

RULE ANALYSIS

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

Short Title: Nuclear Pharmacy

Rule Numbers: §§291.52, 291.53, 291.54

Statutory Authority: Texas Pharmacy Act, Chapter 551-566 and 568-569, 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, updated the definitions; require nuclear pharmacies to be inspected prior to renewal; and clarify the requirements for compounding non-sterile radiopharmaceuticals.

The Board reviewed and voted to propose the amendments during the August 5, 2014, meeting. The proposed amendments were published in the September 26, 2014, issue of the *Texas Register* at 39 TexReg 7707.

1 **PART 15. TEXAS STATE BOARD OF PHARMACY**

2 **CHAPTER 291. PHARMACIES**

3 **SUBCHAPTER C. NUCLEAR PHARMACY (CLASS B)**

4 **22 TAC §§291.52 - 291.54**

5 The Texas State Board of Pharmacy proposes amendments to §291.52, concerning Definitions;
6 §291.53, concerning Personnel; and §291.54, concerning Operational Standards. The
7 amendments to §291.52, if adopted, update the definitions. The amendments to §291.53, if
8 adopted, clarify the requirements for compounding sterile non-radiopharmaceuticals. The
9 amendments to §291.54, if adopted, require nuclear pharmacies to be inspected prior to renewal.

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

13 Ms. Dodson has determined that, for each year of the first five-year period the rule will be in
14 effect, the public benefit anticipated as a result of enforcing the amendments will ensure nuclear
15 pharmacies compounding sterile preparations will be inspected. There is no fiscal impact for
16 individuals, small or large businesses, or to other entities which are required to comply with this
17 section.

18 Comments on the amendments may be submitted to Allison Benz, R.Ph., M.S., Director of
19 Professional Services, Texas State Board of Pharmacy, by mail at 333 Guadalupe Street, Suite 3-
20 600, Austin, Texas 78701 or by fax at (512) 305-8008. Comments must be received by 5:00
21 p.m., October 31, 2014.

22 The amendments are proposed under §551.002 and §554.051 of the Texas Pharmacy Act
23 (Chapters 551 - 566 and 568 - 569, Texas Occupations Code). The Board interprets §551.002 as
24 authorizing the agency to protect the public through the effective control and regulation of the
25 practice of pharmacy. The Board interprets §554.051(a) as authorizing the agency to adopt rules
26 for the proper administration and enforcement of the Act.

27 The statutes affected by these amendments: Texas Pharmacy Act, Chapters 551 - 566 and 568 -
28 569, Texas Occupations Code.

29 **§291.52. Definitions.**

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

33 (1) - (6) (No change.)

34 (7) Aseptic processing--A mode of processing pharmaceutical and medical products that
35 involves the separate sterilization of the product and of the package (containers/closures or
36 packaging material for medical devices) and the transfer of the product into the container and its
37 closure under at least ISO Class 5 conditions. [~~The technique involving procedures designed to~~
38 ~~preclude contamination of drugs, packaging, equipment, or supplies by microorganisms during~~
39 ~~processing.~~]

40 (8) - (13) (No change.)

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

45 (15) - (17) (No change.)

46 (18) Critical site--A location that includes any component or fluid pathway surfaces (e.g., vial
47 septa, injection ports, beakers) or openings (e.g., opened ampuls, needle hubs) exposed and at
48 risk of direct contact with air (e.g., ambient room or HEPA filtered), moisture (e.g., oral and
49 mucosal secretions), or touch contamination. Risk of microbial particulate contamination of the
50 critical site increases with the size of the openings and exposure time. [~~Sterile ingredients of~~
51 ~~compounded sterile preparations and locations on devices and components used to prepare,~~
52 ~~package, and transfer compounded sterile preparations that provide opportunity for exposure to~~
53 ~~contamination.~~]

54 (19) - (43) (No change.)

55 **§291.53. Personnel.**

56 (a) - (b) (No change.)

57 (c) Authorized nuclear pharmacists.

58 (1) (No change.)

59 (2) Special requirements for compounding of non-radiopharmaceutical preparations.

60 (A) Non-sterile preparations. All pharmacists engaged in compounding non-sterile non-
61 radiopharmaceuticals shall meet the training requirements specified in §291.131 of this title
62 (relating to Pharmacies Compounding Non-Sterile Preparations).

63 (B) Sterile Preparations. All pharmacists engaged in compounding sterile non-
64 radiopharmaceuticals shall meet the training requirements specified in §291.133 of this title
65 (relating to Pharmacies Compounding Sterile Preparations).

66 (3) (No change.)

- 67 (d) Pharmacy Technicians and Pharmacy Technician Trainees.
- 68 (1) (No change.)
- 69 (2) Special requirements for compounding of non-radiopharmaceutical preparations.
- 70 (A) Non-sterile preparations. All pharmacy technicians and pharmacy technician trainees
71 engaged in compounding non-sterile non-radiopharmaceuticals shall meet the training
72 requirements specified in §291.131 of this title.
- 73 (B) Sterile Preparations. All pharmacy technicians and pharmacy technician trainees engaged in
74 compounding sterile non- radiopharmaceuticals shall meet the training requirements specified in
75 §291.133 of this title.
- 76 (3) - (4) (No change.)
- 77 ~~[(e) Special education, training, and evaluation requirements for pharmacy personnel
78 compounding or responsible for the direct supervision of pharmacy personnel compounding
79 sterile radiopharmaceuticals. All pharmacy personnel preparing sterile radiopharmaceuticals
80 shall meet the training requirements specified in §291.133 of this title.]~~
- 81 **§291.54. Operational Standards.**
- 82 (a) Licensing requirements.
- 83 (1) - (3) (No change.)
- 84 (4) A Class B pharmacy may not renew a pharmacy license unless the pharmacy has been
85 inspected by the board within the last renewal period.
- 86 (5) [(4)] A Class B pharmacy which changes ownership shall notify the board within ten days of
87 the change of ownership and apply for a new and separate license as specified in §291.3 of this
88 title (relating to Required Notifications).
- 89 (6) [(5)] A Class B pharmacy which changes location and/or name shall notify the board within
90 ten days of the change and file for an amended license as specified in §291.3 of this title.
- 91 (7) [(6)] A Class B pharmacy owned by a partnership or corporation which changes managing
92 officers shall notify the board in writing of the names of the new managing officers within ten
93 days of the change, following the procedures in §291.3 of this title.
- 94 (8) [(7)] A Class B pharmacy shall notify the board in writing within ten days of closing,
95 following the procedures in §291.5 of this title (relating to Closing a Pharmacy).
- 96 (9) [(8)] A separate license is required for each principal place of business and only one
97 pharmacy license may be issued to a specific location.

98 ~~(10)~~ [(9)] A fee as specified in §291.6 of this title (relating to Pharmacy License Fees) will be
99 charged for the issuance and renewal of a license and the issuance of an amended license.

100 ~~(11)~~ [(10)] A Class B pharmacy, licensed under the provisions of the Act, §560.051(a)(2), which
101 also operates another type of pharmacy which would otherwise be required to be licensed under
102 the Act, §560.051(a)(1), concerning community pharmacy (Class A), is not required to secure a
103 license for such other type of pharmacy; provided, however, such licensee is required to comply
104 with the provisions of §291.31 of this title (relating to Definitions); §291.32 of this title (relating
105 to Personnel); §291.33 of this title (relating to Operational Standards); §291.34 of this title
106 (relating to Records); and §291.35 of this title (relating to Official Prescription Requirements), to
107 the extent such rules are applicable to the operation of the pharmacy.

108 ~~(12)~~ [(11)] A Class B (nuclear) pharmacy engaged in the compounding of non-sterile non-
109 radioactive preparations shall comply with the provisions of §291.131 of this title (relating to
110 Pharmacies Compounding Non-Sterile Preparations).

111 ~~(13)~~ [(12)] A Class B (nuclear) pharmacy engaged in the compounding of sterile non-radioactive
112 preparations shall comply with the provisions of §291.133 of this title (relating to Pharmacies
113 Compounding Sterile Preparations).

114 (b) Risk levels for compounded sterile radiopharmaceuticals. Risk Levels for sterile compounded
115 radiopharmaceuticals shall be as listed below.

116 (1) Low-risk level compounded sterile radiopharmaceuticals.

117 (A) Low-risk level compounded sterile radiopharmaceuticals are those compounded under all of
118 the following conditions.

119 (i) The compounded sterile preparations are compounded with aseptic manipulations entirely
120 within ISO Class 5 or better air quality using only sterile ingredients, products, components, and
121 devices.

122 (ii) The compounding involves only transfer, measuring, and mixing manipulations with closed
123 or sealed packaging systems that are performed promptly and attentively.

124 (iii) Manipulations are limited to aseptically opening ampuls, penetrating sterile stoppers on vials
125 with sterile needles and syringes, and transferring sterile liquids in sterile syringes to sterile
126 administration devices and packages of other sterile products.

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

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

135 (2) Medium-risk level compounded sterile radiopharmaceuticals.

136 (A) Medium-risk level compounded sterile radiopharmaceuticals are those compounded
137 aseptically under low-risk conditions and one or more of the of the following conditions exists.

138 (i) Multiple individual or small doses of sterile products are combined or pooled to prepare [a]
139 compounded sterile radiopharmaceuticals that will be administered either to multiple patients or
140 to one patient on multiple occasions.

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

143 (iii) The compounding process requires unusually long duration, such as that required to
144 complete the dissolution or homogenous mixing.

145 (iv) The sterile compounded radiopharmaceuticals do not contain broad-spectrum bacteriostatic
146 substances, and they are administered over several days.

147 ~~[(v) For a medium risk preparation, in the absence of passing sterility test, the storage periods
148 cannot exceed the following time periods: before administration, the compounded sterile
149 preparations are properly stored and are exposed for not more than 30 hours at controlled room
150 temperature for not more than 7 days at a cold temperature, and for 45 days in solid frozen state
151 at minus 20 degrees or colder.]~~

152 (B) Examples of medium-risk compounding include the following.

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

156 (ii) Filling of reservoirs of injection and infusion devices with multiple sterile drug products and
157 evacuations of air from those reservoirs before the filled device is dispensed.

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

161 (iv) Transfer of volumes from multiple ampuls or vials into a single, final sterile container or
162 product.

163 (3) High-risk level compounded sterile radiopharmaceuticals.

164 (A) High-risk level compounded sterile radiopharmaceuticals are those compounded under any
165 of the following conditions.

166 (i) Non-sterile ingredients, including manufactured products are incorporated, or a non-sterile
167 device is employed before terminal sterilization.

168 (ii) Sterile ingredients, components, devices, and mixtures are exposed to air quality inferior to
169 ISO Class 5. This includes storage in environments inferior to ISO Class 5 of opened or partially
170 used packages of manufactured sterile products that lack antimicrobial preservatives.

171 (iii) Non-sterile preparations are exposed no more than 6 hours before being sterilized.

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

175 ~~[(v) For a high risk preparation, in the absence of passing sterility test, the storage periods cannot
176 exceed the following time periods: before administration, the compounded sterile preparations
177 are properly stored and are exposed for not more than 24 hours at controlled room temperature
178 for not more than 3 days at a cold temperature, and for 45 days in solid frozen state at minus 20
179 degrees or colder.]~~

180 (B) Examples of high-risk compounding include the following.

181 (i) Dissolving non-sterile bulk drug and nutrient powders to make solutions, which will be
182 terminally sterilized.

183 (ii) Sterile ingredients, components, devices, and mixtures are exposed to air quality inferior to
184 ISO Class 5. This includes storage in environments inferior to ISO Class 5 of opened or partially
185 used packages of manufactured sterile products that lack antimicrobial preservatives.

186 (iii) Measuring and mixing sterile ingredients in non-sterile devices before sterilization is
187 performed.

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

191 (c) - (f) (No change.)

192 (g) Radiopharmaceuticals and/or radioactive materials.

193 (1) General requirements.

194 (A) - (B) (No change.)

195 (C) An authorized nuclear pharmacist may transfer to authorized users radioactive materials not
196 intended for drug use in accordance with the requirements of the Texas Department of State
197 Health Services, Radiation Control Program, Texas Administrative Code, Title 25, Part 1,
198 Subchapter F, §289.252 relating to Licensing of Radioactive Material[5].

199 (D) (No change.)

200 (2) - (3) (No change.)

201 (h) - (i) (No change.)

202 The agency certifies that legal counsel has reviewed the proposal and found it to be within the
203 state agency's legal authority to adopt.

204 Filed with the Office of the Secretary of State on September 15, 2014.

205 TRD-201404386

206 Gay Dodson, R.Ph.

207 Executive Director

208 Texas State Board of Pharmacy

209 Earliest possible date of adoption: October 26, 2014

210 For further information, please call: (512) 305-8028

211



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By Overnight Courier

August 1, 2014

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William P. Hobby Building
Tower 3, Suite 600
333 Guadalupe St
Austin, TX 78701

RE: Comments on Proposed Amendments to Rule Numbers §§291.52, 291.53, 291.54

Dear Ms. Dodson:

Cardinal Health Nuclear Pharmacy Services appreciates this opportunity to provide public comments on the proposals by the Texas State Board of Pharmacy to amend sections of Rules §§291.52, 291.53, 291.54 of the Texas State Board of Pharmacy Rules. Cardinal Health Nuclear Pharmacy Services operates nine nuclear pharmacies in Texas, dispensing approximately 58,000 patient doses of diagnostic and therapeutic radiopharmaceuticals every month. Cardinal Health Nuclear Pharmacy Services has 190 employees in Texas of which 35 are pharmacists, accounting for approximately \$12 million dollars in salary paid annually.

Cardinal Health Nuclear Pharmacy Services believes that special consideration for nuclear pharmacy preparation of radiopharmaceuticals should be considered by the Board. At the outset of this discussion is a recognition that the preparation and the very nature of radiopharmaceuticals, among others: an extremely short half-life; the regulation of the preparation of radiopharmaceuticals by the Texas State Board of Pharmacy, the Texas Department of State Health Services Radiation Control Program and the Nuclear Regulatory Commission; and the unique relationship between the prescribing practitioner and the nuclear pharmacist that prepares the prescription, are such that special consideration is warranted.

As proposed the changes to amend sections of the Texas State Board of Pharmacy Rules has the potential to create significant complications for the operation of nuclear pharmacies in Texas. Cardinal Health Nuclear Pharmacy Services proposes consideration of the following suggestions:

Issue 1

- Where the Board proposes to amend in Tab 10, Section 291.54(a)(7):
Aseptic processing-- A mode of processing pharmaceutical and medical products that involves the separate sterilization of the product and of the package (containers– closures or packaging material for medical devices) and the transfer of the product into the container and

its closure under at least ISO Class 5 conditions. ~~[The technique involving procedures designed to preclude contamination of drugs, packaging, equipment, or supplies by microorganisms during processing.]~~

Comment 1

Cardinal Health would opine that such language implies, as applied to a radiopharmaceutical, that the Board anticipates sterility testing on drugs prior to dispensing. As identified above, given the unique short half-life of the radiopharmaceuticals dispensed the Board would be creating an impractical outcome as the product would be decayed beyond its usefulness while awaiting the outcome of the sterility test. When a radiopharmaceutical is prepared from an FDA approved manufacturer of a kit for the preparation of a particular radiopharmaceutical, as Cardinal Health does, the manufacturer has already prepared a sterilized product [kit] whereupon the nuclear pharmacist prepares the dose with the proper radioactivity from another FDA approved manufacturer's product: the Tc99m sodium pertechnetate.

The matter is further complicated by the proposed deletion of the following in Section 291.54(b)(1)(A)(iv):

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

The preparation by a nuclear pharmacist of a dose of a radiopharmaceutical from a kit manufactured by an FDA approved manufacturer of the sterile "kit for the preparation of..." constitutes low-risk preparation as defined by USP <797>. Consequently, Cardinal Health would request recognition by the Board that the preparation of radiopharmaceuticals is low-risk when such radiopharmaceuticals are prepared from a kit manufactured by an FDA approved manufacturer and that such preparation does not require awaiting the outcome of a sterility test.

Issue 2

- Although not an amendment, there is existing language that the Board uses in Section 291.54(b)(2)(ii) that may be better clarified as follows:

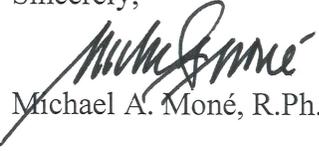
The compounding process includes complex aseptic manipulations other than the single simple volume transfer.

Comment 2

When a radiopharmacist prepares a radiopharmaceutical vial from a kit manufactured by an FDA registered drug manufacturer it requires of the introduction of sterile Tc-99m sodium pertechnetate as well as sterile normal saline. It must not be limited to only one needle puncture / volume transfer.

Cardinal Health Nuclear Pharmacy Services thanks the Texas State Board of Pharmacy for its consideration of these proposed changes to the regulations affecting nuclear pharmacy practice in Texas.

Sincerely,

A handwritten signature in black ink, appearing to read "Michael A. Moné". The signature is written in a cursive style with a prominent initial "M".

Michael A. Moné, R.Ph., J.D., FAPhA