RULE ANALYSIS

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

Short Title: Pharmacies Compounding Sterile Preparations

Rule Numbers: §291.133

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

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

Purpose: The amendments, if adopted, add new definitions for active pharmaceutical ingredient, commercially available product, easily substitutable dosage strength, and essentially a copy of commercially available product.

TITLE 22 EXAMINING BOARDS
PART 15 TEXAS STATE BOARD OF PHARMACY
CHAPTER 291 PHARMACIES
SUBCHAPTER G SERVICES PROVIDED BY PHARMACIES

§291.133. Pharmacies Compounding Sterile Preparations.

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

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

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

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

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

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

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

(2) Active pharmaceutical ingredient---The substance in a drug product that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or function of the body.

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

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

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

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

(4)[~~(3)~~] Ancillary supplies--Supplies necessary for the preparation and administration of compounded sterile preparations.

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

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

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

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

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

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

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

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

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

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

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

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

(14) Commercially available product-- A drug product that is a marketed drug product or available on the market, and subject to federal requirements relating to approval, labeling, and Current Good Manufacturing Practice (CGMP) requirements, the federal copies restrictions under section 503A of the Federal Food Drug and Cosmetic Act, and the copy restrictions described under subsections (d)(1)(C) and (D) of this section.

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

(16)[~~(14)~~] Compounding--The preparation, mixing, assembling, packaging, or labeling of a drug or device:

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

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

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

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

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

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

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

(20)[~~(18)~~] Critical Area--An ISO Class 5 environment.

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

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

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

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

(25) Easily substitutable dosage strength--The dosage strength of a compounded drug preparation that can be achieved by the administration of fractional or multiple doses of a commercially available drug product.

(26) Essentially a copy of a commercially available product--A compounded preparation:

(A) that has the same active pharmaceutical ingredient(s) as the commercially available drug product;

(B) containing an active pharmaceutical ingredient that has:

(i) the same or similar dosage strength; or

(ii) an easily substitutable dosage strength; and

(C) for which the commercially available drug product can be used by the same route of administration as prescribed for the compounded drug preparation.

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

(28)[~~(24)~~] Hazardous Drugs--Drugs that, studies in animals or humans indicate exposure to the drugs, have a potential for causing cancer, development or reproductive toxicity, or harm to organs. For the purposes of this chapter, radiopharmaceuticals are not considered hazardous drugs.

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

(30)[~~(26)~~] HVAC--Heating, ventilation, and air conditioning.

(31)[~~(27)~~] 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.

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

(33)[~~(29)~~] 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.

(34)[~~(30)~~] 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.

(35)[~~(31)~~] 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.

(36)[~~(32)~~] 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.

(37)[~~(33)~~] 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.

(38)[~~(34)~~] 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).

(39)[~~(35)~~] 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.

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

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

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

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

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

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

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

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

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

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

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

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

(49)[~~(45)~~] SOPs--Standard operating procedures.

(50)[~~(46)~~] Sterilizing Grade Membranes--Membranes that are documented to retain 100% of a culture of 107 microorganisms of a strain of Brevundimonas (Pseudomonas) diminuta per square centimeter of membrane surface under a pressure of not less than 30 psi (2.0 bar). Such

filter membranes are nominally at 0.22-micrometer or 0.2-micrometer nominal pore size, depending on the manufacturer's practice.

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

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

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

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

(c)-(g) No change.