Kansas Administrative Regulations

State Board of Pharmacy

Article 13.—Parenteral Products

68-13-4. Sterile preparations.

(a) This regulation shall apply to the following:

(1) Sterile preparations that are compounded in Kansas; and

(2) sterile preparations that are shipped or delivered into Kansas by a pharmacy to be administered to a patient in Kansas.

(b) As used in this regulation, each of the following terms shall have the meaning specified in this subsection:

(1)(A) "High-risk," when used to describe a sterile preparation, means that the sterile preparation meets at least one of the following conditions:

(i) The sterile preparation is compounded from nonsterile ingredients or with nonsterile containers or equipment before terminal sterilization.

(ii) The sterile ingredients or components of the sterile preparation are exposed to air quality inferior to that of an ISO class five environment for more than one hour.

(iii) The sterile preparation contains nonsterile water and is stored for more than six hours before being sterilized.

(iv) The compounding pharmacist cannot verify from documentation received from the supplier or by direct examination that the chemical purity and content strength of the ingredients meet the specifications of an official compendium.

(v) The sterile preparation has been stored at room temperature and administered more than 24 hours after compounding, stored under refrigeration more than three days, or stored frozen from 0° to -20°C (32° to -4°F) or colder for 45 or fewer days, and sterility has not been confirmed by testing.

(B) This term shall apply to sterile preparations including the following:

(i) Alum bladder irrigation solution;

(ii) any morphine preparation made for parenteral administration from nonsterile powder or tablets;

(iii) any total parenteral nutrition solution made from dried amino acids;

(iv) any total parenteral nutrition solution sterilized by final filtration; and

(v) any autoclaved intravenous solution.

(2) "Immediate use" means a situation in which a sterile preparation is compounded pursuant to an order in a medical care facility for administration to the patient within one hour of the start of compounding the sterile preparation.

(3) "Low-risk," when used to describe a sterile preparation, means that the sterile preparation meets the following conditions:

(A) In the absence of sterility testing, is stored at room temperature and administration to the patient has begun not more than 48 hours after compounding, is stored under refrigeration for 14 or fewer days before administration to the patient over a period not to exceed 24 hours, or is stored frozen at -20°C (-4°F) or colder for 45 or fewer days before administration to the patient over a period not to exceed 24 hours;

(B) is prepared for administration to one patient or is batch-prepared and contains suitable preservatives for administration to more than one patient; and

(C) is prepared by a simple or closed-system aseptic transfer of no more than three sterile, nonpyrogenic, finished pharmaceuticals obtained from licensed manufacturers into sterile final containers obtained from licensed manufacturers with no more than two instances in which a transfer device passes through the designated access point into any one sterile container or package.

(4)(A) "Medium-risk," when used to describe a sterile preparation, means that the sterile preparation meets at least one of the following conditions:

(i) In the absence of sterility testing, is stored at room temperature and administered to the patient not more than 30 hours after compounding, is stored under refrigeration for nine or fewer days, or is stored frozen at -20°C (-4°F) or colder for 45 or fewer days;

(ii) is batch-prepared and intended for use by more than one patient or by one patient on multiple occasions;

(iii) is created by a compounding process that includes complex aseptic manipulations other than a single-volume transfer; or

(iv) is compounded by at least four manipulations of sterile ingredients obtained from licensed manufacturers in a sterile container obtained from a licensed manufacturer by using a simple or closed-system aseptic transfer.

(B) This term shall apply to the following:

(i) Sterile preparations for use in a portable pump or reservoir over multiple days;

(ii) batch-reconstituted sterile preparations;

(iii) batch-prefilled syringes; and

(iv) total parenteral nutrient solutions that are compounded by the gravity transfer of carbohydrates and amino acids into an empty container with the addition of sterile additives using a syringe and needle or that are mixed with an automatic compounding device.

(5) "Pharmacy" means a pharmacy, nonresident pharmacy, or outsourcing facility as defined by K.S.A. 2017 Supp. 65-1626, and amendments thereto.

(c) Any sterile preparation for immediate use may be compounded outside a primary engineering control if both of the following conditions are met:

(1) Administration to the patient begins within one hour of the start of compounding the sterile preparation.

(2) The sterile preparation is compounded by a simple or closed-system aseptic transfer of sterile, nonpyrogenic, finished pharmaceuticals obtained from licensed manufacturers into sterile final containers obtained from licensed manufacturers.

(d) When a multiple-dose container with antimicrobial preservatives has been opened or entered, the container shall be labeled with a beyond-use date not to exceed 28 days, unless otherwise specified by the manufacturer.

(e) Each compounding area shall contain a primary engineering control providing unidirectional airflow that will maintain an ISO class five environment for compounding sterile preparations and shall be void of all activities and materials that are extraneous to compounding.

(f) Each sterile preparation compounded in a segregated compounding area shall be labeled with a beyond-use date of no more than 12 hours.

(g) Each single-dose container shall be labeled as such.

(h) The contents of each single-dose container shall be used within one hour if the container is opened or entered in an area with air quality that does not meet the requirements of an ISO class five environment.

(i) The contents of each single-dose container shall be used within six hours if the container is opened or entered in an area that meets the requirements of an ISO class five environment.

(j) For the convenience of any patient, any pharmacist may compound a sterile preparation before receiving an order if the pharmacist has previously filled orders for the sterile preparation and the sterile preparation is based on routine, regularly observed prescribing patterns.

(k) Compounding for non-human animals shall meet the same requirements as those for human prescriptions, except that a pharmacist shall not compound bulk chemicals for food-producing animals.

(l) Each sterile preparation sold by a pharmacy to a practitioner for administration to a patient shall be packaged with a label that includes the following text: "For Office Use Only — Not For Resale."

(m) Any pharmacy may distribute sterile preparations without a prescription, including providing limited quantities to a practitioner in the course of professional practice to administer limited quantities to an individual patient, if the sterile preparations are not intended for resale.

(n) A pharmacist shall not compound a sterile preparation that is essentially a copy.

(o) Any pharmacist may compound a sterile preparation that is commercially available only if there is sufficient documentation of a specific medical need for the prescription or the product is temporarily unavailable due to problems other than safety or effectiveness. Each pharmacist shall document any unavailability in the patient's prescription record, including the date the product was unavailable, and shall maintain documentation from the manufacturer or distributor demonstrating the product's unavailability. The pharmacist shall cease compounding the sterile preparation as soon as the product becomes commercially available.

(p) A pharmacist shall not compound a sterile preparation by any of the following methods:

(1) Using any component withdrawn from the market by the FDA for safety reasons;

(2) receiving, storing, or using any drug component that is not guaranteed or otherwise determined to meet the requirements of an official compendium; or

(3) compounding finished drugs through manufacturing, as defined in K.S.A. 65-1626 and amendments thereto, without first receiving an FDA-sanctioned investigational new drug application in accordance with 21 U.S.C. 355(i) and 21 C.F.R. Part 312.

(q) Each pharmacist or pharmacy compounding sterile preparations shall have the following resources:

(1) A primary engineering control that is currently certified by an inspector certified by the controlled environmental testing association to ensure aseptic conditions within the working area and that has the required documentation. The certification shall be deemed current if the certification occurred within the previous six months or on the date the device was last moved to another location, whichever is more recent. The required documentation shall include the following:

(A) Inspection certificates for the past five years or since the date of installation, whichever is more recent;

(B) records of all filter maintenance for the past five years or since the date of installation, whichever is more recent;

(C) records of all HEPA filter maintenance for the past five years or since the date of installation, whichever is more recent; and

(D) records of all disinfecting and cleaning for the past year or since the date of installation, whichever is more recent;

(2) a sink with hot and cold running water;

(3) a refrigerator capable of maintaining a temperature of 2° to 8°C (36° to 46°F) and, if needed, a freezer capable of maintaining a temperature of -25° to -10°C (-13° to 14°F). The temperature shall be monitored and recorded each business day. Each pharmacy with an electronic system that alerts the pharmacist to noncompliant temperatures shall be exempt from daily recording;

(4) the reference materials required by K.A.R. 68-2-12a and a current copy of a reference text on intravenous incompatibilities and stabilities. If an electronic library is

provided, a workstation shall be readily available for use by pharmacy personnel, students, interns, and board personnel;

(5) a policy and procedure manual, with a documented review at least every two years by the pharmacist-in-charge or designee, which shall include the following subjects:

(A) Sanitation;

(B) storage;

(C) dispensing;

(D) labeling;

(E) destruction and return of controlled substances;

(F) recordkeeping;

(G) recall procedures;

(H) responsibilities and duties of supportive personnel;

(I) aseptic compounding techniques; and

(J) ongoing evaluation of all staff compounding sterile preparations; and

(6) supplies necessary for compounding sterile preparations.

(r) Each pharmacist-in-charge shall maintain a uniform formulation record for each sterile preparation, documenting the following:

(1) The quantities, strength, and dosage form of all components of the sterile preparation;

(2) the equipment used to compound the sterile preparation and the mixing instructions;

(3) the container used in dispensing;

(4) the storage requirements;

(5) the beyond-use date to be assigned;

(6) quality control procedures, which may include monitoring the following, if applicable:

(A) Adequacy of mixing to ensure uniformity and homogeneity; and

(B) the clarity, completeness, or pH of solutions;

(7) the sterilization methods;

(8) the source of the formulation; and

(9) the name of the pharmacist who verified the accuracy of the formulation record and the date of verification.

(s) Each pharmacist-in-charge shall maintain on the original order or on a separate, uniform record a compounding record for each sterile preparation, documenting the following:

(1) The name and strength of the sterile preparation;

(2) the formulation record reference for the sterile preparation;

(3) the name of the manufacturer or repackager and, if applicable, the lot number and the expiration date of each component;

(4) the total number of dosage units or total quantity compounded;

(5) the name of the person or persons who compounded the sterile preparation;

(6) the name of the pharmacist, or the pharmacy student or intern working under the direct supervision and control of the pharmacist, who verified the accuracy of the sterile preparation;

(7) the date of compounding;

(8) the assigned internal identification number, if applicable;

(9) the prescription number, if assigned;

(10) the results of quality control procedures;

(11) the results of the sterility testing and, if applicable, pyrogen testing for the batch; and

(12) the assigned beyond-use-date. In the absence of valid scientific stability information that is applicable to a component or the sterile preparation, the beyond-use date shall be established in accordance with the following criteria:

(A) For nonaqueous and solid formulations, one of the following:

(i) If the manufactured drug product is the source of the active ingredient, six months from the date of compounding or the time remaining until the manufactured drug product's expiration date, whichever is earlier; or

(ii) if the substance listed in an official compendium is the source of an active ingredient, six months from the date of compounding or the time remaining until the expiration date of any component of the formulation, whichever is earlier;

(B) for formulations containing water and made from ingredients in solid form, not more than 14 days when stored under refrigeration; and

(C) for all other formulations, not longer than the intended duration of therapy or 30 days, whichever is earlier.

(t) The compounding record and corresponding formulation record specified in subsections (s) and (r), respectively, shall be retained at the pharmacy for at least five years and shall be made readily available to the pharmacist-in-charge, the board, and the board's designee.

(u) Medical care facility pharmacies shall generate a compounding record and a corresponding formulation record only for batch compounding or for any sterile preparation with a beyond-use date of more than seven days.

(v) Except when compounding in any CAI, each person involved in compounding a sterile preparation shall follow personal garbing and washing procedures that include the following minimum requirements:

(1) Preparing for garbing by removing any outer garments, cosmetics, jewelry, and artificial nails;

(2) performing the following procedures, in the order listed:

(A) Donning dedicated shoes or shoe covers;

(B) donning head and facial hair covers;

(C) either washing the hands with soap for at least 20 seconds or using an antiseptic hand scrub in accordance with the manufacturer's instructions; and

(D) donning a nonshedding gown; and

(3) entering the work area and immediately performing an antiseptic hand-cleaning procedure using an alcohol-based surgical hand scrub and successively donning sterile, powder-free gloves. Sterile gloves shall be disinfected after touching any nonsterile area.

(w) All sterile preparations shall be stored and delivered in a manner that is designed to maintain parenteral product stability and sterility.

(x) All sterile preparations, except for sterile preparations for immediate use, shall be compounded under aseptic conditions as follows:

(1) Each low-risk sterile preparation labeled with a beyond-use date of 12 hours or longer shall be compounded in an ISO class five environment using techniques that ensure sterility. Each low-risk sterile preparation labeled with a beyond-use date of less than 12 hours shall, at a minimum, be made in a segregated compounding area.

(2) Each medium-risk sterile preparation shall be compounded in an ISO class five environment using techniques that ensure sterility.

(3) Each high-risk sterile preparation made with nonsterile components shall be sterilized before being administered to a patient and shall have a certificate of analysis indicating that all nonsterile components meet the standards of the "United States pharmacopeia" and the FDA for identity, purity, and endotoxin levels as verified by a pharmacist.

(y) Each pharmacist engaged in the dispensing of sterile preparations shall meet all labeling requirements under state and federal law. In addition, the label of each sterile preparation shall contain the following information:

(1) The name and quantity of each component;

(2) the beyond-use date;

(3) the prescribed flow rate;

(4) the name or initials of each person who compounded the sterile preparation; and

(5) any special storage instructions.

(z)(1) The pharmacist-in-charge and all personnel involved in compounding sterile preparations shall have practical or academic training in sterile compounding, clean room technology, laminar flow technology, and quality assurance techniques. The training shall include the following:

(A) At least one successful media fill test; and

(B) a successful glove fingertip test.

(2) The pharmacist-in-charge shall ensure that all supportive personnel are trained and successfully demonstrate the following before performing any delegated sterile admixture services:

(A) Comprehensive knowledge of the pharmacy's standard operating procedures with regard to sterile admixture services, as specified in the policy and procedure manual;

(B) familiarity with the compounding techniques; and

(C) aseptic technique, which shall be proven by means of a media fill test and a glove fingertip test.

(3) The pharmacist-in-charge shall be responsible for testing the aseptic technique of all personnel involved in compounding sterile preparations annually by means of a media fill test. All personnel involved in compounding high-risk sterile preparations shall undergo this testing twice each year. Each individual who fails to demonstrate acceptable aseptic technique shall be prohibited from compounding sterile preparations until the individual demonstrates acceptable technique by means of a media fill test.

(aa) The pharmacist-in-charge shall document all training and test results for each person before that person begins compounding sterile preparations. This documentation shall be maintained by the pharmacy for at least five years and shall be made available to the board upon request.

(bb) The pharmacist-in-charge shall be responsible maintaining records documenting the frequency of cleaning and disinfection of all compounding areas, according to the following minimum requirements:

(1) Each ISO class five environment shall be cleaned and disinfected as follows:

(A) At the beginning of each shift;

(B) every 30 minutes during continuous periods of compounding individual sterile preparations;

(C) before each batch; and

(D) after a spill or known contamination.

(2) All counters, work surfaces, and floors shall be cleaned and disinfected daily.

(3) All walls, ceilings, and storage shelves shall be cleaned and disinfected monthly.

(cc) The pharmacist-in-charge shall be responsible for maintaining records documenting the monitoring of the air pressure and air flow and shall initiate immediate corrective action if indicated. The air pressure of the antearea shall be maintained at five pascals, and the air flow shall be maintained at 0.2 meters per second. The air pressure and air flow values shall be checked and recorded at least once daily.

(dd) The pharmacist-in-charge shall be responsible for maintaining records documenting the monitoring of the cleanliness and sterility of the sterile compounding

environment. Environmental sampling shall be performed in each new facility before any sterile preparation in that facility is provided to a patient and, at a minimum, every six months thereafter. The environmental sampling shall include the primary engineering control, antearea and buffer area, and equipment and shall be performed following any repair or service performed at the facility and in response to any identified problem or concern.

Environmental sampling shall consist of the following, at a minimum:

(1) Environmental nonviable particle counts;

(2) environmental viable airborne particle testing by volumetric collection;

(3) environmental viable surface sampling; and

(4) certification of operational efficiency of the primary engineering control by an independent contractor according to the international organization of standardization classification of particulate matter in room air, at least once every six months.

(ee) The environmental sampling records specified in subsection (dd) shall be retained at the pharmacy for at least five years and shall be made readily available to the pharmacist-in-charge, the board, and the board's designee.

(ff) If a microbial growth above acceptable levels is detected in an ISO class five environment, ISO class seven environment, or ISO class eight environment, an immediate reevaluation of the adequacy of compounding practice, cleaning procedures, operational procedures, and air filtration efficiency with the aseptic compounding location shall be conducted and documented. Each investigation into the source of the contamination shall include air sources, personnel garbing, and all filters, at a minimum. The ISO class five environment, ISO class seven environment, or ISO class eight environment shall be cleaned three times and environmental sampling shall be performed and reevaluated. Sterile preparations may be compounded and labeled with a beyond-use date according to subsection (gg) until microbial growth has decreased to acceptable levels.

(1) An ISO class five environment shall have acceptable levels of microbial growth if both of the following conditions are met:

(A) An airborne sample demonstrates no more than one colony-forming unit per cubic meter of air.

(B) A surface sample demonstrates no more than three colony-forming units per contact plate.

(2) An ISO class seven environment shall have acceptable levels of microbial growth if both of the following conditions are met:

(A) An airborne sample demonstrates no more than 10 colony-forming units per cubic meter of air.

(B) A surface sample demonstrates no more than five colony-forming units per contact plate.

(3) An ISO class eight environment shall have acceptable levels of microbial growth if both of the following conditions are met:

(A) An airborne sample demonstrates no more than 100 colony-forming units per cubic meter of air.

(B) A surface sample demonstrates no more than 100 colony-forming units per contact plate.

(gg) Unless sterility has been confirmed by testing, each high-risk sterile preparation shall be administered according to the following:

(1) Within 24 hours of compounding if stored at room temperature;

(2) within three days of compounding if stored under refrigeration; or

(3) within 45 days of compounding if stored frozen at -20°C (-4°F) or colder.

(Authorized by K.S.A. 65-1630 and K.S.A. 2017 Supp. 65-1637e; implementing K.S.A. 2017 Supp. 65-1626a, K.S.A. 65-1634, K.S.A. 2017 Supp. 65-1637c, and K.S.A. 2017 Supp. 65-1642; effective May 11, 2018.)