory surgical center, or pharmacy in accordance with Chapter 562 of the Act, or
1264 for administration or provision by a veterinarian in accordance with §563.054 of the Act.
1265

1266 (33) Pharmacy Bulk Package--A container of a sterile preparation for potential use that
1267 contains many single doses. The contents are intended for use in a pharmacy admixture
1268 program and are restricted to the preparation of admixtures for infusion or, through a sterile
1269 transfer device, for the filling of empty sterile syringes. The closure shall be penetrated only one
1270 time after constitution with a suitable sterile transfer device or dispensing set, which allows
1271 measured dispensing of the contents. The pharmacy bulk package is to be used only in a
1272 suitable work area such as a laminar flow hood (or an equivalent clean air compounding area).
1273

1274 (34) Prepackaging--The act of repackaging and relabeling quantities of drug products from a
1275 manufacturer's original container into unit dose packaging or a multiple dose container for
1276 distribution within a facility licensed as a Class C pharmacy or to other pharmacies under
1277 common ownership for distribution within those facilities. The term as defined does not prohibit
1278 the prepackaging of drug products for use within other pharmacy classes.
1279

1280 (35) Preparation or Compounded Sterile Preparation--A sterile admixture compounded in a
1281 licensed pharmacy or other healthcare-related facility pursuant to the order of a licensed
1282 prescriber. The components of the preparation may or may not be sterile products.
1283

1284 (36) Primary Engineering Control--A device or room that provides an ISO Class 5 environment
1285 for the exposure of critical sites when compounding sterile preparations. Such devices include,
1286 but may not be limited to, laminar airflow workbenches, biological safety cabinets, compounding
1287 aseptic isolators, and compounding aseptic containment isolators.
1288

1289 (37) Product--A commercially manufactured sterile drug or nutrient that has been evaluated for
1290 safety and efficacy by the U.S. Food and Drug Administration (FDA). Products are accompanied
1291 by full prescribing information, which is commonly known as the FDA-approved manufacturer's
1292 labeling or product package insert.
1293

1294 (38) Positive Control--A quality assurance sample prepared to test positive for microbial
1295 growth.
1296

1297 (39) ~~Positive Pressure Room--A room that is at a higher pressure compared to adjacent spaces~~
1298 ~~and, therefore, the net airflow is out of the room.]~~
1299

1300 ~~[(40)]~~ Quality assurance--The set of activities used to ensure that the process used in the
1301 preparation of sterile drug preparations lead to preparations that meet predetermined standards
1302 of quality.
1303

1304 **(40)** ~~[(41)]~~ Quality control--The set of testing activities used to determine that the ingredients,
1305 components (e.g., containers), and final compounded sterile preparations prepared meet
1306 predetermined requirements with respect to identity, purity, non-pyrogenicity, and sterility.
1307

1308 **(41)** ~~[(42)]~~ Reasonable quantity--An amount of a compounded drug that:
1309

1310 (A) does not exceed the amount a practitioner anticipates may be used in the practitioner's
1311 office or facility before the beyond use date of the drug;
1312

1313 (B) is reasonable considering the intended use of the compounded drug and the nature of the
1314 practitioner's practice; and
1315

1316 (C) for any practitioner and all practitioners as a whole, is not greater than an amount the
1317 pharmacy is capable of compounding in compliance with pharmaceutical standards for identity,
1318 strength, quality, and purity of the compounded drug that are consistent with United States
1319 Pharmacopoeia guidelines and accreditation practices.

1320
1321 **(42)** ~~[(43)]~~ Segregated Compounding Area--A designated space, either a demarcated area or
1322 room, that is restricted to preparing low-risk level compounded sterile preparations with 12-hour
1323 or less beyond-use date. Such area shall contain a device that provides unidirectional airflow of
1324 ISO Class 5 air quality for preparation of compounded sterile preparations and shall be void of
1325 activities and materials that are extraneous to sterile compounding.

1326
1327 **(43)** ~~[(44)]~~ Single-dose container--A single-unit container for articles or preparations intended
1328 for parenteral administration only. It is intended for a single use. A single-dose container is
1329 labeled as such. Examples of single-dose containers include pre-filled syringes, cartridges,
1330 fusion-sealed containers, and closure-sealed containers when so labeled.

1331
1332 **(44)** ~~[(45)]~~ SOPs--Standard operating procedures.

1333
1334 **(45)** ~~[(46)]~~ Sterilizing Grade Membranes--Membranes that are documented to retain 100% of a
1335 culture of 10⁷ microorganisms of a strain of *Brevundimonas* (*Pseudomonas*) *diminuta* per
1336 square centimeter of membrane surface under a pressure of not less than 30 psi (2.0 bar). Such
1337 filter membranes are nominally at 0.22- μ m or 0.2- μ m nominal pore size, depending on the
1338 manufacturer's practice.

1339
1340 **(46)** ~~[(47)]~~ Sterilization by Filtration--Passage of a fluid or solution through a sterilizing grade
1341 membrane to produce a sterile effluent.

1342
1343 **(47)** ~~[(48)]~~ Terminal Sterilization--The application of a lethal process, e.g., steam under
1344 pressure or autoclaving, to sealed final preparation containers for the purpose of achieving a
1345 predetermined sterility assurance level of usually less than 10⁻⁶ or a probability of less than one
1346 in one million of a non-sterile unit.

1347
1348 **(48)** ~~[(49)]~~ Unidirectional Flow--An airflow moving in a single direction in a robust and uniform
1349 manner and at sufficient speed to reproducibly sweep particles away from the critical processing
1350 or testing area.

1351
1352 **(49)** ~~[(50)]~~ USP/NF--The current edition of the United States Pharmacopoeia/National Formulary.

1353
1354 (c) Personnel.

1355
1356 (1) Pharmacist-in-charge.

1357
1358 (A) General. The pharmacy shall have a pharmacist-in-charge in compliance with the specific
1359 license classification of the pharmacy.

1360
1361 (B) Responsibilities. In addition to the responsibilities for the specific class of pharmacy, the
1362 pharmacist-in-charge shall have the responsibility for, at a minimum, the following concerning
1363 the compounding of sterile preparations:

1364

1365 (i) developing a system to ensure that all pharmacy personnel responsible for compounding
1366 and/or supervising the compounding of sterile preparations within the pharmacy receive
1367 appropriate education and training and competency evaluation;
1368

1369 (ii) determining that all personnel involved in compounding sterile preparations obtain
1370 continuing education appropriate for the type of compounding done by the personnel;
1371

1372 (iii) supervising a system to ensure appropriate procurement of drugs and devices and
1373 storage of all pharmaceutical materials including pharmaceuticals, components used in the
1374 compounding of sterile preparations, and drug delivery devices;
1375

1376 (iv) ensuring that the equipment used in compounding is properly maintained;
1377

1378 (v) developing a system for the disposal and distribution of drugs from the pharmacy;
1379

1380 (vi) developing a system for bulk compounding or batch preparation of drugs;
1381

1382 (vii) developing a system for the compounding, sterility assurance, quality assurance, and
1383 quality control of sterile preparations; and
1384

1385 (viii) if applicable, ensuring that the pharmacy has a system to dispose of hazardous waste
1386 in a manner so as not to endanger the public health.
1387

1388 (2) Pharmacists.

1389 (A) General.

1390 (i) A pharmacist is responsible for ensuring that compounded sterile preparations are
1391 accurately identified, measured, diluted, and mixed and are correctly purified, sterilized,
1392 packaged, sealed, labeled, stored, dispensed, and distributed.
1393

1394 (ii) A pharmacist shall inspect and approve all components, drug preparation containers,
1395 closures, labeling, and any other materials involved in the compounding process.
1396

1397 (iii) A pharmacist shall review all compounding records for accuracy and conduct in-process
1398 and final checks and verification of calculations to ensure that errors have not occurred in the
1399 compounding process.
1400

1401 (iv) A pharmacist is responsible for ensuring the proper maintenance, cleanliness, and use
1402 of all equipment used in the compounding process.
1403

1404 (v) A pharmacist shall be accessible at all times, 24 hours a day, to respond to patients' and
1405 other health professionals' questions and needs.
1406

1407 (B) Prior to September 1, 2015 - initial training and continuing education.
1408

1409 (i) All pharmacists who compound sterile preparations for administration to patients or
1410 supervise pharmacy technicians and pharmacy technician trainees compounding sterile
1411 preparations shall:
1412
1413
1414

1415 (I) complete through a single course, a minimum of 20 hours of instruction and experience
1416 in the areas listed in paragraph (4)(D) of this subsection. Such training may be obtained
1417 through:

1418
1419 (-a-) completion of a structured on-the-job didactic and experiential training program at
1420 this pharmacy which provides 20 hours of instruction and experience. Such training may not be
1421 transferred to another pharmacy unless the pharmacies are under common ownership and
1422 control and use a common training program; or

1423
1424 (-b-) completion of a recognized course in an accredited college of pharmacy or a course
1425 sponsored by an ACPE accredited provider which provides 20 hours of instruction and
1426 experience;

1427
1428 (II) possess knowledge about:

1429
1430 (-a-) aseptic processing;

1431
1432 (-b-) quality control and quality assurance as related to environmental, component, and
1433 finished preparation release checks and tests;

1434
1435 (-c-) chemical, pharmaceutical, and clinical properties of drugs;

1436
1437 (-d-) container, equipment, and closure system selection; and

1438
1439 (-e-) sterilization techniques.

1440
1441 (ii) The required experiential portion of the training programs specified in this subparagraph
1442 must be supervised by an individual who has already completed training as specified in this
1443 paragraph or paragraph (3) of this subsection.

1444
1445 (iii) All pharmacists engaged in compounding sterile preparations shall obtain continuing
1446 education appropriate for the type of compounding done by the pharmacist.

1447
1448 (C) Effective September 1, 2015 - initial training and continuing education.

1449
1450 (i) All pharmacists who compound sterile preparations or supervise pharmacy technicians
1451 and pharmacy technician trainees compounding sterile preparations shall comply with the
1452 following:

1453
1454 (I) complete through a single course, a minimum of 20 hours of instruction and experience
1455 in the areas listed in paragraph (4)(D) of this subsection. Such training shall be obtained through
1456 completion of a recognized course in an accredited college of pharmacy or a course sponsored
1457 by an ACPE accredited provider;

1458
1459 (II) complete a structured on-the-job didactic and experiential training program at this
1460 pharmacy which provides sufficient hours of instruction and experience in the facility's sterile
1461 compounding processes and procedures. Such training may not be transferred to another
1462 pharmacy unless the pharmacies are under common ownership and control and use a common
1463 training program; and

1464
1465 (III) possess knowledge about:

1466
1467 (-a-) aseptic processing;
1468
1469 (-b-) quality control and quality assurance as related to environmental, component, and
1470 finished preparation release checks and tests;
1471
1472 (-c-) chemical, pharmaceutical, and clinical properties of drugs;
1473
1474 (-d-) container, equipment, and closure system selection; and
1475
1476 (-e-) sterilization techniques.
1477
1478 (ii) The required experiential portion of the training programs specified in this subparagraph
1479 must be supervised by an individual who is actively engaged in performing sterile compounding
1480 and is qualified and has completed training as specified in this paragraph or paragraph (3) of
1481 this subsection.
1482
1483 (iii) In order to renew a license to practice pharmacy, during the previous licensure period, a
1484 pharmacist engaged in sterile compounding shall complete a minimum of:
1485
1486 (I) two hours of ACPE-accredited continuing education relating to one or more of the areas
1487 listed in paragraph (4)(D) of this subsection if the pharmacist is engaged in compounding low
1488 and medium risk sterile preparations; or
1489
1490 (II) four hours of ACPE-accredited continuing education relating to one or more of the
1491 areas listed in paragraph (4)(D) of this subsection if the pharmacist is engaged in compounding
1492 high risk sterile preparations.
1493
1494 (3) Pharmacy technicians and pharmacy technician trainees.
1495
1496 (A) General. All pharmacy technicians and pharmacy technician trainees shall meet the
1497 training requirements specified in §297.6 of this title (relating to Pharmacy Technician and
1498 Pharmacy Technician Trainee Training).
1499
1500 (B) Prior to September 1, 2015 - initial training and continuing education. In addition to
1501 specific qualifications for registration, all pharmacy technicians and pharmacy technician
1502 trainees who compound sterile preparations for administration to patients shall:
1503
1504 (i) have initial training obtained either through completion of:
1505
1506 (I) a single course, a minimum of 40 hours of instruction and experience in the areas listed
1507 in paragraph (4)(D) of this subsection. Such training may be obtained through:
1508
1509 (-a-) completion of a structured on-the-job didactic and experiential training program at
1510 this pharmacy which provides 40 hours of instruction and experience. Such training may not be
1511 transferred to another pharmacy unless the pharmacies are under common ownership and
1512 control and use a common training program; or
1513
1514 (-b-) completion of a course sponsored by an ACPE accredited provider which provides
1515 40 hours of instruction and experience; or
1516

1517 (II) a training program which is accredited by the American Society of Health-System
1518 Pharmacists. Individuals enrolled in training programs accredited by the American Society of
1519 Health-System Pharmacists may compound sterile preparations in a licensed pharmacy
1520 provided:

1521
1522 (-a-) the compounding occurs only during times the individual is assigned to a pharmacy
1523 as a part of the experiential component of the American Society of Health-System Pharmacists
1524 training program;

1525
1526 (-b-) the individual is under the direct supervision of and responsible to a pharmacist who
1527 has completed training as specified in paragraph (2) of this subsection; and

1528
1529 (-c-) the supervising pharmacist conducts in-process and final checks.

1530
1531 (ii) acquire the required experiential portion of the training programs specified in this
1532 subparagraph under the supervision of an individual who has already completed training as
1533 specified in paragraph (2) of this subsection or this paragraph.

1534
1535 (C) Effective September 1, 2015 - initial training and continuing education.

1536
1537 (i) Pharmacy technicians and pharmacy technician trainees may compound sterile
1538 preparations provided the pharmacy technicians and/or pharmacy technician trainees are
1539 supervised by a pharmacist who has completed the training specified in paragraph (2) of this
1540 subsection, conducts in-process and final checks, and affixes his or her initials to the
1541 appropriate quality control records.

1542
1543 (ii) All pharmacy technicians and pharmacy technician trainees who compound sterile
1544 preparations for administration to patients shall:

1545
1546 (I) have initial training obtained either through completion of:

1547
1548 (-a-) a single course, a minimum of 40 hours of instruction and experience in the areas
1549 listed in paragraph (4)(D) of this subsection. Such training shall be obtained through completion
1550 of a course sponsored by an ACPE accredited provider which provides 40 hours of instruction
1551 and experience; or

1552
1553 (-b-) a training program which is accredited by the American Society of Health-System
1554 Pharmacists.

1555
1556 (II) and

1557
1558 (-a-) complete a structured on-the-job didactic and experiential training program at this
1559 pharmacy which provides sufficient hours of instruction and experience in the facility's sterile
1560 compounding processes and procedures. Such training may not be transferred to another
1561 pharmacy unless the pharmacies are under common ownership and control and use a common
1562 training program; and

1563
1564 (-b-) possess knowledge about:

1565
1566 (-1-) aseptic processing;

1567

1568 (-2-) quality control and quality assurance as related to environmental, component, and
1569 finished preparation release checks and tests;

1570
1571 (-3-) chemical, pharmaceutical, and clinical properties of drugs;

1572
1573 (-4-) container, equipment, and closure system selection; and

1574
1575 (-5-) sterilization techniques.

1576
1577 (iii) Individuals enrolled in training programs accredited by the American Society of Health-
1578 System Pharmacists may compound sterile preparations in a licensed pharmacy provided:

1579
1580 (I) the compounding occurs only during times the individual is assigned to a pharmacy as a
1581 part of the experiential component of the American Society of Health-System Pharmacists
1582 training program;

1583
1584 (II) the individual is under the direct supervision of and responsible to a pharmacist who
1585 has completed training as specified in paragraph (2) of this subsection; and

1586
1587 (III) the supervising pharmacist conducts in-process and final checks.

1588
1589 (iv) The required experiential portion of the training programs specified in this subparagraph
1590 must be supervised by an individual who is actively engaged in performing sterile compounding,
1591 is qualified and has completed training as specified in paragraph (2) of this subsection or this
1592 paragraph.

1593
1594 (v) In order to renew a registration as a pharmacy technician, during the previous
1595 registration period, a pharmacy technician engaged in sterile compounding shall complete a
1596 minimum of:

1597
1598 (I) two hours of ACPE accredited continuing education relating to one or more of the areas
1599 listed in paragraph (4)(D) of this subsection if the pharmacy technician is engaged in
1600 compounding low and medium risk sterile preparations; or

1601
1602 (II) four hours of ACPE accredited continuing education relating to one or more of the
1603 areas listed in paragraph (4)(D) of this subsection if pharmacy technician is engaged in
1604 compounding high risk sterile preparations.

1605
1606 (4) Evaluation and testing requirements.

1607
1608 (A) All pharmacy personnel preparing sterile preparations shall be trained conscientiously and
1609 skillfully by expert personnel through multimedia instructional sources and professional
1610 publications in the theoretical principles and practical skills of aseptic manipulations, garbing
1611 procedures, aseptic work practices, achieving and maintaining ISO Class 5 environmental
1612 conditions, and cleaning and disinfection procedures before beginning to prepare compounded
1613 sterile preparations.

1614
1615 (B) All pharmacy personnel preparing sterile preparations shall perform didactic review and
1616 pass written and media-fill testing of aseptic manipulative skills initially followed by:

1617
1618 (i) every 12 months for low- and medium-risk level compounding; and

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

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

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

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

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

(i) aseptic technique;

(ii) critical area contamination factors;

(iii) environmental monitoring;

(iv) structure and engineering controls related to facilities;

(v) equipment and supplies;

(vi) sterile preparation calculations and terminology;

(vii) sterile preparation compounding documentation;

(viii) quality assurance procedures;

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

(x) handling of hazardous drugs, if applicable;

(xi) cleaning procedures; and

(xii) general conduct in the clean room.

(E) The aseptic technique of each person compounding or responsible for the direct supervision of personnel compounding sterile preparations shall be observed and evaluated by expert personnel as satisfactory through written and practical tests, and media-fill challenge testing, and such evaluation documented.

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

1670
1671 (G) Media-fill tests procedures for assessing the preparation of specific types of sterile
1672 preparations shall be representative of the most challenging or stressful conditions encountered
1673 by the pharmacy personnel being evaluated for each risk level and for sterilizing high-risk level
1674 compounded sterile preparations.

1675
1676 (H) Media-fill challenge tests simulating high-risk level compounding shall be used to verify
1677 the capability of the compounding environment and process to produce a sterile preparation.

1678
1679 (I) Commercially available sterile fluid culture media, such as Soybean-Casein Digest
1680 Medium shall be able to promote exponential colonization of bacteria that are most likely to be
1681 transmitted to compounding sterile preparations from the compounding personnel and
1682 environment. Media-filled vials are generally incubated at 20 to 25 **degrees Celsius** or at 30 to
1683 35 **degrees Celsius** for a minimum of 14 days. If two temperatures are used for incubation of
1684 media-filled samples, then these filled containers should be incubated for at least 7 days at each
1685 temperature. Failure is indicated by visible turbidity in the medium on or before 14 days.

1686
1687 (J) The pharmacist-in-charge shall ensure continuing competency of pharmacy personnel
1688 through in-service education, training, and media-fill tests to supplement initial training.
1689 Personnel competency shall be evaluated:

1690 (i) during orientation and training prior to the regular performance of those tasks;

1691
1692 (ii) whenever the quality assurance program yields an unacceptable result;

1693
1694 (iii) whenever unacceptable techniques are observed; and

1695
1696 (iv) at least on an annual basis for low- and medium-risk level compounding, and every six
1697 months for high-risk level compounding.

1698
1699 (K) The pharmacist-in-charge shall ensure that proper hand hygiene and garbing practices of
1700 compounding personnel are evaluated prior to compounding sterile preparations intended for
1701 patient use and whenever an aseptic media fill is performed.

1702
1703 (i) Sampling of compounding personnel glove fingertips shall be performed for all risk level
1704 compounding.

1705
1706 (ii) All compounding personnel shall demonstrate competency in proper hand hygiene and
1707 garbing procedures and in aseptic work practices (e.g., disinfection of component surfaces,
1708 routine disinfection of gloved hands).

1709
1710 (iii) Sterile contact agar plates shall be used to sample the gloved fingertips of compounding
1711 personnel after garbing in order to assess garbing competency and after completing the media-
1712 fill preparation (without applying sterile 70% IPA).

1713
1714 (iv) The visual observation shall be documented and maintained to provide a permanent
1715 record and long-term assessment of personnel competency.

1716
1717 (v) All compounding personnel shall successfully complete an initial competency evaluation
1718 and gloved fingertip/thumb sampling procedure no less than three times before initially being
1719 allowed to compound sterile preparations for patient use. Immediately after the compounding
1720

1721 personnel completes the hand hygiene and garbing procedure (e.g., donning of sterile gloves
1722 prior to any disinfection with sterile 70% IPA), the evaluator will collect a gloved fingertip and
1723 thumb sample from both hands from the compounding personnel onto agar plates by lightly
1724 pressing each fingertip into the agar. The plates will be incubated for the appropriate incubation
1725 period and at the appropriate temperature. Re-evaluation of all compounding personnel shall
1726 occur at least annually for compounding personnel who compound low and medium risk level
1727 preparations and every six months for compounding personnel who compound high risk level
1728 preparations.

1729
1730 (L) The pharmacist-in-charge shall ensure surface sampling shall be conducted in all ISO
1731 classified areas on a periodic basis. Sampling shall be accomplished using contact plates at the
1732 conclusion of compounding. The sample area shall be gently touched with the agar surface by
1733 rolling the plate across the surface to be sampled.

1734
1735 (5) Documentation of Training. The pharmacy shall maintain a record of the training and
1736 continuing education on each person who compounds sterile preparations. The record shall
1737 contain, at a minimum, a written record of initial and in-service training, education, and the
1738 results of written and practical testing and media-fill testing of pharmacy personnel. The record
1739 shall be maintained and available for inspection by the board and contain the following
1740 information:

1741 (A) name of the person receiving the training or completing the testing or media-fill tests;

1742 (B) date(s) of the training, testing, or media-fill challenge testing;

1743 (C) general description of the topics covered in the training or testing or of the process
1744 validated;

1745 (D) name of the person supervising the training, testing, or media-fill challenge testing; and

1746 (E) signature or initials of the person receiving the training or completing the testing or media-
1747 fill challenge testing and the pharmacist-in-charge or other pharmacist employed by the
1748 pharmacy and designated by the pharmacist-in-charge as responsible for training, testing, or
1749 media-fill challenge testing of personnel.

1750
1751 (d) Operational Standards.

1752 (1) General Requirements.

1753 (A) Sterile preparations may be compounded:

1754 (i) upon presentation of a practitioner's prescription drug or medication order based on a
1755 valid pharmacist/patient/prescriber relationship;

1756 (ii) in anticipation of future prescription drug or medication orders based on routine, regularly
1757 observed prescribing patterns; or

1758 (iii) in reasonable quantities for office use by a practitioner and for use by a veterinarian.

1759 (B) Sterile compounding in anticipation of future prescription drug or medication orders must
1760 be based upon a history of receiving valid prescriptions issued within an established
1761

1772 pharmacist/patient/prescriber relationship, provided that in the pharmacist's professional
1773 judgment the quantity prepared is stable for the anticipated shelf time.

1774
1775 (i) The pharmacist's professional judgment shall be based on the criteria used to determine
1776 a beyond-use date outlined in paragraph (6)(G) of this subsection.

1777
1778 (ii) Documentation of the criteria used to determine the stability for the anticipated shelf time
1779 must be maintained and be available for inspection.

1780
1781 (iii) Any preparation compounded in anticipation of future prescription drug or medication
1782 orders shall be labeled. Such label shall contain:

1783
1784 (I) name and strength of the compounded preparation or list of the active ingredients and
1785 strengths;

1786
1787 (II) facility's lot number;

1788
1789 (III) beyond-use date as determined by the pharmacist using appropriate documented
1790 criteria as outlined in paragraph (6)(G) of this subsection;

1791
1792 (IV) quantity or amount in the container;

1793
1794 (V) appropriate ancillary instructions, such as storage instructions or cautionary
1795 statements, including hazardous drug warning labels where appropriate; and

1796
1797 (VI) device-specific instructions, where appropriate.

1798
1799 (C) Commercially available products may be compounded for dispensing to individual
1800 patients or for office use provided the following conditions are met:

1801
1802 (i) the commercial product is not reasonably available from normal distribution channels in a
1803 timely manner to meet **individual** patient's needs;

1804
1805 (ii) the pharmacy maintains documentation that the product is not reasonably available due to
1806 a drug shortage or unavailability from the manufacturer; and

1807
1808 (iii) the prescribing practitioner has requested that the drug be compounded as described in
1809 subparagraph (D) of this paragraph.

1810
1811 (D) A pharmacy may not compound preparations that are essentially copies of commercially
1812 available products (e.g., the preparation is dispensed in a strength that is only slightly different
1813 from a commercially available product) unless the prescribing practitioner specifically orders the
1814 strength or dosage form and specifies why the **individual** patient needs the particular strength
1815 or dosage form of the preparation or why the preparation for office use is needed in the
1816 particular strength or dosage form of the preparation. The prescribing practitioner shall provide
1817 documentation of a patient specific medical need and the preparation produces a clinically
1818 significant therapeutic response (e.g., the physician requests an alternate preparation due to
1819 hypersensitivity to excipients or preservative in the FDA-approved product, or the physician
1820 requests an effective alternate dosage form) or if the drug product is not commercially available.
1821 The unavailability of such drug product must be documented prior to compounding. The
1822 methodology for documenting unavailability includes maintaining a copy of the wholesaler's

1823 notification showing back-ordered, discontinued, or out-of-stock items. This documentation must
1824 be available in hard-copy or electronic format for inspection by the board.

1825
1826 (E) A pharmacy may enter into an agreement to compound and dispense
1827 prescription/medication orders for another pharmacy provided the pharmacy complies with the
1828 provisions of §291.125 of this title (relating to Centralized Prescription Dispensing).

1829
1830 (F) Compounding pharmacies/pharmacists may advertise and promote the fact that they
1831 provide sterile prescription compounding services, which may include specific drug preparations
1832 and classes of drugs.

1833
1834 (G) A pharmacy may not compound veterinary preparations for use in food producing animals
1835 except in accordance with federal guidelines.

1836
1837 **(H) Compounded sterile preparations, including hazardous drugs and**
1838 **radiopharmaceuticals, shall be prepared only under conditions that protect the pharmacy**
1839 **personnel in the preparation and storage areas.**

1840
1841 (2) Microbial Contamination Risk Levels. Risk Levels for sterile compounded preparations shall
1842 be as outlined in Chapter 797, Pharmacy Compounding--Sterile Preparations of the USP/NF
1843 and as listed in this paragraph.

1844
1845 (A) Low-risk level compounded sterile preparations.

1846
1847 (i) Low-Risk conditions. Low-risk level compounded sterile preparations are those
1848 compounded under all of the following conditions.

1849
1850 (I) The compounded sterile preparations are compounded with aseptic manipulations
1851 entirely within ISO Class 5 or better air quality using only sterile ingredients, products,
1852 components, and devices.

1853
1854 (II) The compounding involves only transfer, measuring, and mixing manipulations using
1855 not more than three commercially manufactured packages of sterile products and not more than
1856 two entries into any one sterile container or package (e.g., bag, vial) of sterile product or
1857 administration container/device to prepare the compounded sterile preparation.

1858
1859 (III) Manipulations are limited to aseptically opening ampuls, penetrating disinfected
1860 stoppers on vials with sterile needles and syringes, and transferring sterile liquids in sterile
1861 syringes to sterile administration devices, package containers of other sterile products, and
1862 containers for storage and dispensing.

1863
1864 (IV) For a low-risk preparation, in the absence of direct sterility testing results or
1865 appropriate information sources that justify different limits, the storage periods may not exceed
1866 the following periods: before administration the compounded sterile preparation is stored
1867 properly and are exposed for not more than 48 hours at controlled room temperature, for not
1868 more than 14 days if stored at a cold temperature, and for 45 days if stored in a frozen state
1869 between minus 25 degrees Celsius and minus 10 degrees Celsius. For delayed activation
1870 device systems, the storage period begins when the device is activated.

1871
1872 (ii) Examples of Low-Risk Compounding. Examples of low-risk compounding include the
1873 following.

1874
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(I) Single volume transfers of sterile dosage forms from ampuls, bottles, bags, and vials using sterile syringes with sterile needles, other administration devices, and other sterile containers. The solution content of ampules shall be passed through a sterile filter to remove any particles.

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

(III) Preparation of radiopharmaceuticals from FDA-approved drug products.

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

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

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

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

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

(C) Medium-risk level compounded sterile preparations.

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

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

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

1924 (III) The compounding process requires unusually long duration, such as that required to
1925 complete the dissolution or homogenous mixing (e.g., reconstitution of intravenous
1926 immunoglobulin or other intravenous protein products).

1927
1928 (IV) The compounded sterile preparations do not contain broad spectrum bacteriostatic
1929 substances and they are administered over several days (e.g., an externally worn infusion
1930 device).

1931
1932 (V) For a medium-risk preparation, in the absence of direct sterility testing results the
1933 beyond use dates may not exceed the following time periods: before administration, the
1934 compounded sterile preparations are properly stored and are exposed for not more than 30
1935 hours at controlled room temperature, for not more than 9 days at a cold temperature, and for
1936 45 days in solid frozen state between minus 25 degrees Celsius and minus 10 degrees Celsius.

1937
1938 (ii) Examples of medium-risk compounding. Examples of medium-risk compounding include
1939 the following.

1940
1941 (I) Compounding of total parenteral nutrition fluids using a manual or automated device
1942 during which there are multiple injections, detachments, and attachments of nutrient source
1943 products to the device or machine to deliver all nutritional components to a final sterile
1944 container.

1945
1946 (II) Filling of reservoirs of injection and infusion devices with more than three sterile drug
1947 products and evacuations of air from those reservoirs before the filled device is dispensed.

1948
1949 (III) Filling of reservoirs of injection and infusion devices with volumes of sterile drug
1950 solutions that will be administered over several days at ambient temperatures between 25 and
1951 40 degrees Celsius (77 and 104 degrees Fahrenheit).

1952
1953 (IV) Transfer of volumes from multiple ampuls or vials into a single, final sterile container or
1954 product.

1955
1956 (D) High-risk level compounded sterile preparations.

1957
1958 (i) High-risk Conditions. High-risk level compounded sterile preparations are those
1959 compounded under any of the following conditions.

1960
1961 (I) Non-sterile ingredients, including manufactured products not intended for sterile routes
1962 of administration (e.g., oral) are incorporated or a non-sterile device is employed before terminal
1963 sterilization.

1964
1965 (II) Any of the following are exposed to air quality worse than ISO Class 5 for more than 1
1966 hour:

1967
1968 (-a-) sterile contents of commercially manufactured products;

1969
1970 (-b-) CSPs that lack effective antimicrobial preservatives; and

1971
1972 (-c-) sterile surfaces of devices and containers for the preparation, transfer, sterilization,
1973 and packaging of CSPs.

1974

1975 (III) Compounding personnel are improperly garbed and gloved.
1976
1977 (IV) Non-sterile water-containing preparations are exposed no more than 6 hours before
1978 being sterilized.
1979
1980 (V) It is assumed, and not verified by examination of labeling and documentation from
1981 suppliers or by direct determination, that the chemical purity and content strength of ingredients
1982 meet their original or compendial specifications in unopened or in opened packages of bulk
1983 ingredients.
1984
1985 (VI) For a sterilized high-risk level preparation, in the absence of passing a sterility test, the
1986 storage periods cannot exceed the following time periods: before administration, the
1987 compounded sterile preparations are properly stored and are exposed for not more than 24
1988 hours at controlled room temperature, for not more than 3 days at a cold temperature, and for
1989 45 days in solid frozen state between minus 25 degrees Celsius and minus 10 degrees Celsius.
1990
1991 (VII) All non-sterile measuring, mixing, and purifying devices are rinsed thoroughly with
1992 sterile, pyrogen-free water, and then thoroughly drained or dried immediately before use for
1993 high-risk compounding. All high-risk compounded sterile solutions subjected to terminal
1994 sterilization are prefiltered by passing through a filter with a nominal pore size not larger than
1995 1.2 micron preceding or during filling into their final containers to remove particulate matter.
1996 Sterilization of high-risk level compounded sterile preparations by filtration shall be performed
1997 with a sterile 0.2 micrometer or 0.22 micrometer nominal pore size filter entirely within an ISO
1998 Class 5 or superior air quality environment.
1999
2000 (ii) Examples of high-risk compounding. Examples of high-risk compounding include the
2001 following.
2002
2003 (I) Dissolving non-sterile bulk drug powders to make solutions, which will be terminally
2004 sterilized.
2005
2006 (II) Exposing the sterile ingredients and components used to prepare and package
2007 compounded sterile preparations to room air quality worse than ISO Class 5 for more than one
2008 hour.
2009
2010 (III) Measuring and mixing sterile ingredients in non-sterile devices before sterilization is
2011 performed.
2012
2013 (IV) Assuming, without appropriate evidence or direct determination, that packages of bulk
2014 ingredients contain at least 95% by weight of their active chemical moiety and have not been
2015 contaminated or adulterated between uses.
2016
2017 (3) Immediate Use Compounded Sterile Preparations. For the purpose of emergency or
2018 immediate patient care, such situations may include cardiopulmonary resuscitation, emergency
2019 room treatment, preparation of diagnostic agents, or critical therapy where the preparation of the
2020 compounded sterile preparation under low-risk level conditions would subject the patient to
2021 additional risk due to delays in therapy. Compounded sterile preparations are exempted from
2022 the requirements described in this paragraph for low-risk level compounded sterile preparations
2023 when all of the following criteria are met.
2024

2025 (A) Only simple aseptic measuring and transfer manipulations are performed with not more
2026 than three sterile non-hazardous commercial drug and diagnostic radiopharmaceutical drug
2027 products, including an infusion or diluent solution, from the manufacturers' original containers
2028 and not more than two entries into any one container or package of sterile infusion solution or
2029 administration container/device.

2030
2031 (B) Unless required for the preparation, the compounding procedure occurs continuously
2032 without delays or interruptions and does not exceed 1 hour.

2033
2034 (C) During preparation, aseptic technique is followed and, if not immediately administered,
2035 the finished compounded sterile preparation is under continuous supervision to minimize the
2036 potential for contact with nonsterile surfaces, introduction of particulate matter of biological
2037 fluids, mix-ups with other compounded sterile preparations, and direct contact of outside
2038 surfaces.

2039
2040 (D) Administration begins not later than one hour following the completion of preparing the
2041 compounded sterile preparation.

2042
2043 (E) When the compounded sterile preparations is not administered by the person who
2044 prepared it, or its administration is not witnessed by the person who prepared it, the
2045 compounded sterile preparation shall bear a label listing patient identification information such
2046 as name and identification number(s), the names and amounts of all ingredients, the name or
2047 initials of the person who prepared the compounded sterile preparation, and the exact 1-hour
2048 beyond-use time and date.

2049
2050 (F) If administration has not begun within one hour following the completion of preparing the
2051 compounded sterile preparation, the compounded sterile preparation is promptly and safely
2052 discarded. Immediate use compounded sterile preparations shall not be stored for later use.

2053
2054 (G) Hazardous drugs shall not be prepared as immediate use compounded sterile
2055 preparations.

2056 (4) Single-dose and multiple dose containers.

2057
2058 (A) Opened or needle punctured single-dose containers, such as bags bottles, syringes, and
2059 vials of sterile products shall be used within one hour if opened in worse than ISO Class 5 air
2060 quality. Any remaining contents must be discarded.

2061
2062 (B) Single-dose containers, including single-dose large volume parenteral solutions and
2063 single-dose vials, exposed to ISO Class 5 or cleaner air may be used up to six hours after initial
2064 needle puncture.

2065
2066 (C) Opened single-dose fusion sealed containers shall not be stored for any time period.

2067
2068 (D) Multiple-dose containers may be used up to 28 days after initial needle puncture unless
2069 otherwise specified by the manufacturer.

2070
2071 (5) Library. In addition to the library requirements of the pharmacy's specific license
2072 classification, a pharmacy shall maintain current or updated copies in hard-copy or electronic
2073 format of each of the following:
2074
2075

2076 (A) a reference text on injectable drug preparations, such as Handbook on Injectable Drug
2077 Products;

2078
2079 (B) a specialty reference text appropriate for the scope of pharmacy services provided by the
2080 pharmacy, e.g., if the pharmacy prepares hazardous drugs, a reference text on the preparation
2081 of hazardous drugs; [and]

2082
2083 (C) the United States Pharmacopeia/National Formulary containing USP Chapter 71, Sterility
2084 Tests, USP Chapter 85, Bacterial Endotoxins Test, Pharmaceutical Compounding--Nonsterile
2085 Preparations, USP Chapter 795, USP Chapter 797, Pharmaceutical Compounding--Sterile
2086 Preparations, and USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding; **and**

2087
2088 **(D) any additional USP/NF chapters applicable to the practice of the pharmacy (e.g.,**
2089 **Chapter 800, Hazardous Drugs—Handling in Healthcare Settings, Chapter 823, Positron**
2090 **Emission Tomography Drugs for Compounding, Investigational, and Research Uses.**

2091
2092 (6) Environment. Compounding facilities shall be physically designed and environmentally
2093 controlled to minimize airborne contamination from contacting critical sites.

2094
2095 (A) Low and Medium Risk Preparations.

2096
2097 (i) A pharmacy that prepares low- and medium-risk preparations shall have a clean room for
2098 the compounding of sterile preparations that is constructed to minimize the opportunities for
2099 particulate and microbial contamination. The clean room shall:

2100
2101 (I) be clean, well lit, and of sufficient size to support sterile compounding activities;

2102
2103 (II) be maintained at a comfortable temperature (e.g., 20 degrees Celsius or cooler)
2104 allowing compounding personnel to perform flawlessly when attired in the required aseptic
2105 compounding garb;

2106
2107 (III) be used only for the compounding of sterile preparations;

2108
2109 (IV) be designed such that hand sanitizing and gowning occurs outside the buffer area but
2110 allows hands-free access by compounding personnel to the buffer area;

2111
2112 (V) have non-porous and washable floors or floor covering to enable regular disinfection;

2113
2114 (VI) be ventilated in a manner to avoid disruption from the HVAC system and room cross-
2115 drafts;

2116
2117 (VII) have walls, ceilings, floors, fixtures, shelving, counters, and cabinets that are smooth,
2118 impervious, free from cracks and crevices (e.g., coved), non-shedding and resistant to damage
2119 by disinfectant agents;

2120
2121 (VIII) have junctures of ceilings to walls coved or caulked to avoid cracks and crevices;

2122
2123 (IX) have drugs and supplies stored on shelving areas above the floor to permit adequate
2124 floor cleaning;

2125

2126 (X) contain only the appropriate compounding supplies and not be used for bulk storage for
2127 supplies and materials. Objects that shed particles shall not be brought into the clean room. **A**
2128 **Class B pharmacy may use low-linting absorbent materials in the primary engineering**
2129 **control device;**

2130
2131 (XI) contain an ante-area that [~~provides at least an ISO class 8 air quality and~~] contains a
2132 sink with hot and cold running water that enables hands-free use with a closed system of soap
2133 dispensing to minimize the risk of extrinsic contamination. **A Class B pharmacy may have a**
2134 **sink with hot and cold running water that enables hands-free use with a closed system of**
2135 **soap dispensing immediately outside the ante-area if antiseptic hand cleansing is**
2136 **performed using a waterless alcohol-based surgical hand scrub with persistent activity**
2137 **following manufacturers' recommendations once inside the ante-area;** and

2138
2139 (XII) contain a buffer area [~~designed to maintain at least ISO Class 7 conditions for 0.5-µm~~
2140 ~~and larger particles under dynamic working conditions~~]. The following is applicable for the buffer
2141 area.

2142
2143 (-a-) There shall be some demarcation designation that delineates the ante-area from the
2144 buffer area. The demarcation shall be such that it does not create conditions that could
2145 adversely affect the cleanliness of the area.

2146
2147 (-b-) The buffer area shall be segregated from surrounding, unclassified spaces to reduce
2148 the risk of contaminants being blown, dragged, or otherwise introduced into the filtered
2149 unidirectional airflow environment, and this segregation should be continuously monitored.

2150
2151 (-c-) A buffer area that is not physically separated from the ante-area shall employ the
2152 principle of displacement airflow as defined in Chapter 797, Pharmaceutical Compounding--
2153 Sterile Preparations, of the USP/NF, with limited access to personnel.

2154
2155 (-d-) The buffer area shall not contain sources of water (i.e., sinks) or floor drains **other**
2156 **than distilled or sterile water introduced for facilitating the use of heat block wells for**
2157 **radiopharmaceuticals.**

2158
2159 (ii) The pharmacy shall prepare sterile preparations in a primary engineering control device,
2160 such as a laminar air flow hood, biological safety cabinet, compounding aseptic isolator,
2161 compounding aseptic containment isolator which is capable of maintaining at least ISO Class 5
2162 conditions for 0.5-µm particles while compounding sterile preparations.

2163
2164 (I) The primary engineering control shall:

2165
2166 (-a-) be located in the buffer area and placed in the buffer area in a manner as to avoid
2167 conditions that could adversely affect its operation such as strong air currents from opened
2168 doors, personnel traffic, or air streams from the heating, ventilating and air condition system.

2169
2170 (-b-) be certified by a qualified independent contractor according to the International
2171 Organization of Standardization (ISO) Classification of Particulate Matter in Room Air (ISO
2172 14644-1) for operational efficiency at least every six months and whenever the device or room is
2173 relocated or altered or major service to the facility is performed, in accordance with the
2174 manufacturer's specifications;

2175

2176 (-c-) have pre-filters inspected periodically and replaced as needed, in accordance with
2177 written policies and procedures and the manufacturer's specification, and the inspection and/or
2178 replacement date documented; and

2179
2180 (-d-) be located in a buffer area that has a minimum differential positive pressure of 0.02
2181 to 0.05 inches water column **as applicable**.

2182
2183 (II) The compounding aseptic isolator or compounding aseptic containment isolator must
2184 be placed in ~~the [an ISO Class 7]~~ buffer area unless the isolator meets all of the following
2185 conditions.

2186
2187 (-a-) The isolator must provide isolation from the room and maintain ISO Class 5 during
2188 dynamic operating conditions including transferring ingredients, components, and devices into
2189 and out of the isolator and during preparation of compounded sterile preparations.

2190
2191 (-b-) Particle counts sampled approximately 6 to 12 inches upstream of the critical
2192 exposure site must maintain ISO Class 5 levels during compounding operations.

2193
2194 (-c-) The pharmacy shall maintain documentation from the manufacturer that the isolator
2195 meets this standard when located in worse than ISO Class 7 environments.

2196
2197 (B) High-risk Preparations.

2198
2199 (i) In addition to the requirements in subparagraph (A) of this paragraph, when high-risk
2200 preparations are compounded, the primary engineering control shall be located in a buffer area
2201 that provides a physical separation, through the use of walls, doors and pass-throughs and has
2202 a minimum differential positive pressure of 0.02 to 0.05 inches water column.

2203
2204 (ii) Presterilization procedures for high-risk level compounded sterile preparations, such as
2205 weighing and mixing, shall be completed in no worse than an ISO Class 8 environment.

2206
2207 (C) Automated compounding device. ~~If automated compounding devices are used, the~~
2208 ~~pharmacy shall have a method to calibrate and verify the accuracy of automated compounding~~
2209 ~~devices used in aseptic processing and document the calibration and verification on a daily~~
2210 ~~basis, based on the manufacturer's recommendations, and review the results at least weekly.~~

2211
2212 **(i) General. If automated compounding devices are used, the pharmacy shall have a**
2213 **method to calibrate and verify the accuracy of automated compounding devices used in**
2214 **aseptic processing and document the calibration and verification on a daily basis, based**
2215 **on the manufacturer's recommendations, and review the results at least weekly.**

2216
2217 **(ii) Loading bulk drugs into automated compounding devices.**

2218
2219 **(I) Automated compounding device may be loaded with bulk drugs only by a pharmacist**
2220 **or by pharmacy technicians or pharmacy technician trainees under the direction and**
2221 **direct supervision of a pharmacist.**

2222
2223 **(II) The label of an automated compounding device container shall indicate the brand**
2224 **name and strength of the drug; or if no brand name, then the generic name, strength, and**
2225 **name of the manufacturer or distributor.**

2227 **(III) Records of loading bulk drugs into an automated compounding device shall be**
2228 **maintained to show:**
2229
2230 **(-a) name of the drug, strength, and dosage form;**
2231
2232 **(-b) manufacturer or distributor;**
2233
2234 **(-c) manufacturer's lot number;**
2235
2236 **(-d) manufacturer's expiration date;**
2237
2238 **(-e) quantity added to the automated compounding device;**
2239
2240 **(-f) date of loading;**
2241
2242 **(-g) name, initials, or electronic signature of the person loading the automated**
2243 **compounding device; and**
2244
2245 **(-h) name, initials, or electronic signature of the responsible pharmacist.**
2246
2247 **(IV) The automated compounding device shall not be used until a pharmacist verifies**
2248 **that the system is properly loaded and affixes his or her signature or electronic signature**
2249 **to the record specified in clause (III) of this subparagraph.**
2250
2251 (D) Hazardous drugs. If the preparation is hazardous, the following is also applicable.
2252
2253 (i) General.
2254
2255 (I) Hazardous drugs shall be prepared only under conditions that protect personnel during
2256 preparation and storage.
2257
2258 (II) Hazardous drugs shall be stored separately from other inventory in a manner to prevent
2259 contamination and personnel exposure.
2260
2261 (III) All personnel involved in the compounding of hazardous drugs shall wear appropriate
2262 protective apparel, such as gowns, face masks, eye protection, hair covers, shoe covers or
2263 dedicated shoes, and appropriate gloving at all times when handling hazardous drugs, including
2264 receiving, distribution, stocking, inventorying, preparation, for administration and disposal.
2265
2266 (IV) Appropriate safety and containment techniques for compounding hazardous drugs
2267 shall be used in conjunction with aseptic techniques required for preparing sterile preparations.
2268
2269 (V) Disposal of hazardous waste shall comply with all applicable local, state, and federal
2270 requirements.
2271
2272 (VI) Prepared doses of hazardous drugs must be dispensed, labeled with proper
2273 precautions inside and outside, and distributed in a manner to minimize patient contact with
2274 hazardous agents.
2275
2276 (ii) Primary engineering control device. Hazardous drugs shall be prepared in a Class II or III
2277 vertical flow biological safety cabinet or compounding aseptic containment isolator located in an

2278 ISO Class 7 area that is physically separated from other preparation areas. The area for
2279 preparation of sterile chemotherapeutic preparations shall:

2280
2281 (I) have not less than 0.01 inches water column negative pressure to the adjacent positive
2282 pressure ISO Class 7 or better ante-area; and

2283
2284 (II) have a pressure indicator that can be readily monitored for correct room pressurization.
2285

2286 (iii) Facilities that prepare a low volume of hazardous drugs. Pharmacies that prepare a low
2287 volume of hazardous drugs, are not required to comply with the provisions of clause (ii) of this
2288 subparagraph if the pharmacy uses a device that provides two tiers of containment (e.g.,
2289 closed-system vial transfer device within a BSC or CACI that is located in a non-negative
2290 pressure room).

2291
2292 **(E) Blood-labeling procedures. When compounding activities require the manipulation**
2293 **of a patient's blood-derived material (e.g., radiolabeling a patient's or donor's white blood**
2294 **cells), the manipulations shall be clearly separated from routine material-handling**
2295 **procedures and equipment used in preparation activities to avoid any cross-**
2296 **contamination. The preparations shall not require sterilization.**

2297
2298 **(F) [(E)]** Cleaning and disinfecting the sterile compounding areas. The following cleaning and
2299 disinfecting practices and frequencies apply to direct and contiguous compounding areas, which
2300 include ISO Class 5 compounding areas for exposure of critical sites as well as buffer areas,
2301 ante-areas, and segregated compounding areas.

2302
2303 (i) The pharmacist-in-charge is responsible for developing written procedures for cleaning
2304 and disinfecting the direct and contiguous compounding areas and assuring the procedures are
2305 followed.

2306
2307 (ii) These procedures shall be conducted at the beginning of each work shift, before each
2308 batch preparation is started, every 30 minutes during continuous compounding of individual
2309 compounded sterile preparations, when there are spills, and when surface contamination is
2310 known or suspected from procedural breaches.

2311
2312 (iii) Before compounding is performed, all items shall be removed from the direct and
2313 contiguous compounding areas and all surfaces are cleaned by removing loose material and
2314 residue from spills, followed by an application of a residue-free disinfecting agent (e.g., IPA),
2315 which is allowed to dry before compounding begins. **In a Class B pharmacy, objects used in**
2316 **preparing sterile radiopharmaceuticals (e.g., dose calibrator) which cannot be reasonably**
2317 **removed from the compounding area shall be sterilized with an application of a residue-**
2318 **free disinfection agent.**

2319
2320 (iv) Work surfaces in the [~~ISO Class 7~~] buffer areas and [~~ISO Class 8~~] ante-areas, as well as
2321 segregated compounding areas, shall be cleaned and disinfected at least daily. Dust and debris
2322 shall be removed when necessary from storage sites for compounding ingredients and supplies
2323 using a method that does not degrade the ISO Class 7 or 8 air quality.

2324
2325 (v) Floors in the buffer area, ante-area, and segregated compounding area are cleaned by
2326 mopping with a cleaning and disinfecting agent at least once daily when no aseptic operations
2327 are in progress. Mopping shall be performed by trained personnel using approved agents and

2328 procedures described in the written SOPs. It is incumbent on compounding personnel to ensure
2329 that such cleaning is performed properly.

2330

2331 (vi) In the buffer area, ante-area, and segregated compounding area, walls, ceilings, and
2332 shelving shall be cleaned and disinfected monthly. Cleaning and disinfecting agents shall be
2333 used with careful consideration of compatibilities, effectiveness, and inappropriate or toxic
2334 residues.

2335

2336 (vii) All cleaning materials, such as wipers, sponges, and mops, shall be non-shedding, and
2337 dedicated to use in the buffer area, ante-area, and segregated compounding areas and shall not
2338 be removed from these areas except for disposal. Floor mops may be used in both the buffer
2339 area and ante-area, but only in that order. If cleaning materials are reused, procedures shall be
2340 developed that ensure that the effectiveness of the cleaning device is maintained and that
2341 repeated use does not add to the bio-burden of the area being cleaned.

2342

2343 (viii) Supplies and equipment removed from shipping cartons must be wiped with a
2344 disinfecting agent, such as sterile IPA. After the disinfectant is sprayed or wiped on a surface to
2345 be disinfected, the disinfectant shall be allowed to dry, during which time the item shall not be
2346 used for compounding purposes. However, if sterile supplies are received in sealed pouches,
2347 the pouches may be removed as the supplies are introduced into the ISO Class 5 area without
2348 the need to disinfect the individual sterile supply items. No shipping or other external cartons
2349 may be taken into the buffer area or segregated compounding area.

2350

2351 (ix) Storage shelving emptied of all supplies, walls, and ceilings are cleaned and disinfected
2352 at planned intervals, monthly, if not more frequently.

2353

2354 (x) Cleaning must be done by personnel trained in appropriate cleaning techniques.

2355

2356 (xi) Proper documentation and frequency of cleaning must be maintained and shall contain
2357 the following:

2358

(I) date and time of cleaning;

2359

(II) type of cleaning performed; and

2360

(III) name of individual who performed the cleaning.

2361

2362 (F) Security requirements. The pharmacist-in-charge may authorize personnel to gain access
2363 to that area of the pharmacy containing dispensed sterile preparations, in the absence of the
2364 pharmacist, for the purpose of retrieving dispensed prescriptions to deliver to patients. If the
2365 pharmacy allows such after-hours access, the area containing the dispensed sterile
2366 preparations shall be an enclosed and lockable area separate from the area containing
2367 undispensed prescription drugs. A list of the authorized personnel having such access shall be
2368 in the pharmacy's policy and procedure manual.

2369

(G) Storage requirements and beyond-use dating.

2370

(i) Storage requirements. All drugs shall be stored at the proper temperature and conditions,
2371 as defined in the USP/NF and in §291.15 of this title (relating to Storage of Drugs).

2372

(ii) Beyond-use dating.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

2430 (iv) routinely inspected, calibrated(if necessary), or checked to ensure proper performance;

2431

2432 (F) appropriate disposal containers for used needles, syringes, etc., and if applicable,
2433 hazardous waste from the preparation of hazardous drugs and/or biohazardous waste;

2434

2435 (G) appropriate packaging or delivery containers to maintain proper storage conditions for
2436 sterile preparations;

2437

2438 (H) infusion devices, if applicable; and

2439

2440 (I) all necessary supplies, including:

2441

2442 (i) disposable needles, syringes, and other supplies for aseptic mixing;

2443

2444 (ii) disinfectant cleaning solutions;

2445

2446 (iii) hand washing agents with bactericidal action;

2447

2448 (iv) disposable, lint free towels or wipes;

2449

2450 (v) appropriate filters and filtration equipment;

2451

2452 (vi) hazardous spill kits, if applicable; and

2453

2454 (vii) masks, caps, coveralls or gowns with tight cuffs, shoe covers, and gloves, as
2455 applicable.

2456

2457 (8) Labeling.

2458

2459 (A) Prescription drug or medication orders. In addition to the labeling requirements for the
2460 pharmacy's specific license classification, the label dispensed or distributed pursuant to a
2461 prescription drug or medication order shall contain the following:

2462

2463 (i) the generic name(s) or the official name(s) of the principal active ingredient(s) of the
2464 compounded sterile preparation;

2465

2466 (ii) for outpatient prescription orders **other than sterile radiopharmaceuticals** ~~[only]~~, a
2467 statement that the compounded sterile preparation has been compounded by the pharmacy.
2468 (An auxiliary label may be used on the container to meet this requirement);

2469

2470 (iii) a beyond-use date. The beyond-use date shall be determined as outlined in Chapter
2471 797, Pharmacy Compounding--Sterile Preparations of the USP/NF, and paragraph (7)(G) of this
2472 subsection;

2473

2474 (B) Batch. If the sterile preparation is compounded in a batch, the following shall also be
2475 included on the batch label:

2476

2477 (i) unique lot number assigned to the batch;

2478

2479 (ii) quantity;

2480

2481 (iii) appropriate ancillary instructions, such as storage instructions or cautionary statements,
2482 including hazardous drug warning labels where appropriate; and

2483
2484 (iv) device-specific instructions, where appropriate.

2485
2486 (C) Pharmacy bulk package. The label of a pharmacy bulk package shall:

2487
2488 (i) state prominently "Pharmacy Bulk Package--Not for Direct Infusion;"

2489
2490 (ii) contain or refer to information on proper techniques to help ensure safe use of the
2491 preparation; and

2492
2493 (iii) bear a statement limiting the time frame in which the container may be used once it has
2494 been entered, provided it is held under the labeled storage conditions.

2495
2496 (9) Written drug information for prescription drug orders only. Written information about the
2497 compounded preparation or its major active ingredient(s) shall be given to the patient at the time
2498 of dispensing a prescription drug order. A statement which indicates that the preparation was
2499 compounded by the pharmacy must be included in this written information. If there is no written
2500 information available, the patient shall be advised that the drug has been compounded and how
2501 to contact a pharmacist, and if appropriate, the prescriber, concerning the drug. **This**
2502 **paragraph does not apply to the preparation of radiopharmaceuticals.**

2503
2504 (10) Pharmaceutical Care Services. In addition to the pharmaceutical care requirements for the
2505 pharmacy's specific license classification, the following requirements for sterile preparations
2506 compounded pursuant to prescription drug orders must be met. **This paragraph does not**
2507 **apply to the preparation of radiopharmaceuticals.**

2508
2509 (A) Primary provider. There shall be a designated physician primarily responsible for the
2510 patient's medical care. There shall be a clear understanding between the physician, the patient,
2511 and the pharmacy of the responsibilities of each in the areas of the delivery of care, and the
2512 monitoring of the patient. This shall be documented in the patient medication record (PMR).

2513
2514 (B) Patient training. The pharmacist-in-charge shall develop policies to ensure that the patient
2515 and/or patient's caregiver receives information regarding drugs and their safe and appropriate
2516 use, including instruction when applicable, regarding:

2517
2518 (i) appropriate disposition of hazardous solutions and ancillary supplies;

2519
2520 (ii) proper disposition of controlled substances in the home;

2521
2522 (iii) self-administration of drugs, where appropriate;

2523
2524 (iv) emergency procedures, including how to contact an appropriate individual in the event of
2525 problems or emergencies related to drug therapy; and

2526
2527 (v) if the patient or patient's caregiver prepares sterile preparations in the home, the
2528 following additional information shall be provided:

2529

2530 (I) safeguards against microbial contamination, including aseptic techniques for
2531 compounding intravenous admixtures and aseptic techniques for injecting additives to premixed
2532 intravenous solutions;

2533

2534 (II) appropriate storage methods, including storage durations for sterile pharmaceuticals
2535 and expirations of self-mixed solutions;

2536

2537 (III) handling and disposition of premixed and self-mixed intravenous admixtures; and

2538

2539 (IV) proper disposition of intravenous admixture compounding supplies such as syringes,
2540 vials, ampules, and intravenous solution containers.

2541

2542 (C) Pharmacist-patient relationship. It is imperative that a pharmacist-patient relationship be
2543 established and maintained throughout the patient's course of therapy. This shall be
2544 documented in the patient's medication record (PMR).

2545

2546 (D) Patient monitoring. The pharmacist-in-charge shall develop policies to ensure that:

2547

2548 (i) the patient's response to drug therapy is monitored and conveyed to the appropriate
2549 health care provider;

2550

2551 (ii) the first dose of any new drug therapy is administered in the presence of an individual
2552 qualified to monitor for and respond to adverse drug reactions; and

2553

2554 (iii) reports of adverse events with a compounded sterile preparation are reviewed promptly
2555 and thoroughly to correct and prevent future occurrences.

2556

2557 (11) Drugs, components, and materials used in sterile compounding.

2558

2559 (A) Drugs used in sterile compounding shall be a USP/NF grade substances manufactured in
2560 an FDA-registered facility.

2561

2562 (B) If USP/NF grade substances are not available shall be of a chemical grade in one of the
2563 following categories:

2564

2565 (i) Chemically Pure (CP);

2566

2567 (ii) Analytical Reagent (AR);

2568

2569 (iii) American Chemical Society (ACS); or

2570

2571 (iv) Food Chemical Codex.

2572

2573 (C) If a drug, component or material is not purchased from a FDA-registered facility, the
2574 pharmacist shall establish purity and stability by obtaining a Certificate of Analysis from the
2575 supplier and the pharmacist shall compare the monograph of drugs in a similar class to the
2576 Certificate of Analysis.

2577

2578 (D) All components shall:

2579

2580 (i) be manufactured in an FDA-registered facility; or

2581
2582 (ii) in the professional judgment of the pharmacist, be of high quality and obtained from
2583 acceptable and reliable alternative sources; and
2584
2585 (iii) stored in properly labeled containers in a clean, dry area, under proper temperatures.
2586
2587 (E) Drug preparation containers and closures shall not be reactive, additive, or absorptive so
2588 as to alter the safety, identity, strength, quality, or purity of the compounded drug preparation
2589 beyond the desired result.
2590
2591 (F) Components, drug preparation containers, and closures shall be rotated so that the oldest
2592 stock is used first.
2593
2594 (G) Container closure systems shall provide adequate protection against foreseeable external
2595 factors in storage and use that can cause deterioration or contamination of the compounded
2596 drug preparation.
2597
2598 (H) A pharmacy may not compound a preparation that contains ingredients appearing on a
2599 federal Food and Drug Administration list of drug products withdrawn or removed from the
2600 market for safety reasons.
2601
2602 (12) Compounding process.
2603
2604 (A) Standard operating procedures (SOPs). All significant procedures performed in the
2605 compounding area shall be covered by written SOPs designed to ensure accountability,
2606 accuracy, quality, safety, and uniformity in the compounding process. At a minimum, SOPs shall
2607 be developed and implemented for:
2608
2609 (i) the facility;
2610
2611 (ii) equipment;
2612
2613 (iii) personnel;
2614
2615 (iv) preparation evaluation;
2616
2617 (v) quality assurance;
2618
2619 (vi) preparation recall;
2620
2621 (vii) packaging; and
2622
2623 (viii) storage of compounded sterile preparations.
2624
2625 (B) USP/NF. Any compounded formulation with an official monograph in the USP/NF shall be
2626 compounded, labeled, and packaged in conformity with the USP/NF monograph for the drug.
2627
2628 (C) Personnel Cleansing and Garbing.
2629
2630 (i) Any person with an apparent illness or open lesion, including rashes, sunburn, weeping
2631 sores, conjunctivitis, and active respiratory infection, that may adversely affect the safety or

2632 quality of a drug preparation being compounded shall be excluded from working in ISO Class 5,
2633 ~~and~~ ISO Class 7, **and ISO Class 8** compounding areas until the condition is remedied.

2634
2635 (ii) Before entering the buffer area, compounding personnel must remove the following:

2636
2637 (I) personal outer garments (e.g., bandanas, coats, hats, jackets, scarves, sweaters,
2638 vests);

2639
2640 (II) all cosmetics, because they shed flakes and particles; and

2641
2642 (III) all hand, wrist, and other body jewelry or piercings (e.g., earrings, lip or eyebrow
2643 piercings) that can interfere with the effectiveness of personal protective equipment (e.g., fit of
2644 gloves and cuffs of sleeves).

2645
2646 (iii) The wearing of artificial nails or extenders is prohibited while working in the sterile
2647 compounding environment. Natural nails shall be kept neat and trimmed.

2648
2649 (iv) Personnel shall don personal protective equipment and perform hand hygiene in an
2650 order that proceeds from the dirtiest to the cleanest activities as follows:

2651
2652 (I) Activities considered the dirtiest include donning of dedicated shoes or shoe covers,
2653 head and facial hair covers (e.g., beard covers in addition to face masks), and face mask/eye
2654 shield. Eye shields are optional unless working with irritants like germicidal disinfecting agents
2655 or when preparing hazardous drugs.

2656
2657 (II) After donning dedicated shoes or shoe covers, head and facial hair covers, and face
2658 masks, personnel shall perform a hand hygiene procedure by removing debris from underneath
2659 fingernails using a nail cleaner under running warm water followed by vigorous hand washing.
2660 Personnel shall begin washing arms at the hands and continue washing to elbows for at least
2661 30 seconds with either a plain (non-antimicrobial) soap, or antimicrobial soap, and water while in
2662 the ante-area. Hands and forearms to the elbows shall be completely dried using lint-free
2663 disposable towels, an electronic hands-free hand dryer, or a HEPA filtered hands dryer.

2664
2665 (III) After completion of hand washing, personnel shall don clean non-shedding gowns with
2666 sleeves that fit snugly around the wrists and enclosed at the neck.

2667
2668 (IV) Once inside the buffer area or segregated compounding area, and prior to donning
2669 sterile powder-free gloves, antiseptic hand cleansing shall be performed using a waterless
2670 alcohol-based surgical hand scrub with persistent activity following manufacturers'
2671 recommendations. Hands shall be allowed to dry thoroughly before donning sterile gloves.

2672
2673 (V) Sterile gloves that form a continuous barrier with the gown shall be the last item
2674 donned before compounding begins. Routine application of sterile 70% IPA shall occur
2675 throughout the compounding day and whenever nonsterile surfaces are touched.

2676
2677 (v) When compounding personnel shall temporarily exit the **buffer area** [~~ISO Class 7~~
2678 ~~environment~~] during a work shift, the exterior gown, if not visibly soiled, may be removed and
2679 retained in the [~~ISO Class 8~~] ante-area, to be re-donned during that same work shift only.
2680 However, shoe covers, hair and facial hair covers, face mask/eye shield, and gloves shall be
2681 replaced with new ones before re-entering the **buffer area** [~~ISO Class 7 clean environment~~]
2682 along with performing proper hand hygiene.

2683
2684 (vi) During high-risk compounding activities that precede terminal sterilization, such as
2685 weighing and mixing of non-sterile ingredients, compounding personnel shall be garbed and
2686 gloved the same as when performing compounding in an ISO Class 5 environment. Properly
2687 garbed and gloved compounding personnel who are exposed to air quality that is either known
2688 or suspected to be worse than ISO Class 7 shall re-garb personal protective equipment along
2689 with washing their hands properly, performing antiseptic hand cleansing with a waterless
2690 alcohol-based surgical hand scrub, and donning sterile gloves upon re-entering the ISO Class 7
2691 buffer area.

2692
2693 (vii) When compounding aseptic isolators or compounding aseptic containment isolators are
2694 the source of the ISO Class 5 environment, the compounding personnel should follow the
2695 requirements as specified in this subparagraph, unless the isolator manufacturer can provide
2696 written documentation based on validated environmental testing that any components of
2697 personal protective equipment or cleansing are not required.

2698
2699 (13) Quality Assurance.
2700
2701 (A) Initial Formula Validation. Prior to routine compounding of a sterile preparation, a
2702 pharmacy shall conduct an evaluation that shows that the pharmacy is capable of compounding
2703 a preparation that is sterile and that contains the stated amount of active ingredient(s).

2704
2705 (i) Low risk preparations.

2706
2707 (I) Quality assurance practices include, but are not limited to the following:

2708
2709 (-a-) Routine disinfection and air quality testing of the direct compounding environment to
2710 minimize microbial surface contamination and maintain ISO Class 5 air quality.

2711
2712 (-b-) Visual confirmation that compounding personnel are properly donning and wearing
2713 appropriate items and types of protective garments and goggles.

2714
2715 (-c-) Review of all orders and packages of ingredients to ensure that the correct identity
2716 and amounts of ingredients were compounded.

2717
2718 (-d-) Visual inspection of compounded sterile preparations, **except for sterile**
2719 **radiopharmaceuticals**, to ensure the absence of particulate matter in solutions, the absence of
2720 leakage from vials and bags, and the accuracy and thoroughness of labeling.

2721
2722 (II) Example of a Media-Fill Test Procedure. This, or an equivalent test, is performed at
2723 least annually by each person authorized to compound in a low-risk level under conditions that
2724 closely simulate the most challenging or stressful conditions encountered during compounding
2725 of low-risk level sterile preparations. Once begun, this test is completed without interruption
2726 within an ISO Class 5 air quality environment. Three sets of four 5-milliliter aliquots of sterile
2727 Soybean-Casein Digest Medium are transferred with the same sterile 10-milliliter syringe and
2728 vented needle combination into separate sealed, empty, sterile 30-milliliter clear vials (i.e., four
2729 5-milliliter aliquots into each of three 30-milliliter vials). Sterile adhesive seals are aseptically
2730 affixed to the rubber closures on the three filled vials. The vials are incubated within a range of
2731 20 - 35 degrees Celsius for a minimum of 14 days. Failure is indicated by visible turbidity in the
2732 medium on or before 14 days. The media-fill test must include a positive-control sample.

2733

2734 (ii) Medium risk preparations.

2735

2736 (I) Quality assurance procedures for medium-risk level compounded sterile preparations
2737 include all those for low-risk level compounded sterile preparations, as well as a more
2738 challenging media-fill test passed annually, or more frequently.

2739

2740 (II) Example of a Media-Fill Test Procedure. This, or an equivalent test, is performed at
2741 least annually under conditions that closely simulate the most challenging or stressful conditions
2742 encountered during compounding. This test is completed without interruption within an ISO
2743 Class 5 air quality environment. Six 100-milliliter aliquots of sterile Soybean-Casein Digest
2744 Medium are aseptically transferred by gravity through separate tubing sets into separate
2745 evacuated sterile containers. The six containers are then arranged as three pairs, and a sterile
2746 10-milliliter syringe and 18-gauge needle combination is used to exchange two 5-milliliter
2747 aliquots of medium from one container to the other container in the pair. For example, after a 5-
2748 milliliter aliquot from the first container is added to the second container in the pair, the second
2749 container is agitated for 10 seconds, then a 5-milliliter aliquot is removed and returned to the
2750 first container in the pair. The first container is then agitated for 10 seconds, and the next 5-
2751 milliliter aliquot is transferred from it back to the second container in the pair. Following the two
2752 5-milliliter aliquot exchanges in each pair of containers, a 5-milliliter aliquot of medium from each
2753 container is aseptically injected into a sealed, empty, sterile 10-milliliter clear vial, using a sterile
2754 10-milliliter syringe and vented needle. Sterile adhesive seals are aseptically affixed to the
2755 rubber closures on the three filled vials. The vials are incubated within a range of 20 - 35
2756 degrees Celsius for a minimum of 14 days. Failure is indicated by visible turbidity in the medium
2757 on or before 14 days. The media-fill test must include a positive-control sample.

2758

2759 (iii) High risk preparations.

2760

2761 (I) Procedures for high-risk level compounded sterile preparations include all those for low-
2762 risk level compounded sterile preparations. In addition, a media-fill test that represents high-risk
2763 level compounding is performed twice a year by each person authorized to compound high-risk
2764 level compounded sterile preparations.

2765

2766 (II) Example of a Media-Fill Test Procedure Compounded Sterile Preparations Sterilized by
2767 Filtration. This test, or an equivalent test, is performed under conditions that closely simulate the
2768 most challenging or stressful conditions encountered when compounding high-risk level
2769 compounded sterile preparations. Note: Sterility tests for autoclaved compounded sterile
2770 preparations are not required unless they are prepared in batches of more than 25 units. This
2771 test is completed without interruption in the following sequence:

2772

2773 (-a-) Dissolve 3 grams of nonsterile commercially available Soybean-Casein Digest
2774 Medium in 100 milliliters of non-bacteriostatic water to make a 3% nonsterile solution.

2775

2776 (-b-) Draw 25 milliliters of the medium into each of three 30-milliliter sterile syringes.
2777 Transfer 5 milliliters from each syringe into separate sterile 10-milliliter vials. These vials are the
2778 positive controls to generate exponential microbial growth, which is indicated by visible turbidity
2779 upon incubation.

2780

2781 (-c-) Under aseptic conditions and using aseptic techniques, affix a sterile 0.2-micron
2782 porosity filter unit and a 20-gauge needle to each syringe. Inject the next 10 milliliters from each
2783 syringe into three separate 10-milliliter sterile vials. Repeat the process for three more vials.
2784 Label all vials, affix sterile adhesive seals to the closure of the nine vials, and incubate them at

2785 20 to 35 degrees Celsius for a minimum of 14 days. Inspect for microbial growth over 14 days
2786 as described in Chapter 797 Pharmaceutical Compounding--Sterile Preparations, of the
2787 USP/NF.

2788

2789 (B) Finished preparation release checks and tests.

2790

2791 (i) All high-risk level compounded sterile preparations that are prepared in groups of more
2792 than 25 identical individual single-dose packages (such as ampuls, bags, syringes, and vials), or
2793 in multiple dose vials for administration to multiple patients, or are exposed longer than 12 hours
2794 at 2 - 8 degrees Celsius and longer than six hours at warmer than 8 degrees Celsius before
2795 they are sterilized shall be tested to ensure they are sterile and do not contain excessive
2796 bacterial endotoxins as specified in Chapter 71, Sterility Tests of the USP/NF before being
2797 dispensed or administered.

2798

2799 (ii) All compounded sterile preparations, except for sterile radiopharmaceuticals, that are
2800 intended to be solutions must be visually examined for the presence of particulate matter and
2801 not administered or dispensed when such matter is observed.

2802

2803 (iii) The prescription drug and medication orders, written compounding procedure,
2804 preparation records, and expended materials used to make compounded sterile preparations at
2805 all contamination risk levels shall be inspected for accuracy of correct identities and amounts of
2806 ingredients, aseptic mixing and sterilization, packaging, labeling, and expected physical
2807 appearance before they are dispensed or administered.

2808

2809 (C) Viable and nonviable environmental sampling testing. Environmental sampling shall
2810 occur, at a minimum, every six months as part of a comprehensive quality management
2811 program and under any of the following conditions:

2812

2813 (i) as part of the commissioning and certification of new facilities and equipment;

2814

2815 (ii) following any servicing of facilities and equipment;

2816

2817 (iii) as part of the re-certification of facilities and equipment;

2818

2819 (iv) in response to identified problems with end products or staff technique; or

2820

2821 (v) in response to issues with compounded sterile preparations, observed compounding
2822 personnel work practices, or patient-related infections (where the compounded sterile
2823 preparation is being considered as a potential source of the infection).

2824

2825 (D) Total particle counts. Certification that each ISO classified area (e.g., ISO Class 5, 7, and
2826 8), is within established guidelines shall be performed no less than every six months and
2827 whenever the equipment is relocated or the physical structure of the buffer area or ante-area
2828 has been altered. All certification records shall be maintained and reviewed to ensure that the
2829 controlled environments comply with the proper air cleanliness, room pressures, and air
2830 changes per hour. Testing shall be performed by qualified operators using current, state-of-the-
2831 art equipment, with results of the following:

2832

2833 (i) ISO Class 5 - not more than 3520 particles 0.5 µm and larger size per cubic meter of air;

2834

2835 (ii) ISO Class 7 - not more than 352,000 particles of 0.5 µm and larger size per cubic meter
2836 of air for any buffer area; and

2837
2838 (iii) ISO Class 8 - not more than 3,520,000 particles of 0.5 µm and larger size per cubic
2839 meter of air for any ante-area.

2840
2841 (E) Pressure differential monitoring. A pressure gauge or velocity meter shall be installed to
2842 monitor the pressure differential or airflow between the buffer area and the ante-area and
2843 between the ante-area and the general environment outside the compounding area. The results
2844 shall be reviewed and documented on a log at least every work shift (minimum frequency shall
2845 be at least daily) or by a continuous recording device. The pressure between the ISO Class 7 **or**
2846 **ISO Class 8** and the general pharmacy area shall not be less than 0.02 inch water column.

2847
2848 (F) Sampling plan. An appropriate environmental sampling plan shall be developed for
2849 airborne viable particles based on a risk assessment of compounding activities performed.
2850 Selected sampling sites shall include locations within each ISO Class 5 environment and in the
2851 ISO Class 7 and 8 areas and in the segregated compounding areas at greatest risk of
2852 contamination. The plan shall include sample location, method of collection, frequency of
2853 sampling, volume of air sampled, and time of day as related to activity in the compounding area
2854 and action levels.

2855
2856 (G) Viable air sampling. Evaluation of airborne microorganisms using volumetric collection
2857 methods in the controlled air environments shall be performed by properly trained individuals for
2858 all compounding risk levels. For low-, medium-, and high-risk level compounding, air sampling
2859 shall be performed at locations that are prone to contamination during compounding activities
2860 and during other activities such as staging, labeling, gowning, and cleaning. Locations shall
2861 include zones of air backwash turbulence within the laminar airflow workbench and other areas
2862 where air backwash turbulence may enter the compounding area. For low-risk level
2863 compounded sterile preparations within 12-hour or less beyond-use-date prepared in a primary
2864 engineering control that maintains an ISO Class 5, air sampling shall be performed at locations
2865 inside the ISO Class 5 environment and other areas that are in close proximity to the ISO Class
2866 5 environment during the certification of the primary engineering control.

2867
2868 (H) Air sampling frequency and process. Air sampling shall be performed at least every 6
2869 months as a part of the re-certification of facilities and equipment. A sufficient volume of air shall
2870 be sampled and the manufacturer's guidelines for use of the electronic air sampling equipment
2871 followed. At the end of the designated sampling or exposure period for air sampling activities,
2872 the microbial growth media plates are recovered and their covers secured and they are inverted
2873 and incubated at a temperature and for a time period conducive to multiplication of
2874 microorganisms. Sampling data shall be collected and reviewed on a periodic basis as a means
2875 of evaluating the overall control of the compounding environment. If an activity consistently
2876 shows elevated levels of microbial growth, competent microbiology personnel shall be
2877 consulted.

2878
2879 (I) Compounding accuracy checks. Written procedures for double-checking compounding
2880 accuracy shall be followed for every compounded sterile preparation during preparation and
2881 immediately prior to release, including label accuracy and the accuracy of the addition of all
2882 drug products or ingredients used to prepare the finished preparation and their volumes or
2883 quantities. At each step of the compounding process, the pharmacist shall ensure that
2884 components used in compounding are accurately weighed, measured, or subdivided as
2885 appropriate to conform to the formula being prepared.

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(14) Quality control.

(A) Quality control procedures. The pharmacy shall follow established quality control procedures to monitor the compounding environment and quality of compounded drug preparations for conformity with the quality indicators established for the preparation. When developing these procedures, pharmacy personnel shall consider the provisions of USP Chapter 71, Sterility Tests, USP Chapter 85, Bacterial Endotoxins Test, Pharmaceutical Compounding-Nonsterile Preparations, USP Chapter 795, USP Chapter 797, Pharmaceutical Compounding--Sterile Preparations, **Chapter 800, Hazardous Drugs—Handling in Healthcare Settings, Chapter 823, Positron Emission Tomography Drugs for Compounding, Investigational, and Research Uses**, Chapter 1075, Good Compounding Practices, and Chapter 1160, Pharmaceutical Calculations in Prescription Compounding, and USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding of the current USP/NF. Such procedures shall be documented and be available for inspection.

(B) Verification of compounding accuracy and sterility.

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

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

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

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

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

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

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

(2) Compounding records.

2936 (A) Compounding pursuant to patient specific prescription drug orders. Compounding records
2937 for all compounded preparations shall be maintained by the pharmacy electronically or manually
2938 as part of the prescription drug or medication order, formula record, formula book, or
2939 compounding log and shall include:

2940
2941 (i) the date of preparation;

2942
2943 (ii) a complete formula, including methodology and necessary equipment which includes the
2944 brand name(s) of the raw materials, or if no brand name, the generic name(s) or official name
2945 and name(s) of the manufacturer(s) or distributor of the raw materials and the quantities of
2946 each;

2947
2948 (iii) signature or initials of the pharmacist or pharmacy technician or pharmacy technician
2949 trainee performing the compounding;

2950
2951 (iv) signature or initials of the pharmacist responsible for supervising pharmacy technicians
2952 or pharmacy technician trainees and conducting in-process and finals checks of compounded
2953 pharmaceuticals if pharmacy technicians or pharmacy technician trainees perform the
2954 compounding function;

2955
2956 (v) the quantity in units of finished preparation or amount of raw materials;

2957
2958 (vi) the container used and the number of units prepared; and

2959
2960 (vii) a reference to the location of the following documentation which may be maintained with
2961 other records, such as quality control records:

2962
2963 (I) the criteria used to determine the beyond-use date; and

2964
2965 (II) documentation of performance of quality control procedures.

2966
2967 (B) Compounding records when batch compounding or compounding in anticipation of future
2968 prescription drug or medication orders.

2969
2970 (i) Master work sheet. A master work sheet shall be developed and approved by a
2971 pharmacist for preparations prepared in batch. Once approved, a duplicate of the master work
2972 sheet shall be used as the preparation work sheet from which each batch is prepared and on
2973 which all documentation for that batch occurs. The master work sheet shall contain at a
2974 minimum:

2975
2976 (I) the formula;

2977
2978 (II) the components;

2979
2980 (III) the compounding directions;

2981
2982 (IV) a sample label;

2983
2984 (V) evaluation and testing requirements;

2985
2986 (VI) specific equipment used during preparation; and

2987
2988 (VII) storage requirements.
2989
2990 (ii) Preparation work sheet. The preparation work sheet for each batch of preparations shall
2991 document the following:
2992
2993 (I) identity of all solutions and ingredients and their corresponding amounts,
2994 concentrations, or volumes;
2995
2996 (II) lot number for each component;
2997
2998 (III) component manufacturer/distributor or suitable identifying number;
2999
3000 (IV) container specifications (e.g., syringe, pump cassette);
3001
3002 (V) unique lot or control number assigned to batch;
3003
3004 (VI) expiration date of batch-prepared preparations;
3005
3006 (VII) date of preparation;
3007
3008 (VIII) name, initials, or electronic signature of the person(s) involved in the preparation;
3009
3010 (IX) name, initials, or electronic signature of the responsible pharmacist;
3011
3012 (X) finished preparation evaluation and testing specifications, if applicable; and
3013
3014 (XI) comparison of actual yield to anticipated or theoretical yield, when appropriate.
3015
3016 (f) Office Use Compounding and Distribution of Sterile Compounded Preparations
3017
3018 (1) General.
3019
3020 (A) A pharmacy may compound, dispense, deliver, and distribute a compounded sterile
3021 preparation as specified in Subchapter D, Texas Pharmacy Act Chapter 562.
3022
3023 (B) A Class A-S pharmacy is not required to register or be licensed under Chapter 431,
3024 Health and Safety Code, to distribute sterile compounded preparations to a Class C or Class C-
3025 S pharmacy.
3026
3027 (C) A Class C-S pharmacy is not required to register or be licensed under Chapter 431,
3028 Health and Safety Code, to distribute sterile compounded preparations that the Class C-S
3029 pharmacy has compounded for other Class C or Class C-S pharmacies under common
3030 ownership.
3031
3032 (D) To compound and deliver a compounded preparation under this subsection, a pharmacy
3033 must:
3034
3035 (i) verify the source of the raw materials to be used in a compounded drug;
3036

3037 (ii) comply with applicable United States Pharmacopoeia guidelines, including the testing
3038 requirements, and the Health Insurance Portability and Accountability Act of 1996 (Pub. L. No.
3039 104-191);

3040
3041 (iii) enter into a written agreement with a practitioner for the practitioner's office use of a
3042 compounded preparation;

3043
3044 (iv) comply with all applicable competency and accrediting standards as determined by the
3045 board; and

3046
3047 (v) comply with the provisions of this subsection.
3048

3049 **(E) This subsection does not apply to Class B pharmacies compounding sterile**
3050 **radiopharmaceuticals that are furnished for departmental or physicians' use if such**
3051 **authorized users maintain a Texas radioactive materials license.**

3052
3053 (2) Written Agreement. A pharmacy that provides sterile compounded preparations to
3054 practitioners for office use or to another pharmacy shall enter into a written agreement with the
3055 practitioner or pharmacy. The written agreement shall:

3056
3057 (A) address acceptable standards of practice for a compounding pharmacy and a practitioner
3058 and receiving pharmacy that enter into the agreement including a statement that the
3059 compounded drugs may only be administered to the patient and may not be dispensed to the
3060 patient or sold to any other person or entity except to a veterinarian as authorized by §563.054
3061 of the Act;

3062
3063 (B) require the practitioner or receiving pharmacy to include on a patient's chart, medication
3064 order or medication administration record the lot number and beyond-use date of a
3065 compounded preparation administered to a patient;

3066
3067 (C) describe the scope of services to be performed by the pharmacy and practitioner or
3068 receiving pharmacy, including a statement of the process for:

3069
3070 (i) a patient to report an adverse reaction or submit a complaint; and

3071
3072 (ii) the pharmacy to recall batches of compounded preparations.

3073
3074 (3) Recordkeeping.

3075
3076 (A) Maintenance of Records.

3077
3078 (i) Records of orders and distribution of sterile compounded preparations to a practitioner for
3079 office use or to an institutional pharmacy for administration to a patient shall:

3080
3081 (I) be kept by the pharmacy and be available, for at least two years from the date of the
3082 record, for inspecting and copying by the board or its representative and to other authorized
3083 local, state, or federal law enforcement agencies;

3084
3085 (II) maintained separately from the records of preparations dispensed pursuant to a
3086 prescription or medication order; and
3087

3088 (III) supplied by the pharmacy within 72 hours, if requested by an authorized agent of the
3089 Texas State Board of Pharmacy or its representative. If the pharmacy maintains the records in
3090 an electronic format, the requested records must be provided in an electronic format. Failure to
3091 provide the records set out in this subsection, either on site or within 72 hours for whatever
3092 reason, constitutes prima facie evidence of failure to keep and maintain records.
3093

3094 (ii) Records may be maintained in an alternative data retention system, such as a data
3095 processing system or direct imaging system provided the data processing system is capable of
3096 producing a hard copy of the record upon the request of the board, its representative, or other
3097 authorized local, state, or federal law enforcement or regulatory agencies.
3098

3099 (B) Orders. The pharmacy shall maintain a record of all sterile compounded preparations
3100 ordered by a practitioner for office use or by an institutional pharmacy for administration to a
3101 patient. The record shall include the following information:
3102

3103 (i) date of the order;
3104

3105 (ii) name, address, and phone number of the practitioner who ordered the preparation and if
3106 applicable, the name, address and phone number of the institutional pharmacy ordering the
3107 preparation; and
3108

3109 (iii) name, strength, and quantity of the preparation ordered.
3110

3111 (C) Distributions. The pharmacy shall maintain a record of all sterile compounded
3112 preparations distributed pursuant to an order to a practitioner for office use or by an institutional
3113 pharmacy for administration to a patient. The record shall include the following information:
3114

3115 (i) date the preparation was compounded;
3116

3117 (ii) date the preparation was distributed;
3118

3119 (iii) name, strength and quantity in each container of the preparation;
3120

3121 (iv) pharmacy's lot number;
3122

3123 (v) quantity of containers shipped; and
3124

3125 (vi) name, address, and phone number of the practitioner or institutional pharmacy to whom
3126 the preparation is distributed.
3127

3128 (D) Audit Trail.
3129

3130 (i) The pharmacy shall store the order and distribution records of preparations for all sterile
3131 compounded preparations ordered by and or distributed to a practitioner for office use or by a
3132 pharmacy licensed to compound sterile preparations for administration to a patient in such a
3133 manner as to be able to provide an audit trail for all orders and distributions of any of the
3134 following during a specified time period:
3135

3136 (l) any strength and dosage form of a preparation (by either brand or generic name or
3137 both);
3138

3139 (II) any ingredient;
3140
3141 (III) any lot number;
3142
3143 (IV) any practitioner;
3144
3145 (V) any facility; and
3146
3147 (VI) any pharmacy, if applicable.
3148
3149 (ii) The audit trail shall contain the following information:
3150
3151 (I) date of order and date of the distribution;
3152
3153 (II) practitioner's name, address, and name of the institutional pharmacy, if applicable;
3154
3155 (III) name, strength and quantity of the preparation in each container of the preparation;
3156
3157 (IV) name and quantity of each active ingredient;
3158
3159 (V) quantity of containers distributed; and
3160
3161 (VI) pharmacy's lot number.
3162
3163 (4) Labeling. The pharmacy shall affix a label to the preparation containing the following
3164 information:
3165
3166 (A) name, address, and phone number of the compounding pharmacy;
3167
3168 (B) the statement: "For Institutional or Office Use Only--Not for Resale"; or if the preparation
3169 is distributed to a veterinarian the statement: "Compounded Preparation";
3170
3171 (C) name and strength of the preparation or list of the active ingredients and strengths;
3172
3173 (D) pharmacy's lot number;
3174
3175 (E) beyond-use date as determined by the pharmacist using appropriate documented criteria;
3176
3177 (F) quantity or amount in the container;
3178
3179 (G) appropriate ancillary instructions, such as storage instructions or cautionary statements,
3180 including hazardous drug warning labels where appropriate; and
3181
3182 (H) device-specific instructions, where appropriate.
3183
3184 (g) Recall Procedures.
3185
3186 (1) The pharmacy shall have written procedures for the recall of any compounded sterile
3187 preparation provided to a patient, to a practitioner for office use, or a pharmacy for
3188 administration. Written procedures shall include, but not be limited to the requirements as
3189 specified in paragraph (3) of this subsection.

3190
3191 (2) The pharmacy shall immediately initiate a recall of any sterile preparation compounded by
3192 the pharmacy upon identification of a potential or confirmed harm to a patient.

3193
3194 (3) In the event of a recall, the pharmacist-in-charge shall ensure that:

3195
3196 (A) each practitioner, facility, and/or pharmacy to which the preparation was distributed is
3197 notified, in writing, of the recall;

3198
3199 (B) each patient to whom the preparation was dispensed is notified, in writing, of the recall;

3200
3201 (C) the board is notified of the recall, in writing, not later than 24 hours after the recall is
3202 issued;

3203
3204 (D) if the preparation is distributed for office use, the Texas Department of State Health
3205 Services, Drugs and Medical Devices Group, is notified of the recall, in writing;

3206
3207 (E) the preparation is quarantined; and

3208
3209 (F) the pharmacy keeps a written record of the recall including all actions taken to notify all
3210 parties and steps taken to ensure corrective measures.

3211
3212 (4) If a pharmacy fails to initiate a recall, the board may require a pharmacy to initiate a recall if
3213 there is potential for or confirmed harm to a patient.

3214
3215 (5) A pharmacy that compounds sterile preparations shall notify the board immediately of any
3216 adverse effects reported to the pharmacy or that are known by the pharmacy to be potentially
3217 attributable to a sterile preparation compounded by the pharmacy. The agency certifies that
3218 legal counsel has reviewed the proposal and found it to be within the state agency's legal
3219 authority to adopt.