

## **RULE ANALYSIS**

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

**Short Title:** Pharmacies Compounding Sterile Preparations

**Rule Numbers:** §291.133

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

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

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

**The Board reviewed and voted to propose the amendments during the November 4, 2014, meeting. The proposed amendments were published in the December 26, 2014, issue of the *Texas Register* at 40 TexReg 1788.**

## SUBCHAPTER G. SERVICES PROVIDED BY PHARMACIES

### 22 TAC §291.133

The Texas State Board of Pharmacy proposes amendments to §291.133 concerning Pharmacies Compounding Sterile Preparations. The amendments, if adopted, add a definition for compounding personnel; clarify the in-process checks and evaluation of aseptic technique procedures; require media-fill tests for the most challenging or stressful conditions; and update requirements to be consistent with USP 797 requirements.

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

Ms. Dodson has determined that, for each year of the first five-year period the rule will be in effect, the public benefit anticipated as a result of enforcing the amendments will be to ensure pharmacies are preparing sterile preparations under appropriate and safe conditions. Ms. Dodson has also determined that, for each year of the first five-year period the rule will be in effect, an economic cost may exist for entities/persons required to comply with the rule as described below.

There might be an adverse economic effect on micro, small, and large businesses or to other entities/persons who are required to comply with the rules for pharmacies compounding sterile preparations. Based on the significant variances in pharmacies' physical structure and layout, it is difficult for TSBP to determine the actual cost to businesses required to comply with this rule. These costs would involve bringing the sterile compounding area of pharmacies into compliance with the new provisions of the rules. In addition, TSBP is unable to reduce these costs because to do so would compromise the purposes of this rule which is intended to protect the health and safety of the public.

Comments on the amendments may be submitted to Allison Benz, R.Ph., M.S., Director of Professional Services, Texas State Board of Pharmacy, 333 Guadalupe Street, Suite 3-600, Austin, Texas 78701, FAX (512) 305-8008. Comments must be received by 5:00 p.m., April 30, 2015.

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

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

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

37 (a) (No change.)

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

41 (1) - (16) (No change.)

42 (17) Compounding Personnel--A pharmacist, pharmacy technician, or pharmacy technician  
43 trainee who performs the actual compounding; a pharmacist who supervises pharmacy  
44 technicians or pharmacy technician trainees compounding sterile preparations, and a pharmacist  
45 who performs an intermediate or final verification of a compounded sterile preparation.

46 (18) [(17)] Critical Area--An ISO Class 5 environment.

47 (19) [(18)] Critical Sites--A location that includes any component or fluid pathway surfaces (e.g.,  
48 vial septa, injection ports, beakers) or openings (e.g., opened ampuls, needle hubs) exposed and  
49 at risk of direct contact with air (e.g., ambient room or HEPA filtered), moisture (e.g., oral and  
50 mucosal secretions), or touch contamination. Risk of microbial particulate contamination of the  
51 critical site increases with the size of the openings and exposure time.

52 (20) [(19)] Device--An instrument, apparatus, implement, machine, contrivance, implant, in-vitro  
53 reagent, or other similar or related article, including any component part or accessory, that is  
54 required under federal or state law to be ordered or prescribed by a practitioner.

55 (21) [(20)] Direct Compounding Area--A critical area within the ISO Class 5 primary  
56 engineering control where critical sites are exposed to unidirectional HEPA-filtered air, also  
57 known as first air.

58 (22) [(21)] Disinfectant--An agent that frees from infection, usually a chemical agent but  
59 sometimes a physical one, and that destroys disease-causing pathogens or other harmful  
60 microorganisms but may not kill bacterial and fungal spores. It refers to substances applied to  
61 inanimate objects.

62 (23) [(22)] First Air--The air exiting the HEPA filter in a unidirectional air stream that is  
63 essentially particle free.

64 (24) [(23)] Hazardous Drugs--Drugs that, studies in animals or humans indicate exposure to the  
65 drugs, have a potential for causing cancer, development or reproductive toxicity, or harm to  
66 organs.

67 (25) [(24)] Hot water--The temperature of water from the pharmacy's sink maintained at a  
68 minimum of 105 degrees F (41 degrees C).

69 (26) [(25)] HVAC--Heating, ventilation, and air conditioning.

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

(28) [~~(27)~~] IPA--Isopropyl alcohol (2-propanol).

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

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

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

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

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

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

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

108 (36) ~~[(35)]~~ Preparation or Compounded Sterile Preparation--A sterile admixture compounded in  
109 a licensed pharmacy or other healthcare-related facility pursuant to the order of a licensed  
110 prescriber. The components of the preparation may or may not be sterile products.

111 (37) ~~[(36)]~~ Primary Engineering Control--A device or room that provides an ISO Class 5  
112 environment for the exposure of critical sites when compounding sterile preparations. Such  
113 devices include, but may not be limited to, laminar airflow workbenches, biological safety  
114 cabinets, compounding aseptic isolators, and compounding aseptic containment isolators.

115 (38) ~~[(37)]~~ Product--A commercially manufactured sterile drug or nutrient that has been  
116 evaluated for safety and efficacy by the U.S. Food and Drug Administration (FDA). Products are  
117 accompanied by full prescribing information, which is commonly known as the FDA-approved  
118 manufacturer's labeling or product package insert.

119 (39) ~~[(38)]~~ Positive Control--A quality assurance sample prepared to test positive for microbial  
120 growth.

121 (40) ~~[(39)]~~ Positive Pressure Room--A room that is at a higher pressure compared to adjacent  
122 spaces and, therefore, the net airflow is out of the room.

123 (41) ~~[(40)]~~ Quality assurance--The set of activities used to ensure that the process used in the  
124 preparation of sterile drug preparations lead to preparations that meet predetermined standards of  
125 quality.

126 (42) ~~[(41)]~~ Quality control--The set of testing activities used to determine that the ingredients,  
127 components (e.g., containers), and final compounded sterile preparations prepared meet  
128 predetermined requirements with respect to identity, purity, non-pyrogenicity, and sterility.

129 (43) ~~[(42)]~~ Reasonable quantity--An amount of a compounded drug that:

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

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

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

138 (44) ~~[(43)]~~ Segregated Compounding Area--A designated space, either a demarcated area or  
139 room, that is restricted to preparing low-risk level compounded sterile preparations with 12-hour  
140 or less beyond-use date. Such area shall contain a device that provides unidirectional airflow of  
141 ISO Class 5 air quality for preparation of compounded sterile preparations and shall be void of  
142 activities and materials that are extraneous to sterile compounding.

143 (45) [(44)] Single-dose container--A single-unit container for articles or preparations intended  
144 for parenteral administration only. It is intended for a single use. A single-dose container is  
145 labeled as such. Examples of single-dose containers include pre-filled syringes, cartridges,  
146 fusion-sealed containers, and closure-sealed containers when so labeled.

147 (46) [(45)] SOPs--Standard operating procedures.

148 (47) [(46)] Sterilizing Grade Membranes--Membranes that are documented to retain 100% of a  
149 culture of 10<sup>7</sup> microorganisms of a strain of *Brevundimonas* (*Pseudomonas*) *diminuta* per square  
150 centimeter of membrane surface under a pressure of not less than 30 psi (2.0 bar). Such filter  
151 membranes are nominally at 0.22-micrometer [~~µm~~] or 0.2-micrometer [~~µm~~] nominal pore size,  
152 depending on the manufacturer's practice.

153 (48) [(47)] Sterilization by Filtration--Passage of a fluid or solution through a sterilizing grade  
154 membrane to produce a sterile effluent.

155 (49) [(48)] Terminal Sterilization--The application of a lethal process, e.g., steam under pressure  
156 or autoclaving, to sealed final preparation containers for the purpose of achieving a  
157 predetermined sterility assurance level of usually less than 10<sup>-6</sup> or a probability of less than one  
158 in one million of a non-sterile unit.

159 (50) [(49)] Unidirectional Flow--An airflow moving in a single direction in a robust and uniform  
160 manner and at sufficient speed to reproducibly sweep particles away from the critical processing  
161 or testing area.

162 (51) [(50)] USP/NF--The current edition of the United States Pharmacopeia/National Formulary.

163 (c) Personnel.

164 (1) - (2) (No change.)

165 (3) Pharmacy technicians and pharmacy technician trainees.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

209 (II) and

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

215 (-b-) possess knowledge about:

216 (-1-) aseptic processing;

217 (-2-) quality control and quality assurance as related to environmental, component, and finished  
218 preparation release checks and tests;

219 (-3-) chemical, pharmaceutical, and clinical properties of drugs;

220 (-4-) container, equipment, and closure system selection; and

221 (-5-) sterilization techniques.

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

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

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

229 (III) ~~the~~ supervising pharmacist conducts periodic in-process checks as documented in the  
230 pharmacy's policy and procedures and a final check ~~checks~~.

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

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

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



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

243 (4) Evaluation and testing requirements.

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

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

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

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

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

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

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

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

262 (i) aseptic technique;

263 (ii) critical area contamination factors;

264 (iii) environmental monitoring;

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

266 (v) equipment and supplies;

267 (vi) sterile preparation calculations and terminology;

268 (vii) sterile preparation compounding documentation;

269 (viii) quality assurance procedures;

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

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

272 (xi) cleaning procedures; and

273 (xii) general conduct in the clean room.

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

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

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

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

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

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

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

- (ii) whenever the quality assurance program yields an unacceptable result;
- (iii) whenever unacceptable techniques are observed; and
- (iv) at least on an annual basis for low- and medium-risk level compounding, and every six months for high-risk level compounding.
- (K) The pharmacist-in-charge shall ensure that proper hand hygiene and garbing practices of compounding personnel are evaluated prior to compounding, supervising, or verifying sterile preparations intended for patient use and whenever an aseptic media fill is performed.
- (i) Sampling of compounding personnel glove fingertips shall be performed for all risk level compounding.
- (ii) All compounding personnel shall demonstrate competency in proper hand hygiene and garbing procedures and in aseptic work practices (e.g., disinfection of component surfaces, routine disinfection of gloved hands).
- (iii) Sterile contact agar plates shall be used to sample the gloved fingertips of compounding personnel after garbing in order to assess garbing competency and after completing the media-fill preparation (without applying sterile 70% IPA).
- (iv) The visual observation shall be documented and maintained to provide a permanent record and long-term assessment of personnel competency.
- (v) All compounding personnel shall successfully complete an initial competency evaluation and gloved fingertip/thumb sampling procedure no less than three times before initially being allowed to compound sterile preparations for patient use. Immediately after the compounding personnel completes the hand hygiene and garbing procedure (i.e., after donning of sterile gloves and before any disinfecting [e.g., donning of sterile gloves prior to any disinfection]) with sterile 70% IPA), the evaluator will collect a gloved fingertip and thumb sample from both hands of ~~from~~ the compounding personnel onto agar plates or media test paddles by having the individual lightly touching [pressing] each fingertip onto [into] the agar. The test plates or test paddles will be incubated for the appropriate incubation period and at the appropriate temperature. Results of the initial gloved fingertip evaluations shall indicate zero colony-forming units (0 CFU) growth on the agar plates or media test paddles, or the test shall be considered a failure. In the event of a failed gloved fingertip test, the evaluation shall be repeated until the individual can successfully don sterile gloves and pass the gloved fingertip evaluation, defined as zero CFUs growth. No preparation intended for patient use shall be compounded by an individual until the results of the initial gloved fingertip evaluation indicate that the individual can competently perform aseptic procedures except that a pharmacist may temporarily supervise pharmacy technicians compounding sterile preparations while waiting for the results of the evaluation for no more than three days. [Re-evaluation of all compounding personnel shall occur at least annually for compounding personnel who compound low and medium risk level preparations and every six months for compounding personnel who compound high risk level preparations.]

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

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

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

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

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

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

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

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

(d) Operational Standards.

(1) (No change.)

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

(A) Low-risk level compounded sterile preparations.

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

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

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

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

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

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

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

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

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

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

409 (ii) The primary engineering control device shall be certified and maintain ISO Class 5 for  
410 exposure of critical sites and shall be located in a segregated compounding area restricted to

411 sterile compounding activities that minimizes the risk of contamination of the compounded  
412 sterile preparation.

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

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

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

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

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

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

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

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

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

439 (ii) Examples of medium-risk compounding. Examples of medium-risk compounding include the  
440 following.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

473 (VII) All non-sterile measuring, mixing, and purifying devices are rinsed thoroughly with sterile,  
474 pyrogen-free water, and then thoroughly drained or dried immediately before use for high-risk  
475 compounding. All high-risk compounded sterile solutions subjected to terminal sterilization are



476 prefiltered by passing through a filter with a nominal pore size not larger than 1.2 micron  
477 preceding or during filling into their final containers to remove particulate matter. Sterilization of  
478 high-risk level compounded sterile preparations by filtration shall be performed with a sterile 0.2  
479 micrometer or 0.22 micrometer nominal pore size filter entirely within an ISO Class 5 or  
480 superior air quality environment.

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

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

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

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

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

492 (3) - (5) (No change.)

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

495 (A) Low and Medium Risk Preparations.

496 ~~[(+)]~~ A pharmacy that prepares low- and medium-risk preparations shall have a clean room for  
497 the compounding of sterile preparations that is constructed to minimize the opportunities for  
498 particulate and microbial contamination. The clean room shall:

499 (i) ~~[(+)]~~ be clean, well lit, and of sufficient size to support sterile compounding activities;

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

503 (iii) ~~[(+)]~~ be used only for the compounding of sterile preparations;

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

506 (v) ~~[(+)]~~ have non-porous and washable floors or floor covering to enable regular disinfection;



507 (vi) [~~(VI)~~] be ventilated in a manner to avoid disruption from the HVAC system and room cross-  
508 drafts;

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

512 (viii) [~~(VIII)~~] have junctures of ceilings to walls coved or caulked to avoid cracks and crevices;

513 (ix) [~~(IX)~~] have drugs and supplies stored on shelving areas above the floor to permit adequate  
514 floor cleaning;

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

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

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

523 (I) [~~(a)~~] There shall be some demarcation designation that delineates the ante-area from the  
524 buffer area. The demarcation shall be such that it does not create conditions that could adversely  
525 affect the cleanliness of the area.

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

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

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

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

537 [~~(I) The primary engineering control shall:]~~

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

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

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

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

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

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

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

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

(B) High-risk Preparations.

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

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

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

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

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

574 (i) ~~[(H)]~~ Hazardous drugs shall be prepared only under conditions that protect personnel during  
575 preparation and storage.

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

578 (iii) ~~[(H)]~~ All personnel involved in the compounding of hazardous drugs shall wear appropriate  
579 protective apparel, such as gowns, face masks, eye protection, hair covers, shoe covers or  
580 dedicated shoes, and appropriate gloving at all times when handling hazardous drugs, including  
581 receiving, distribution, stocking, inventorying, preparation, for administration and disposal.

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

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

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

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

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

595 ~~[(II) have a pressure indicator that can be readily monitored for correct room pressurization.]~~

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

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

- 605 (i) The pharmacist-in-charge is responsible for developing written procedures for cleaning and  
606 disinfecting the direct and contiguous compounding areas and assuring the procedures are  
607 followed.
- 608 (ii) These procedures shall be conducted at the beginning of each work shift, before each batch  
609 preparation is started, when there are spills, and when surface contamination is known or  
610 suspected resulting from procedural breaches, and every 30 minutes during continuous  
611 compounding of individual compounded sterile preparations, unless a particular compounding  
612 procedure requires more than 30 minutes to complete, in which case, the direct compounding  
613 area is to be cleaned immediately after the compounding activity is completed. ~~[when there are~~  
614 ~~spills, and when surface contamination is known or suspected from procedural breaches.]~~
- 615 (iii) Before compounding is performed, all items shall be removed from the direct and  
616 contiguous compounding areas and all surfaces are cleaned by removing loose material and  
617 residue from spills, followed by an application of a residue-free disinfecting agent (e.g., IPA),  
618 which is allowed to dry before compounding begins.
- 619 (iv) Work surfaces in the ISO Class 7 buffer areas and ISO Class 8 ante-areas, as well as  
620 segregated compounding areas, shall be cleaned and disinfected at least daily. Dust and debris  
621 shall be removed when necessary from storage sites for compounding ingredients and supplies  
622 using a method that does not degrade the ISO Class 7 or 8 air quality.
- 623 (v) Floors in the buffer area, ante-area, and segregated compounding area are cleaned by  
624 mopping with a cleaning and disinfecting agent at least once daily when no aseptic operations  
625 are in progress. Mopping shall be performed by trained personnel using approved agents and  
626 procedures described in the written SOPs. It is incumbent on compounding personnel to ensure  
627 that such cleaning is performed properly.
- 628 (vi) In the buffer area, ante-area, and segregated compounding area, walls, ceilings, and shelving  
629 shall be cleaned and disinfected monthly. Cleaning and disinfecting agents shall be used with  
630 careful consideration of compatibilities, effectiveness, and inappropriate or toxic residues.
- 631 (vii) All cleaning materials, such as wipers, sponges, and mops, shall be non-shedding, and  
632 dedicated to use in the buffer area, ante-area, and segregated compounding areas and shall not be  
633 removed from these areas except for disposal. Floor mops may be used in both the buffer area  
634 and ante-area, but only in that order. If cleaning materials are reused, procedures shall be  
635 developed that ensure that the effectiveness of the cleaning device is maintained and that  
636 repeated use does not add to the bio-burden of the area being cleaned.
- 637 (viii) Supplies and equipment removed from shipping cartons must be wiped with a disinfecting  
638 agent, such as sterile IPA. After the disinfectant is sprayed or wiped on a surface to be  
639 disinfected, the disinfectant shall be allowed to dry, during which time the item shall not be used  
640 for compounding purposes. However, if sterile supplies are received in sealed pouches, the  
641 pouches may be removed as the supplies are introduced into the ISO Class 5 area without the  
642 need to disinfect the individual sterile supply items. No shipping or other external cartons may be  
643 taken into the buffer area or segregated compounding area.

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

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

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

649 (I) date and time of cleaning;

650 (II) type of cleaning performed; and

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

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

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

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

662 (ii) Beyond-use dating.

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

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

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

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

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

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

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

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

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

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

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

701 (B) Biological safety cabinet.

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

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

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

710 (ii) Pharmacies that prepare a low volume of hazardous drugs, are not required to comply with  
711 the provisions of clause (i) of this subparagraph if the pharmacy uses a device that provides two

712 tiers of containment (e.g., closed-system vial transfer device within a BSC or CACI that is  
713 located in a non-negative pressure room).

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

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

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

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

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

730 (C) Compounding aseptic isolator.

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

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

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

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

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

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



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

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

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

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

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

758 (D) Compounding aseptic containment isolator.

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

762 (I) be vented to the outside of the building in which the pharmacy is located; provide at least 0.01  
763 inches water column negative pressure compared to the other areas of the pharmacy;

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

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

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

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

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

774 (ii) If the CACI meets all conditions specified in clause (i) of this subparagraph, the CACI shall  
775 not be located in the same room as a CAI, but shall be located in a separate room in the  
776 pharmacy, that is not required to maintain ISO classified air. The room in which the CACI is



777 located shall provide a minimum of 0.01 inches water column negative pressure compared with  
778 the other areas of the pharmacy and shall meet the following requirements:

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

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

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

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

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

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

792 (8) [(7)] Additional Equipment and Supplies. [Equipment and supplies.] Pharmacies  
793 compounding sterile preparations shall have the following equipment and supplies:

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

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

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

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

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

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

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

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

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

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

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

815 (H) infusion devices, if applicable; and

816 (I) all necessary supplies, including:

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

818 (ii) disinfectant cleaning solutions;

819 (iii) sterile 70% isopropyl alcohol;

820 (iv) sterile gloves, both for hazardous and non-hazardous drug compounding;

821 (v) sterile alcohol-based or water-less alcohol based surgical scrub;

822 (vi) [~~(iii)~~] hand washing agents with bactericidal action;

823 (vii) [~~(iv)~~] disposable, lint free towels or wipes;

824 (viii) [~~(v)~~] appropriate filters and filtration equipment;

825 (ix) [~~(vi)~~] hazardous spill kits, if applicable; and

826 (x) [~~(vii)~~] masks, caps, coveralls or gowns with tight cuffs, shoe covers, and gloves, as  
827 applicable.

828 (9) [~~(8)~~] Labeling.

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

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

834 (ii) for outpatient prescription orders only, a statement that the compounded sterile preparation  
835 has been compounded by the pharmacy. (An auxiliary label may be used on the container to  
836 meet this requirement);

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

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

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

843 (ii) quantity;

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

846 (iv) device-specific instructions, where appropriate.

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

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

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

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

853 (10) ~~[(9)]~~ Written drug information for prescription drug orders only. Written information about  
854 the compounded preparation or its major active ingredient(s) shall be given to the patient at the  
855 time of dispensing a prescription drug order. A statement which indicates that the preparation  
856 was compounded by the pharmacy must be included in this written information. If there is no  
857 written information available, the patient shall be advised that the drug has been compounded  
858 and how to contact a pharmacist, and if appropriate, the prescriber, concerning the drug.

859 (11) ~~[(10)]~~ Pharmaceutical Care Services. In addition to the pharmaceutical care requirements for  
860 the pharmacy's specific license classification, the following requirements for sterile preparations  
861 compounded pursuant to prescription drug orders must be met.

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

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

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

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

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

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

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

876 (I) safeguards against microbial contamination, including aseptic techniques for compounding  
877 intravenous admixtures and aseptic techniques for injecting additives to premixed intravenous  
878 solutions;

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

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

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

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

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

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

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

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

894 (12) ~~(14)~~ Drugs, components, and materials used in sterile compounding.

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

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

899 (i) Chemically Pure (CP);

900 (ii) Analytical Reagent (AR);

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

902 (iv) Food Chemical Codex.

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

907 (D) All components shall:

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

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

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

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

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

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

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

923 (13) ~~[(42)]~~ Compounding process.

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

928 (i) the facility;

929 (ii) equipment;

930 (iii) personnel;

931 (iv) preparation evaluation;

932 (v) quality assurance;

933 (vi) preparation recall;

934 (vii) packaging; and

935 (viii) storage of compounded sterile preparations.

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

938 (C) Personnel Cleansing and Garbing.

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

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

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

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

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

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

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

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

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

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

966 (IV) Once inside the buffer area or segregated compounding area, and prior to donning sterile  
967 powder-free gloves, antiseptic hand cleansing shall be performed using a sterile 70% IPA-based  
968 or another suitable sterile ~~waterless~~ alcohol-based surgical hand scrub with persistent activity  
969 following manufacturers' recommendations. Hands shall be allowed to dry thoroughly before  
970 donning sterile gloves.

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

978 (v) When compounding personnel shall temporarily exit the ISO Class 7 environment during a  
979 work shift, the exterior gown, if not visibly soiled, may be removed and retained in the ISO Class  
980 8 ante-area, to be re-donned during that same work shift only. However, shoe covers, hair and  
981 facial hair covers, face mask/eye shield, and gloves shall be replaced with new ones before re-  
982 entering the ISO Class 7 clean environment along with performing proper hand hygiene.

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

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

(14) ~~[(13)]~~ Quality Assurance.

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

(i) Low risk preparations.

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

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

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

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

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

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

(ii) Medium risk preparations.



1024 (I) Quality assurance procedures for medium-risk level compounded sterile preparations include  
1025 all those for low-risk level compounded sterile preparations, as well as a more challenging  
1026 media-fill test passed annually, or more frequently.

1027 (II) Example of a Media-Fill Test Procedure. This, or an equivalent test, is performed at least  
1028 annually under conditions that closely simulate the most challenging or stressful conditions  
1029 encountered during compounding. This test is completed without interruption within an ISO  
1030 Class 5 air quality environment. Six 100-milliliter aliquots of sterile Soybean-Casein Digest  
1031 Medium are aseptically transferred by gravity through separate tubing sets into separate  
1032 evacuated sterile containers. The six containers are then arranged as three pairs, and a sterile 10-  
1033 milliliter syringe and 18-gauge needle combination is used to exchange two 5-milliliter aliquots  
1034 of medium from one container to the other container in the pair. For example, after a 5-milliliter  
1035 aliquot from the first container is added to the second container in the pair, the second container  
1036 is agitated for 10 seconds, then a 5-milliliter aliquot is removed and returned to the first container  
1037 in the pair. The first container is then agitated for 10 seconds, and the next 5-milliliter aliquot is  
1038 transferred from it back to the second container in the pair. Following the two 5-milliliter aliquot  
1039 exchanges in each pair of containers, a 5-milliliter aliquot of medium from each container is  
1040 aseptically injected into a sealed, empty, sterile 10-milliliter clear vial, using a sterile 10-  
1041 milliliter syringe and vented needle. Sterile adhesive seals are aseptically affixed to the rubber  
1042 closures on the three filled vials. The vials are incubated within a range of 20 - 35 degrees  
1043 Celsius for a minimum of 14 days. Failure is indicated by visible turbidity in the medium on or  
1044 before 14 days. The media-fill test must include a positive-control sample.

1045 (iii) High risk preparations.

1046 (I) Procedures for high-risk level compounded sterile preparations include all those for low-risk  
1047 level compounded sterile preparations. In addition, a media-fill test that represents high-risk level  
1048 compounding is performed twice a year by each person authorized to compound high-risk level  
1049 compounded sterile preparations.

1050 (II) Example of a Media-Fill Test Procedure Compounded Sterile Preparations Sterilized by  
1051 Filtration. This test, or an equivalent test, is performed under conditions that closely simulate the  
1052 most challenging or stressful conditions encountered when compounding high-risk level  
1053 compounded sterile preparations. Note: Sterility tests for autoclaved compounded sterile  
1054 preparations are not required unless they are prepared in batches of more than 25 units. This test  
1055 is completed without interruption in the following sequence:

1056 (-a-) Dissolve 3 grams of non-sterile commercially available Soybean-Casein Digest Medium in  
1057 100 milliliters of non-bacteriostatic water to make a 3% non-sterile solution.

1058 (-b-) Draw 25 milliliters of the medium into each of three 30-milliliter sterile syringes. Transfer 5  
1059 milliliters from each syringe into separate sterile 10-milliliter vials. These vials are the positive  
1060 controls to generate exponential microbial growth, which is indicated by visible turbidity upon  
1061 incubation.

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

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

(B) Finished preparation release checks and tests.

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

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

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

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

(C) Environmental Testing.

1099 (i) ~~[(C)]~~ Viable and nonviable environmental sampling testing. Environmental sampling shall  
1100 occur, at a minimum, every six months as part of a comprehensive quality management program  
1101 and under any of the following conditions:

1102 (I) ~~[(i)]~~ as part of the commissioning and certification of new facilities and equipment;

1103 (II) ~~[(ii)]~~ following any servicing of facilities and equipment;

1104 (III) ~~[(iii)]~~ as part of the re-certification of facilities and equipment;

1105 (IV) ~~[(iv)]~~ in response to identified problems with end products or staff technique; or

1106 (V) ~~[(v)]~~ in response to issues with compounded sterile preparations, observed compounding  
1107 personnel work practices, or patient-related infections (where the compounded sterile preparation  
1108 is being considered as a potential source of the infection).

1109 (ii) ~~[(D)]~~ Total particle counts. Certification that each ISO classified area (e.g., ISO Class 5, 7,  
1110 and 8), is within established guidelines shall be performed no less than every six months and  
1111 whenever the equipment is relocated or the physical structure of the buffer area or ante-area has  
1112 been altered. All certification records shall be maintained and reviewed to ensure that the  
1113 controlled environments comply with the proper air cleanliness, room pressures, and air changes  
1114 per hour. Testing shall be performed by qualified operators using current, state-of-the-art  
1115 equipment, with results of the following:

1116 (I) ~~[(i)]~~ ISO Class 5 - not more than 3520 particles 0.5 micrometer ~~[µm]~~ and larger size per cubic  
1117 meter of air;

1118 (II) ~~[(ii)]~~ ISO Class 7 - not more than 352,000 particles of 0.5 micrometer ~~[µm]~~ and larger size  
1119 per cubic meter of air for any buffer area; and

1120 (III) ~~[(iii)]~~ ISO Class 8 - not more than 3,520,000 particles of 0.5 micrometer ~~[µm]~~ and larger  
1121 size per cubic meter of air for any ante-area.

1122 (iii) ~~[(E)]~~ Pressure differential monitoring. A pressure gauge or velocity meter shall be installed  
1123 to monitor the pressure differential or airflow between the buffer area and the ante-area and  
1124 between the ante-area and the general environment outside the compounding area. The results  
1125 shall be reviewed and documented on a log at least every work shift (minimum frequency shall  
1126 be at least daily) or by a continuous recording device. The pressure between the ISO Class 7 and  
1127 the general pharmacy area shall not be less than 0.02 inch water column.

1128 (iv) ~~[(F)]~~ Sampling plan. An appropriate environmental sampling plan shall be developed for  
1129 airborne viable particles based on a risk assessment of compounding activities performed.  
1130 Selected sampling sites shall include locations within each ISO Class 5 environment and in the  
1131 ISO Class 7 and 8 areas and in the segregated compounding areas at greatest risk of  
1132 contamination. The plan shall include sample location, method of collection, frequency of

1133 sampling, volume of air sampled, and time of day as related to activity in the compounding area  
1134 and action levels.

1135 (v) [~~(G)~~] Viable air sampling. Evaluation of airborne microorganisms using volumetric collection  
1136 methods in the controlled air environments shall be performed by properly trained individuals for  
1137 all compounding risk levels. For low-, medium-, and high-risk level compounding, air sampling  
1138 shall be performed at locations that are prone to contamination during compounding activities  
1139 and during other activities such as staging, labeling, gowning, and cleaning. Locations shall  
1140 include zones of air backwash turbulence within the laminar airflow workbench and other areas  
1141 where air backwash turbulence may enter the compounding area. For low-risk level compounded  
1142 sterile preparations within 12-hour or less beyond-use-date prepared in a primary engineering  
1143 control that maintains an ISO Class 5, air sampling shall be performed at locations inside the ISO  
1144 Class 5 environment and other areas that are in close proximity to the ISO Class 5 environment  
1145 during the certification of the primary engineering control.

1146 (vi) [~~(H)~~] Air sampling frequency and process. Air sampling shall be performed at least every 6  
1147 months as a part of the re-certification of facilities and equipment. A sufficient volume of air  
1148 shall be sampled and the manufacturer's guidelines for use of the electronic air sampling  
1149 equipment followed. At the end of the designated sampling or exposure period for air sampling  
1150 activities, the microbial growth media plates are recovered and their covers secured and they are  
1151 inverted and incubated at a temperature and for a time period conducive to multiplication of  
1152 microorganisms. Sampling data shall be collected and reviewed on a periodic basis as a means of  
1153 evaluating the overall control of the compounding environment. If an activity consistently shows  
1154 elevated levels of microbial growth, competent microbiology personnel shall be consulted.

1155 (vii) [~~(I)~~] Compounding accuracy checks. Written procedures for double-checking compounding  
1156 accuracy shall be followed for every compounded sterile preparation during preparation and  
1157 immediately prior to release, including label accuracy and the accuracy of the addition of all drug  
1158 products or ingredients used to prepare the finished preparation and their volumes or quantities.  
1159 At each step of the compounding process, the pharmacist shall ensure that components used in  
1160 compounding are accurately weighed, measured, or subdivided as appropriate to conform to the  
1161 formula being prepared.

1162 (15) [~~(14)~~] Quality control.

1163 (A) Quality control procedures. The pharmacy shall follow established quality control  
1164 procedures to monitor the compounding environment and quality of compounded drug  
1165 preparations for conformity with the quality indicators established for the preparation. When  
1166 developing these procedures, pharmacy personnel shall consider the provisions of USP Chapter  
1167 71, Sterility Tests, USP Chapter 85, Bacterial Endotoxins Test, Pharmaceutical Compounding--  
1168 Non-sterile Preparations, USP Chapter 795, USP Chapter 797, Pharmaceutical Compounding--  
1169 Sterile Preparations, Chapter 1075, Good Compounding Practices, and Chapter 1160,  
1170 Pharmaceutical Calculations in Prescription Compounding, and USP Chapter 1163, Quality  
1171 Assurance in Pharmaceutical Compounding of the current USP/NF. Such procedures shall be  
1172 documented and be available for inspection.

- 1173 (B) Verification of compounding accuracy and sterility.
- 1174 (i) The accuracy of identities, concentrations, amounts, and purities of ingredients in  
1175 compounded sterile preparations shall be confirmed by reviewing labels on packages, observing  
1176 and documenting correct measurements with approved and correctly standardized devices, and  
1177 reviewing information in labeling and certificates of analysis provided by suppliers.
- 1178 (ii) If the correct identity, purity, strength, and sterility of ingredients and components of  
1179 compounded sterile preparations cannot be confirmed such ingredients and components shall be  
1180 discarded immediately. Any compounded sterile preparation that fails sterility testing following  
1181 sterilization by one method (e.g., filtration) is to be discarded and not subjected to a second  
1182 method of sterilization.
- 1183 (iii) If individual ingredients, such as bulk drug substances, are not labeled with expiration dates,  
1184 when the drug substances are stable indefinitely in their commercial packages under labeled  
1185 storage conditions, such ingredients may gain or lose moisture during storage and use and shall  
1186 require testing to determine the correct amount to weigh for accurate content of active chemical  
1187 moieties in compounded sterile preparations.
- 1188 (e) Records. Any testing, cleaning, procedures, or other activities required in this subsection shall  
1189 be documented and such documentation shall be maintained by the pharmacy.
- 1190 (1) Maintenance of records. Every record required under this section must be:
- 1191 (A) kept by the pharmacy and be available, for at least two years for inspecting and copying by  
1192 the board or its representative and to other authorized local, state, or federal law enforcement  
1193 agencies; and
- 1194 (B) supplied by the pharmacy within 72 hours, if requested by an authorized agent of the Texas  
1195 State Board of Pharmacy. If the pharmacy maintains the records in an electronic format, the  
1196 requested records must be provided in an electronic format. Failure to provide the records set out  
1197 in this section, either on site or within 72 hours, constitutes prima facie evidence of failure to  
1198 keep and maintain records in violation of the Act.
- 1199 (2) Compounding records.
- 1200 (A) Compounding pursuant to patient specific prescription drug orders. Compounding records  
1201 for all compounded preparations shall be maintained by the pharmacy electronically or manually  
1202 as part of the prescription drug or medication order, formula record, formula book, or  
1203 compounding log and shall include:
- 1204 (i) the date of preparation;
- 1205 (ii) a complete formula, including methodology and necessary equipment which includes the  
1206 brand name(s) of the raw materials, or if no brand name, the generic name(s) or official name  
1207 and name(s) of the manufacturer(s) or distributor of the raw materials and the quantities of each;

1208 (iii) signature or initials of the pharmacist or pharmacy technician or pharmacy technician trainee  
1209 performing the compounding;

1210 (iv) signature or initials of the pharmacist responsible for supervising pharmacy technicians or  
1211 pharmacy technician trainees and conducting in-process and finals checks of compounded  
1212 pharmaceuticals if pharmacy technicians or pharmacy technician trainees perform the  
1213 compounding function;

1214 (v) the quantity in units of finished preparation or amount of raw materials;

1215 (vi) the container used and the number of units prepared; and

1216 (vii) a reference to the location of the following documentation which may be maintained with  
1217 other records, such as quality control records:

1218 (I) the criteria used to determine the beyond-use date; and

1219 (II) documentation of performance of quality control procedures.

1220 (B) Compounding records when batch compounding or compounding in anticipation of future  
1221 prescription drug or medication orders.

1222 (i) Master work sheet. A master work sheet shall be developed and approved by a pharmacist for  
1223 preparations prepared in batch. Once approved, a duplicate of the master work sheet shall be  
1224 used as the preparation work sheet from which each batch is prepared and on which all  
1225 documentation for that batch occurs. The master work sheet shall contain at a minimum:

1226 (I) the formula;

1227 (II) the components;

1228 (III) the compounding directions;

1229 (IV) a sample label;

1230 (V) evaluation and testing requirements;

1231 (VI) specific equipment used during preparation; and

1232 (VII) storage requirements.

1233 (ii) Preparation work sheet. The preparation work sheet for each batch of preparations shall  
1234 document the following:

1235 (I) identity of all solutions and ingredients and their corresponding amounts, concentrations, or  
1236 volumes;

- 1237 (II) lot number for each component;
- 1238 (III) component manufacturer/distributor or suitable identifying number;
- 1239 (IV) container specifications (e.g., syringe, pump cassette);
- 1240 (V) unique lot or control number assigned to batch;
- 1241 (VI) expiration date of batch-prepared preparations;
- 1242 (VII) date of preparation;
- 1243 (VIII) name, initials, or electronic signature of the person(s) involved in the preparation;
- 1244 (IX) name, initials, or electronic signature of the responsible pharmacist;
- 1245 (X) finished preparation evaluation and testing specifications, if applicable; and
- 1246 (XI) comparison of actual yield to anticipated or theoretical yield, when appropriate.
- 1247 (f) - (g) (No change.)
- 1248 The agency certifies that legal counsel has reviewed the proposal and found it to be within the
- 1249 state agency's legal authority to adopt.





April 8, 2015

Attention: Allison Benz  
Texas State Board of Pharmacy  
333 Guadalupe St. Tower 3, Suite 600  
Austin, TX 78701

RE: Comment Submission for TAC 291.133

Dear Ms. Benz,

We would like to submit the following comment to the Board for the proposed rule revisions of TAC 291.133.

Section, subdivision	Proposed Language	Recommendation
(9)(d)(13)(C) (iv)(IV)	Once inside the buffer area or segregated compounding area, and prior to donning sterile powder-free gloves, antiseptic hand cleansing shall be performed using a <u>sterile 70% IPA</u> <del>[waterless alcohol]</del> based surgical hand scrub with persistent activity following manufacturers' recommendations.	Once inside the buffer area or segregated compounding area, and prior to donning sterile powder-free gloves, antiseptic cleansing shall be performed using <u>a</u> <del>waterless alcohol-based</del> surgical hand scrub with persistent activity following manufacturers' recommendations.

Institution/Contact: Hartley Medical (#26729), William Stuart, RPh

Rationale:

1. We recommend that the language remain consistent with the text of USP <797>.
2. To the best of our knowledge, a "sterile 70% IPA based surgical hand scrub" does not exist on the market. We have researched many products available and all contain ethyl alcohol. Additionally, the reference products are not sterile. Therefore I ask for the Board to remove the wording; "sterile 70% IPA based hand scrub".

Sincerely,

William A. Stuart, RPh  
President  
Hartley Medical Center Pharmacy, Inc.