

**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 (Community), Class C (Institutional), and Class E (Non-resident) pharmacies;

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

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

(4) compounding of sterile preparations by a Class C (Institutional) pharmacy and the distribution of the compounded preparations to other Class C (Institutional) 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) 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).

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

(4) Anteroom--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.

(5) Aseptic Processing--The technique involving procedures designed to preclude contamination of drugs, packaging, equipment, or supplies by microorganisms during preparation.

(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.

(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.

(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.

(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.

(10) Biological Safety Cabinet, Class II--A ventilated cabinet for personnel, product, 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.

(11) Buffer Area, Buffer or Core Room, Buffer or Clean Room Areas, Buffer Room Area, Buffer or Clean Area, or Buffer Zone--An ISO Class 7 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.

(12) Clean room or controlled area--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.

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

(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.

(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).

(16) Critical Area--A critical area is an ISO Class 5 environment.

(17) Critical Sites--Sterile ingredients of compounded sterile preparations and locations on devices and components used to prepare, package, and transfer compounded sterile preparations that provide opportunity for exposure to contamination.

(18) Cytotoxic--A pharmaceutical that has the capability of killing living cells.

(19) 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.

(20) Disinfectant--A disinfectant is 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 spores. It refers to substances applied to inanimate objects.

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

(22) HVAC--Heating, ventilation, and air conditioning.

(23) 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.

(24) IPA--Isopropyl alcohol (2-propanol).

(25) Media-Fill Test--A media-fill test is 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 (SCDM) is substituted for the actual drug product 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.

(26) 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.

(27) 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.

(28) 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.

(29) 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).

(30) 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.

(31) 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.

(32) 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, and compounding aseptic isolators.

(33) Product--A product is 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.

(34) Positive Control--A quality assurance sample prepared to test positive for microbial growth.

(35) Positive Pressure Room--A room that is at a higher pressure compared to adjacent spaces and, therefore, the net airflow is out of the room.

(36) 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.

(37) 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.

(38) 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.

(39) Single-dose container--A container intended for a single use, other than single-dose vials and single-dose large volume potential solutions. Examples of single-dose containers include pre-filled syringes, cartridges, and fusion-sealed containers without preservatives.

(40) Single-dose vial--A vial intended for a single use. Exceptions to this definition would be single dose vials routinely used to compound total potential nutrition (TPN) preparations (e.g., sodium chloride, sodium acetate, sodium phosphate, potassium chloride, potassium acetate, potassium phosphate, calcium gluconate, magnesium sulfate, multivitamin for injection, multi-trace elements, ascorbic acid, folic acid, heparin, phytonadione, L-carnitine, cysteine, selenium, injectable zinc).

(41) Single-dose large volume parenteral (LVP) solution--LVP solutions (i.e., containers of solution of at least 1000 mL) routinely used for compounding sterile TPN preparations or for batch compounding (e.g., sterile water for injection (SWFI); 5%, 10%, and 70% dextrose in SWFI; 0.9% sodium chloride; 0.45% sodium chloride; 5% dextrose/0.9% sodium chloride; 5% dextrose/0.45% sodium chloride).

(42) SOPs--Standard operating procedures.

(43) 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} , i.e., or a probability of less than one in one million of a non-sterile unit.

(44) USP/NF--The current edition of the United States Pharmacopeia/National Formulary.

(c) Personnel.

(1) Pharmacist-in-charge.

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

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

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

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

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

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

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

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

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

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

(2) Pharmacists. Special requirements for compounding sterile preparations.

(A) All pharmacists engaged in compounding sterile preparations shall:

(i) possess the education, training, and proficiency necessary to properly and safely perform compounding duties undertaken or supervised; and

(ii) obtain continuing education appropriate for the type of compounding done by the pharmacist.

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

(C) A pharmacist shall review all compounding records for accuracy and conduct in-process and final checks to ensure that errors have not occurred in the compounding process.

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

(E) A pharmacist shall be accessible at all times to respond to patients' and other health professionals' questions and needs. Such access may be through a telephone or pager which is answered 24 hours a day.

(3) Pharmacy technicians and pharmacy technician trainees. Pharmacy technicians and pharmacy technician trainees may compound sterile preparations provided the pharmacy technicians and/or pharmacy technician trainees:

(A) have completed the education and training specified in paragraph (4) of this subsection; and

(B) are supervised by a pharmacist who has completed the training specified in paragraph (4) of this subsection, conducts in-process and final checks, and affixes his or her initials to the appropriate quality control records.

(4) Special education, training, and evaluation requirements for pharmacy personnel compounding or responsible for the direct supervision of pharmacy personnel compounding sterile preparations.

(A) General.

(i) All pharmacy personnel preparing sterile preparations shall receive didactic and experiential training and competency evaluation through demonstration, testing (written and practical) as outlined by the pharmacist-in-charge and described in the policy and procedure or training manual. Such training shall include instruction and experience in the following areas:

(I) aseptic technique;

(II) critical area contamination factors;

(III) environmental monitoring;

(IV) structure and engineering controls related to facilities;

(V) equipment and supplies;

(VI) sterile preparation calculations and terminology;

(VII) sterile preparation compounding documentation;

(VIII) quality assurance procedures;

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

(X) handling of cytotoxic and hazardous drugs, if applicable; and

(XI) general conduct in the controlled area.

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

(iii) Although media-fill tests may be incorporated into the experiential portion of a training program, media-fill tests must be conducted at each pharmacy where an individual compounds sterile preparations. No preparation intended for patient use shall be compounded by an individual until the on-site media-fill tests test indicates that the individual can competently perform aseptic procedures, except that a pharmacist may temporarily compound sterile preparations and supervise pharmacy technicians compounding sterile preparations without media-fill tests provided the pharmacist:

(I) has completed a recognized course in an accredited college of pharmacy or a course sponsored by an ACPE accredited provider which provides 20 hours of instruction and experience in the areas listed in this subparagraph; and

(II) completes the on-site media-fill tests within seven days of commencing work at the pharmacy.

(iv) Media-fill tests procedures for assessing the preparation of specific types of sterile preparations shall be representative of all types of manipulations, products, risk levels, and batch sizes that personnel preparing that type of sterile preparation are likely to encounter.

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

(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.

(B) Pharmacists.

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

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

(-a-) completion of a structured on-the-job didactic and experiential training program at this pharmacy which provides 20 hours of instruction and experience in the areas listed in paragraph (1) of this subsection. Such training may not be transferred to another pharmacy unless the pharmacies are under common ownership and control and use a common training program; or

(-b-) completion of a recognized course in an accredited college of pharmacy or a course sponsored by an ACPE accredited provider which provides 20 hours of instruction and experience in the areas listed in subparagraph (A) of this paragraph.

(II) possess knowledge about:

(-a-) aseptic processing;

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

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

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

(-e-) sterilization techniques.

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

(C) Pharmacy technicians and pharmacy technician trainees. In addition to specific qualifications for registration, all pharmacy technicians and pharmacy technician trainees who compound sterile preparations for administration to patients shall:

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

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

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

(-b-) completion of a course sponsored by an ACPE accredited provider which provides 40 hours of instruction and experience in the areas listed in subparagraph (A) of this paragraph; or

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

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

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

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

(ii) acquire the required experiential portion of the training programs specified in this subparagraph under the supervision of an individual who has already completed training as specified in subparagraph (B) or (C) of this paragraph.

(D) Documentation of Training. The pharmacy shall maintain a record 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 contain the following information:

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

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

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

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

(v) 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) General Requirements.

(A) Sterile preparations may be compounded in licensed pharmacies:

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

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

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

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

(i) The pharmacist's professional judgment shall be based on the criteria used to determine a beyond-use date outlined in paragraph (5)(G) of this subsection.

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

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

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

(II) facility's lot number;

(III) beyond-use date as determined by the pharmacist using appropriate documented criteria as outlined in paragraph (5)(G) of this subsection;

(IV) quantity or amount in the container;

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

(VI) device-specific instructions, where appropriate.

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

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

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

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

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

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

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

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

(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 below.

(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.

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

(II) The compounding involves only transfer, measuring, and mixing manipulations with closed or sealed packaging systems that are preformed promptly and attentively.

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

(IV) For a low-risk preparation, in the absence of direct sterility testing results or appropriate information sources that justify different limits, the storage periods may not exceed the following periods: before administration, 48 hours at controlled room temperature, for not more than 14 days if stored at a cold temperature, 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.

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

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

(II) Manually measuring and mixing no more than three manufactured products to compound drug admixtures.

(B) Medium-risk level compounded sterile preparations.

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

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

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

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

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

(V) For a medium-risk preparation, in the absence of direct sterility testing results or appropriate information sources that justify different limits the beyond use dates may not exceed the following time periods: before administration, the compounded sterile preparations are properly stored and are exposed for not more than 30 hours at controlled room temperature, for not more than 7 days at a cold temperature, and for 45 days in solid frozen state at minus 20 degrees Celsius or colder.

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

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

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

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

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

(C) High-risk level compounded sterile preparations.

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

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

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

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

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

(V) For a high-risk preparation, in the absence of direct sterility testing results or appropriate information sources that justify different limits, the storage periods cannot exceed the following time periods: before administration, the compounded sterile preparations are properly stored and are exposed for not more than 24 hours at controlled room temperature, for not more than 3 days at a cold temperature, and for 45 days in solid frozen state at minus 20 degrees or colder.

(VI) All non-sterile measuring, mixing, and purifying equipment is rinsed thoroughly with sterile, pyrogen-free water, and then thoroughly drained or dried immediately before use for high-risk compounding while assuring cleanliness. All high-risk compounded sterile aqueous solutions subjected to terminal sterilization are passed through a filter with a nominal porosity not larger than 1.2 micron preceding or during filling into their final containers to remove particulate matter. Sterilization of high-risk level compounded sterile preparations by filtration shall be performed entirely within an ISO Class 5 or superior air quality environment.

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

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

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

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

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

(3) Immediate Use Compounded Sterile Preparations. For the purpose of emergency or immediate patient care, compounded sterile preparations are exempted from the requirements described in this paragraph for low-risk, medium-risk, and high-risk level compounded sterile preparations when all of the following criteria are met.

(A) Only simple aseptic measuring and transfer manipulations are performed with not more than three sterile non-hazardous commercial drug and diagnostic radiopharmaceutical drug products, including an infusion or diluent solution.

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

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

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

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

(F) Cytotoxic drugs shall not be prepared as immediate use compounded sterile preparations.

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

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

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

(C) the United States Pharmacopeia/National Formulary or the USP Pharmacist's Pharmacopeia containing USP Chapter 797, Pharmaceutical Compounding--Sterile Preparations.

(5) Environment. Compounding facilities shall be physically designed and environmentally controlled to minimize airborne contamination of critical sites.

(A) Prior to September 1, 2008.

(i) Controlled area.

(I) Low and Medium Risk Preparations. The pharmacy shall have a designated controlled area for the compounding of sterile pharmaceuticals that is functionally separate from areas for the preparation of non-sterile pharmaceuticals and is constructed to minimize the opportunities for particulate and microbial contamination. This controlled area for the preparation of sterile pharmaceuticals shall:

(-a-) have a controlled environment that is aseptic or contains an aseptic environmental control device(s). If the aseptic environmental control device is located within the controlled area, the controlled area must extend a minimum of six feet from the device and clearly marked to identify the separation between the controlled and non-controlled area;

(-b-) be clean, well lighted, and of sufficient size to support sterile compounding activities;

(-c-) be used only for the compounding of sterile pharmaceuticals;

(-d-) be designed to avoid outside traffic and air flow;

(-e-) be designed such that hand sanitizing and gowning occurs outside the controlled area but is accessible without use of the hands of the compounding personnel;

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

(-g-) be ventilated in a manner not interfering with aseptic environmental control conditions;

(-h-) have walls, ceilings, and fixtures, shelving, counters, and cabinets that are smooth, impervious, free from cracks and crevices, and nonshedding. (acoustical ceiling tiles that are coated with an acrylic paint are acceptable);

(-i-) have drugs and supplies stored on shelving areas above the floor to permit adequate floor cleaning; and

(-j-) contain only the appropriate compounding supplies and not be used for bulk storage for supplies and materials. Objects that shed particles may not be brought into the controlled area.

(II) High-risk Preparations. In addition to the requirements in subclause (I) of this clause, when high-risk preparations are compounded, the aseptic environment control device(s) shall be located in a controlled area that maintains at least an ISO Class 8 (formerly Class 100,000) environment.

(ii) Aseptic environment control device(s). The pharmacy shall prepare sterile pharmaceuticals in an appropriate aseptic environmental control device(s) or area, such as

a laminar air flow hood, biological safety cabinet, clean room which is capable of maintaining at least ISO Class 5 (formerly Class 100) conditions during normal activity, or other aseptic environmental control devices that produce ISO Class 5 (formerly Class 100) environmental conditions or better. The aseptic environmental control device(s) shall:

(I) be certified by an 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 or when it is relocated; and

(II) have pre-filters inspected periodically and replaced as needed, in accordance with written policies and procedures, and the inspection and/or replacement date documented.

(iii) Automated compounding or counting device. If automated compounding or counting devices are used, the pharmacy shall have a method to calibrate and verify the accuracy of automated compounding or counting devices used in aseptic processing and document the calibration and verification on a routine basis.

(B) Low and Medium Risk Preparations.

(i) Effective September 1, 2008, a pharmacy that prepares low- and medium-risk preparations shall have a clean room/controlled area for the compounding of sterile preparations that is constructed to minimize the opportunities for particulate and microbial contamination. The clean room/controlled area shall:

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

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

(III) be designed such that hand sanitizing and gowning occurs outside the buffer area but is accessible without use of the hands of the compounding personnel;

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

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

(VI) have walls, ceilings, floors, fixtures, shelving, counters, and cabinets that are smooth, impervious, free from cracks and crevices (e.g., coved), nonshedding and resistant to damage by disinfectant agents.

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

(VIII) have drugs and supplies stored on shelving areas above the floor to permit adequate floor cleaning;

(IX) contain only the appropriate compounding supplies and not be used for bulk storage for supplies and materials. Objects that shed particles shall not be brought into the controlled area;

(X) contain an anteroom/ante-zone that provides at least an ISO class 8 air quality which may contain a sink that enables hands-free use with a closed system of soap dispensing to minimize the risk of extrinsic contamination; and

(XI) contain a buffer zone or buffer room designed to maintain at least ISO Class 7 conditions. The following is applicable for the buffer area.

(-a-) There shall be some demarcation designation that delineates the anteroom or area from the buffer area.

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

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

(-d-) The buffer area shall not contain sources of water (i.e., sinks) or floor drains.

(ii) The pharmacy shall prepare sterile pharmaceuticals in a primary engineering control device, such as a laminar air flow hood, biological safety cabinet, compounding aseptic isolator which is capable of maintaining at least ISO Class 5 conditions during normal activity.

(I) The primary engineering control shall:

(-a-) be located in the buffer area or room 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 an 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 when it is relocated, in accordance with the manufacturer's specifications; and

(-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.

(II) The compounding aseptic isolator must be placed in an ISO Class 7 cleanroom unless the compounding aseptic 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 compounding aseptic isolator meets this standard when located in worse than ISO Class 7 environments.

(C) High-risk Preparations. In addition to the requirements in subparagraph (B) of this paragraph, when high-risk preparations are compounded, the primary engineering control shall be located in a buffer room 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.

(D) 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 routine basis, based on the manufacturer's recommendations.

(E) Cytotoxic drugs. If the preparation is cytotoxic, the following is also applicable.

(i) General.

(I) All personnel involved in the compounding of cytotoxic products shall wear appropriate protective apparel, such as gowns, face masks, eye protection, hair covers, shoe covers or dedicated shoes, and appropriate gloving.

(II) Appropriate safety and containment techniques for compounding cytotoxic drugs shall be used in conjunction with aseptic techniques required for preparing sterile preparations.

(III) Disposal of cytotoxic waste shall comply with all applicable local, state, and federal requirements.

(IV) Prepared doses of cytotoxic drugs must be dispensed, labeled with proper precautions inside and outside, and distributed in a manner to minimize patient contact with cytotoxic agents.

(ii) Primary engineering control device. Cytotoxic drugs must be prepared in a Class II or III vertical flow biological safety cabinet or compounding aseptic isolator.

(F) Cleaning and disinfecting the sterile compounding areas. The following cleaning and disinfecting practices and frequencies apply to direct and contiguous compounding areas, which include ISO Class 5 compounding areas for exposure of critical sites as well as buffer rooms, anterooms, and ante-areas.

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

(ii) These procedures shall be conducted prior to and after each work shift (at a minimum of every 12 hours while the pharmacy is open) and when there are spills or environmental quality breaches.

(iii) Before compounding is performed, all items are removed from the direct and contiguous compounding areas and all surfaces are cleaned of loose material and residue from spills, followed by an application of a residue-free disinfecting agent (e.g., IPA), that is left on for a time sufficient to exert its antimicrobial effect.

(iv) Work surfaces near the direct and contiguous compounding areas in the buffer or clean area are cleaned of loose material and residue from spills, followed by an application

of a residue-free disinfecting agent that is left on for a time sufficient to exert its antimicrobial effect.

(v) Floors in the buffer or clean area are cleaned by mopping at least once daily when no aseptic operations are in progress preceding from the buffer or clean room area to the anteroom area.

(vi) In the anteroom area, walls, ceilings, and shelving shall be cleaned monthly.

(vii) Supplies and equipment removed from shipping cartons must be wiped with a disinfecting agent, such as IPA. However, if supplies are received in sealed pouches, the pouches may be removed as the supplies are introduced into the buffer or clean area without the need to disinfect the individual supply items. No shipping or other external cartons may be taken into the buffer or clean area.

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

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

(H) Storage requirements and beyond-use dating.

(i) Storage requirements. All drugs shall be stored at the proper temperature and conditions, as defined in the USP/NF. The most commonly used definitions are as follows:

(I) freezer--A place where the temperature is maintained thermostatically between minus 25 degrees and minus 10 degrees Celsius (minus 13 degrees Fahrenheit and 14 degrees Fahrenheit).

(II) cold temperature--A temperature not exceeding 8 degrees Celsius (46 degrees Fahrenheit). A refrigerator is a cold place in which the temperature maintained thermostatically between 2 degrees and 8 degrees Celsius (36 degrees and 46 degrees Fahrenheit);

(III) cool--A temperature between 8 degrees and 15 degrees Celsius (46 degrees and 59 degrees Fahrenheit). An article for which storage in a cool place is directed may, alternatively, be stored in a refrigerator unless otherwise specified on the labeling; and

(IV) controlled room temperature--A temperature maintained thermostatically between 15 degrees and 30 degrees Celsius (59 degrees and 86 degrees Fahrenheit).

(ii) Beyond-use dating.

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

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

(III) Beyond-use dates for compounded sterile preparations that lack justification from either appropriate literature sources or by direct testing evidence must be assigned as described in Chapter 797, Pharmaceutical Compounding--Sterile Preparations of the USP/NF.

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

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

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

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

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

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

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

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

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

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

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

(G) infusion devices, if applicable; and

(H) all necessary supplies, including:

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

(ii) disinfectant cleaning solutions;

(iii) hand washing agents with bactericidal action;

- (iv) disposable, lint free towels or wipes;
- (v) appropriate filters and filtration equipment;
- (vi) cytotoxic spill kits, if applicable; and

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

(7) Labeling.

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

(i) The generic name(s) or the official name(s) of the principal active ingredient(s) of the compounded sterile preparation.

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

(iii) A beyond-use date. The beyond-use date shall be determined as outlined in Chapter 797, Pharmacy Compounding--Sterile Preparations of the USP/NF, and paragraph (4) of this subsection.

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

(i) unique lot number assigned to the batch;

(ii) quantity;

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

(iv) device-specific instructions, where appropriate.

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

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

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

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

(8) Written drug information for prescription drug orders only. Written information about the compounded preparation or its major active ingredient(s) shall be given to the patient at the time of dispensing a prescription drug order. A statement which indicates that the preparation was compounded by the pharmacy must be included in this written information. If there is no written information available, the patient shall be advised that the drug has

been compounded and how to contact a pharmacist, and if appropriate, the prescriber, concerning the drug.

(9) **Pharmaceutical Care Services.** In addition to the pharmaceutical care requirements for the pharmacy's specific license classification, the following requirements for sterile preparations compounded pursuant to prescription drug orders must be met.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

(10) **Drugs, components, and materials used in sterile compounding.**

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

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

(i) Chemically Pure (CP);

(ii) Analytical Reagent (AR);

(iii) American Chemical Society (ACS); or

(iv) Food Chemical Codex.

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

(D) All components shall:

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

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

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

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

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

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

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

(11) Compounding process.

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

(i) the facility;

- (ii) equipment;
- (iii) personnel;
- (iv) preparation evaluation;
- (v) quality assurance;
- (vi) preparation recall;
- (vii) packaging; and
- (viii) storage of compounded sterile preparations.

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

(C) Personnel Cleansing and Garbing.

(i) Any person with an apparent illness or open lesion that may adversely affect the safety or quality of a drug preparation being compounded shall be excluded from direct contact with components, drug preparation containers, closures, any materials involved in the compounding process, and drug products until the condition is corrected.

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

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

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

(III) all hand, wrist, and other body jewelry.

(iii) The wearing of artificial nails or extenders is prohibited while working in the sterile compounding environment.

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

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

(II) After donning dedicated shoes or shoe covers, head and facial hair covers, and face masks, personnel shall perform a hand hygiene procedure by removing debris from underneath fingernails using a nail cleaner under running warm water followed by vigorous hand washing. Personnel shall begin washing arms at the hands and continue washing to elbows for at least 30 seconds with either a plain (non-antimicrobial) soap, or antimicrobial soap, and water while in the anteroom/ante-area.

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

(IV) Gloves that form a continuous barrier with the gown shall be the last item donned before compounding begins.

(V) Gloves, either those which are sterile or have been disinfected by applying 70% IPA or appropriate disinfectant to all contact surface areas and allowed to dry, that form a continuous barrier with the gown shall be the last item donned before compounding begins. Routine application of 70% IPA shall occur throughout the compounding day and whenever nonsterile surfaces are touched.

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

(D) At each step of the compounding process, the pharmacist shall ensure that components used in compounding are accurately weighed, measured, or subdivided as appropriate to conform to the formula being prepared.

(12) 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 product that is sterile and that contains the stated amount of active ingredient(s).

(i) Low risk preparations.

(l) 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 produce. 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 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.

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

(II) Example of a Media-Fill Test Procedure. This, or an equivalent test, is performed at least annually under conditions that closely simulate the most challenging or stressful conditions encountered during compounding. This test is completed without interruption within an ISO Class 5 air quality environment. Six 100-milliliter aliquots of sterile Soybean-Casein Digest Medium are aseptically transferred by gravity through separate tubing sets into separate evacuated sterile containers. The six containers are then arranged as three pairs, and a sterile 10-milliliter syringe and 18-gauge needle combination is used to exchange two 5-milliliter aliquots of medium from one container to the other container in the pair. For example, after a 5-milliliter aliquot from the first container is added to the second container in the pair, the second container is agitated for 10 seconds, then a 5-milliliter aliquot is removed and returned to the first container in the pair. The first container is then agitated for 10 seconds, and the next 5-milliliter aliquot is transferred from it back to the second container in the pair. Following the two 5-milliliter aliquot exchanges in each pair of containers, a 5-milliliter aliquot of medium from each container is aseptically injected into a sealed, empty, sterile 10-milliliter clear vial, using a sterile 10-milliliter syringe and vented needle. 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 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.

(iii) High risk preparations.

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

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

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

(-b-) Draw 25 milliliters of the medium into each of three 30-milliliter sterile syringes. Transfer 5 milliliters from each syringe into separate sterile 10-milliliter vials. These vials are the positive controls to generate exponential microbial growth, which is indicated by visible turbidity upon 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. Inspect for microbial growth over 14 days as described in Chapter 797 Pharmaceutical Compounding--Sterile Preparations, of the USP/NF.

(B) Finished preparation release checks and tests.

(i) High-risk level compounded sterile preparations. 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 (36 - 46 degrees Fahrenheit) and longer than six hours at warmer than 8 degrees Celsius (46 degrees Fahrenheit) 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.

(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 administered or dispensed.

(13) Quality control.

(A) Quality control procedures. The pharmacy shall follow established quality control procedures to monitor the compounding environment and quality of compounded drug preparations for conformity with the quality indicators established for the preparation. When developing these procedures, pharmacy personnel shall consider the provisions of Chapter 797, Pharmaceutical Compounding--Sterile Preparations, Chapter 1075, Good Compounding Practices, and Chapter 1160, Pharmaceutical Calculations in Prescription Compounding of the current USP/NF. Such procedures shall be documented and be available for inspection.

(B) Verification of compounding accuracy and sterility.

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

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

(iii) If individual ingredients, such as bulk drug substances, are not labeled with expiration dates, when the drug substances are stable indefinitely in their commercial packages under labeled storage conditions, such ingredients may gain or lose moisture

during storage and use and shall require testing to determine the correct amount to weigh for accurate content of active chemical moieties in compounded sterile preparations.

(e) Records.

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

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

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

(2) Compounding records.

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

(i) the date of preparation;

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

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

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

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

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

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

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

(II) documentation of performance of quality control procedures.

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

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

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

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

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

(f) Office Use Compounding and Distribution of Compounded Preparations to Class C Pharmacies or Veterinarians in Accordance with Section 563.054 of the Act.

(1) General.

(A) A pharmacy may dispense and deliver a reasonable quantity of a compounded preparation to a practitioner for office use by the practitioner in accordance with this subsection.

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

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

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

(i) verify the source of the raw materials to be used in a compounded drug;

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

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

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

(v) comply with the provisions of this subsection.

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

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

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

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

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

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

(3) Recordkeeping.

(A) Maintenance of Records.

(i) Records of orders and distribution of sterile compounded preparations to a practitioner for office use or to a Class C pharmacy for administration to a patient shall:

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

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

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

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

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

(i) date of the order;

(ii) name, address, and phone number of the practitioner who ordered the preparation and if applicable, the name, address and phone number of the Class C Pharmacy ordering the preparation; and

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

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

(i) date the preparation was compounded;

(ii) date the preparation was distributed;

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

(iv) pharmacy's lot number;

(v) quantity of containers shipped; and

(vi) name, address, and phone number of the practitioner or Class C Pharmacy to whom the preparation is distributed.

(D) Audit Trail.

(i) The pharmacy shall store the order and distribution records of preparations for all sterile compounded preparations ordered by and or distributed to a practitioner for office use or by a Class C pharmacy for administration to a patient in such a manner as to be able to

provide an audit trail for all orders and distributions of any of the following during a specified time period.

(I) any strength and dosage form of a preparation (by either brand or generic name or both);

(II) any ingredient;

(III) any lot number;

(IV) any practitioner;

(V) any facility; and

(VI) any pharmacy, if applicable.

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

(I) date of order and date of the distribution;

(II) practitioner's name, address, and name of the Class C pharmacy, if applicable;

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

(IV) name and quantity of each active ingredient;

(V) quantity of containers distributed; and

(VI) pharmacy's lot number;

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

(A) name, address, and phone number of the compounding pharmacy;

(B) the statement: "For Institutional or Office Use Only--Not for Resale"; or if the preparation is distributed to a veterinarian the statement: "Compounded Preparation";

(C) name and strength of the preparation or list of the active ingredients and strengths;

(D) pharmacy's lot number;

(E) beyond-use date as determined by the pharmacist using appropriate documented criteria;

(F) quantity or amount in the container;

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

(H) device-specific instructions, where appropriate.

(g) Recall Procedures.

(1) The pharmacy shall have written procedure for the recall of any compounded sterile preparations provided to a patient, to a practitioner for office use, or to a pharmacy for administration. The recall procedures shall require:

(A) notification to each practitioner, facility, and/or pharmacy to which the preparation was distributed;

(B) notification to each patient to whom the preparation was dispensed;

(C) quarantine of the product if there is a suspicion of harm to a patient; and

(D) a recall if there is probable or confirmed harm to a patient.

(2) If the pharmacy identifies a suspicion of, probable, or confirmed harm to a patient, the pharmacy shall immediately notify and provide information as required by the board to the following:

(A) the Texas Department of State Health Services, Drugs and Medical Devices Group, if the preparation is distributed for office use; and

(B) the board.

(3) The board may require a pharmacy to institute a recall if there is probable or confirmed harm to a patient.