compound high-risk level CSPs using one or more sample collections during any media-fill test procedure before they are allowed to continue compounding CSPs for human use.

Immediately prior to sampling, gloves shall not be disinfected with sterile 70% IPA. Disinfecting gloves immediately before sampling will provide false negative results. Plates filled with nutrient agar with neutralizing agents such as lecithin and polysorbate 80 added shall be used when sampling personnel fingertips. Personnel shall "touch" the agar with the fingertips of both hands in separate plates in a manner to create a slight impression in the agar. The sampled gloves shall be immediately discarded and proper hand hygiene performed after sampling. The nutrient agar plates shall be incubated as stated below (see *Incubation Period*). Results should be reported separately as number of cfu per employee per hand (left hand, right hand). The cfu action level for gloved hands will be based on the total number of cfu on both gloves, not per hand.

Incubation Period—At the end of the designated sampling period for compounding personnel competency assessment activities (surface or personnel), the agar plates are recovered and covers secured and they are inverted and incubated at a temperature and for a time period conducive to multiplication of microorganisms. TSA with lecithin and polysorbate 80 shall be incubated at 30° to 35° for 48 to 72 hours.

Aseptic Manipulation Competency Evaluation—After successful completion of an initial Hand Hygiene and Garbing Competency Evaluation, all compounding personnel shall have their aseptic technique and related practice competency evaluated initially during the *Media-Fill Test Procedure* and subsequent annual or semi-annual *Media-Fill Test Procedures*. Records of these evaluations will be maintained using a form such as the *Sample Form for Assessing Aseptic Technique and Related Practices of Compounding Personnel* (see *Appendix IV*) and maintained to provide a permanent record of and long-term assessment of personnel competency.

Media-Fill Test Procedure—The skill of personnel to aseptically prepare CSPs shall be evaluated using sterile fluid bacterial culture media-fill verification, (i.e., sterile bacterial culture medium transfer via a sterile syringe and needle). Media-fill testing is used to assess the quality of the aseptic skill of compounding personnel. Media-fill tests shall represent the most challenging or stressful conditions actually encountered by the personnel being evaluated when they prepare low- and medium-risk level CSPs and when sterilizing high-risk level CSPs. Media-fill challenge tests are also used to verify the capability of the compounding environment and processes to produce sterile preparations.

A commercially available sterile fluid culture media, such as Soybean–Casein Digest Medium (see *Sterility Tests* ⟨71⟩), that is able to promote exponential colonization of bacteria that are most likely to be transmitted to CSPs from the compounding personnel and environment is commonly used. For high-risk level CSPs nonsterile commercially available Soybean–Casein Digest Medium may be used to make a 3% solution. Normal processing steps, including filter sterilization, shall be mimicked. Media-filled vials shall be incubated at 20° to 25° or at 30° to 35° for a minimum of 14 days. If two temperatures are used for incubation of media-filled samples, then these filled containers should be incubated for at least 7 days at each temperature (see *Microbiological Evaluation of Clean Rooms and Other Controlled Environments* ⟨1116⟩). Failure is indicated by visible turbidity in any one of the media-fill units on or before 14 days. Other methodologies recommended by a competent microbiologist to enhance recovery time and sensitivity to detect microbial contamination may be considered (see *CSP Microbial Contamination Risk Levels* for examples of media-fill procedures).

SURFACE CLEANING AND DISINFECTION SAMPLING AND ASSESSMENT

Surface sampling is an important component of the maintenance of a suitable microbially con-

trolled environment for compounding CSPs, especially since transfer of microbial contamination from improperly disinfected work surfaces via inadvertent touch contact by compounding personnel can be a potential source of contamination into CSPs. It is useful for evaluating facility and work surface cleaning and disinfecting procedures and employee competency in work practices such as disinfection of component/vial surface cleaning. Surface sampling shall be performed in all ISO classified areas on a periodic basis. Sampling can be accomplished using contact plates or swabs, and it shall be done at the conclusion of compounding. Locations to be sampled shall be defined in a sample plan or on a form. The size of the plate to be used for each sampled location usually ranges from 24 to 30 cm^2. Contact plates are filled with general solid agar growth medium and neutralizing agents above the rim of the plate, and they are used for sampling regular or flat surfaces. Swabs may be used for sampling irregular surfaces, especially for equipment (see *Microbiological Evaluation of Clean Rooms and Other Controlled Environments* ⟨1116⟩).

Cleaning and Disinfecting Competency Evaluation—Compounding personnel and other personnel responsible for cleaning shall be visually observed during the process of performing cleaning and disinfecting procedures, during initial personnel training on cleaning procedures, during changes in cleaning staff, and at the completion of any media-fill test procedure (see *Cleaning and Disinfecting of Compounding Areas*).

The visual observation shall be documented using a form such as the *Sample Form for Assessing Cleaning and Disinfection Procedures* (see *Appendix V*) and maintained to provide a permanent record and long-term assessment of personnel competency.

Surface Collection Methods—To sample surfaces using a contact plate, gently touch the sample area with the agar surface and roll the plate across the surface to be sampled. The contact plate will leave a growth media residue behind; therefore, immediately after sampling with the contact plate, the sampled area shall be thoroughly wiped with a nonshedding wipe soaked in sterile 70% IPA.

If an area is sampled via the swab method, collection of the sample is processed by using appropriate procedures that will result in the surface location equivalent to that of a contact plate. After swabbing the surface to be sampled, swabs are placed in an appropriate diluent; an aliquot is planted on or in the specified nutrient agar. Results should be reported as cfu per unit of surface area.

Action Levels, Documentation, and Data Evaluation

The value of viable microbial monitoring of gloved fingertips and surfaces of components and the compounding environment are realized when the data are used to identify and correct an unacceptable work practice. Sampling data shall be collected and reviewed on a routine basis as a means of evaluating the overall control of the compounding environment. If an activity consistently shows elevated levels of microbial growth, competent microbiology personnel shall be consulted.

Any cfu count that exceeds its respective action level (see *Table 4*) should prompt a re-evaluation of the adequacy of personnel work practices, cleaning procedures, operational procedures, and air filtration efficiency within the aseptic compounding location. An investigation into the source of the contamination shall be conducted. Sources could include HVAC systems, damaged HEPA filters, and changes in personnel garbing or working practices. The source of the problem shall be eliminated, the affected area cleaned, and resampling performed.

When gloved fingertip sample results exceed action levels after proper incubation, a review of hand hygiene and garbing procedures as well as glove and surface disinfection procedures and work practices shall be performed and documented. Employee training may be required to correct the source of the problem.

Counts of cfu are to be used as an approximate measure of the environmental microbial bioburden. Action levels are determined on the basis

of cfu data gathered at each sampling location and trended over time. The numbers in *Table 4* should be used only as guidelines. Regardless of the number of cfu identified in the compounding facility, further corrective actions will be dictated by the identification of microorganisms recovered (at least the genus level) by an appropriate credentialed laboratory of any microbial bioburden captured as a cfu using an impaction air sampler. Highly pathogenic microorganisms (e.g., Gram-negative rods, coagulase positive staphylococcus, molds and yeasts) can be potentially fatal to patients receiving CSPs and shall be immediately remedied, regardless of cfu count, with the assistance of a competent microbiologist, infection control professional, or industrial hygienist.

Table 4. Recommended Action Levels for Microbial Contamination*

Classification	Fingertip Sample	Surface Sample (Contact Plate) (cfu per plate)
ISO Class 5	> 3	> 3
ISO Class 7	N/A	> 5
ISO Class 8 or worse	N/A	> 100

*Pharmaceutical Inspection Co-operation Scheme (PIC/S) Guide to Good Manufacturing Practice for Medicinal Products Annexes PE 009-6, 5 April 2007.

SUGGESTED STANDARD OPERATING PROCEDURES (SOPs)

The compounding facility shall have written, properly approved SOPs designed to ensure the quality of the environment in which a CSP is prepared. The following procedures are recommended:

1. Access to the buffer area is restricted to qualified personnel with specific responsibilities or assigned tasks in the compounding area.
2. All cartoned supplies are decontaminated in the area by removing them from shipping cartons and wiping or spraying them with a nonresidue-generating disinfecting agent while they are being transferred to a clean and properly disinfected cart or other conveyance for introduction into the buffer area. Manufacturers' directions or published data for minimum contact time will be followed. Individual pouched sterile supplies need not be wiped because the pouches can be removed as these sterile supplies are introduced into the buffer area.
3. Supplies that are required frequently or otherwise needed close at hand but not necessarily needed for the scheduled operations of the shift are decontaminated and stored on shelving in the ante-area.
4. Carts used to bring supplies from the storeroom cannot be rolled beyond the demarcation line in the ante-area, and carts used in the buffer area cannot be rolled outward beyond the demarcation line unless cleaned and disinfected before returning.
5. Generally, supplies required for the scheduled operations of the shift are wiped down with an appropriate disinfecting agent and brought into the buffer area, preferably on one or more movable carts. Supplies that are required for back-up or general support of operations may be stored on the designated shelving in the buffer area, but excessive amounts of supplies are to be avoided.
6. Nonessential objects that shed particles shall not be brought into the buffer area, including pencils, cardboard cartons, paper towels, and cotton items (e.g., gauze pads).
7. Essential paper-related products (e.g., paper syringe overwraps, work records contained in a protective sleeve) shall be wiped down with an appropriate disinfecting agent prior to being brought into the buffer area.
8. Traffic flow in and out of the buffer area shall be minimized.
9. Personnel preparing to enter the buffer area shall remove all personal outer garments, cosmetics (because they shed flakes and particles), and all hand, wrist, and other visible jewelry or piercings that can interfere with the effectiveness of PPE.
10. Personnel entering the ante-area shall don at-

tire as described in *Personnel Cleansing and Garbing* and *Personnel Training and Competency Evaluation of Garbing, Aseptic Work Practices and Cleaning/Disinfection Procedures*.

11. Personnel shall then thoroughly wash hands and forearms to the elbow with soap and water for at least 30 seconds. An air dryer or disposable nonshedding towels are used to dry hands and forearms after washing.
12. Personnel entering the buffer area shall perform antiseptic hand cleansing prior to donning sterile gloves using a waterless alcohol-based surgical hand scrub with persistent activity.
13. Chewing gum, drinks, candy, or food items shall not be brought into the buffer area or ante-area. Materials exposed in patient care and treatment areas shall never be introduced into areas where components and ingredients for CSPs are present.
14. At the beginning of each compounding activity session, and whenever liquids are spilled, the surfaces of the direct compounding environment are first cleaned with USP Purified Water to remove water-soluble residues. Immediately thereafter, the same surfaces are disinfected with a nonresidue-generating agent using a nonlinting wipe.
15. Primary engineering controls shall be operated continuously during compounding activity. When the blower is turned off and before other personnel enter to perform compounding activities, only one person shall enter the buffer area for the purposes of turning on the blower (for at least 30 minutes) and disinfecting the work surfaces.
16. Traffic in the area of the DCA is minimized and controlled.
17. Supplies used in the DCA for the planned procedures are accumulated and then decontaminated by wiping or spraying the outer surface with sterile 70% IPA or removing the outer wrap at the edge of the DCA as the item is introduced into the aseptic work area.
18. All supply items are arranged in the DCA so as to reduce clutter and provide maximum efficiency and order for the flow of work.
19. After proper introduction into the DCA of supply items required for and limited to the assigned operations, they are so arranged that a clear, uninterrupted path of HEPA-filtered air will bathe all critical sites at all times during the planned procedures. That is, no objects may be placed between the first air from HEPA filters and an exposed critical site.
20. All procedures are performed in a manner designed to minimize the risk of touch contamination. Gloves are disinfected with adequate frequency with an approved disinfectant such as sterile 70% IPA.
21. All rubber stoppers of vials and bottles and the necks of ampuls are disinfected by wiping with sterile 70% IPA and waiting for at least 10 seconds before they are used to prepare CSPs.
22. After the preparation of every CSP, the contents of the container are thoroughly mixed and then inspected for the presence of particulate matter, evidence of incompatibility, or other defects.
23. After procedures are completed, used syringes, bottles, vials, and other supplies are removed, but with a minimum of exit and reentry into the DCA so as to minimize the risk of introducing contamination into the aseptic workspace.

ELEMENTS OF QUALITY CONTROL

A written description of specific training and performance evaluation program for individuals involved in the use of aseptic techniques for the preparation of sterile products shall be developed for each site. This program equips personnel with the appropriate knowledge and trains them in the required skills necessary to perform the assigned tasks. Each person assigned to the aseptic area in the preparation of sterile products shall successfully complete specialized training in aseptic techniques and aseptic area practices prior to preparing CSPs (see *Personnel Training and Evaluation in*

Aseptic Manipulation Skills and *Personnel Training and Competency Evaluation of Garbing, Aseptic Work Practices and Cleaning/Disinfection Procedures*).

Ingredients and Devices

Compounding personnel ascertain that ingredients for CSPs are of the correct identity and appropriate quality using the following information: vendor labels, labeling, certificates of analysis, direct chemical analysis, and knowledge of compounding facility storage conditions.

STERILE INGREDIENTS AND DEVICES

Commercially available sterile drug products, sterile ready-to-use containers, and devices are examples of sterile components. A written procedure for unit-by-unit physical inspection preparatory to use is followed to ensure that these components are sterile, free from defects, and otherwise suitable for their intended use.

NONSTERILE INGREDIENTS AND DEVICES

If any nonsterile components, including containers and ingredients, are used to make a CSP, such CSPs must be high risk. Nonsterile active ingredients and added substances or excipients for CSPs should preferably be official *USP* or *NF* articles. When nonofficial ingredients are used, they shall be accompanied by certificates of analysis from their suppliers to aid compounding personnel in judging the identity, quality, and purity in relation to the intended use in a particular CSP. Physical inspection of a package of ingredients is necessary in order to detect breaks in the container, looseness in the cap or closure, and deviation from the expected appearance, aroma, and texture of the contents.

Bulk or unformulated drug substances and added substances or excipients shall be stored in tightly closed containers under temperature, humidity, and lighting conditions that are either indicated in official monographs or approved by suppliers. The date of receipt by the compounding facility shall be clearly and indelibly marked on each package of ingredient. After receipt by the compounding facility, packages of ingredients that lack a supplier's expiration date cannot be used after 1 year unless either appropriate inspection or testing indicates that the ingredient has retained its purity and quality for use in CSPs.

Careful consideration and evaluation of nonsterile ingredient sources is especially warranted when the CSP will be administered into the vascular system, central nervous system, or eyes.

Upon receipt of each lot of the bulk drug substance or excipient used for CSPs, the individual compounding the preparation performs a visual inspection of the lot for evidence of deterioration, other types of unacceptable quality, and wrong identification. For bulk drug substances or excipients, visual inspection is performed on a routine basis as described in the written protocol.

Equipment

It is necessary that equipment, apparatus, and devices used to compound a CSP be consistently capable of operating properly and within acceptable tolerance limits. Written procedures outlining required equipment calibration, annual maintenance, monitoring for proper function, and controlled procedures for use of the equipment and specified time frames for these activities are established and followed. Routine maintenance and frequencies shall be outlined in these SOPs. Results from the equipment calibration, annual maintenance reports, and routine maintenance are kept on file for the lifetime of the equipment. Personnel are prepared through an appropriate combination of specific training and experience to operate or manipulate any piece of equipment, apparatus, or device they may use when preparing CSPs. Training includes gaining the ability to determine whether any item of equipment is operating properly or is malfunctioning.

VERIFICATION OF AUTOMATED COMPOUNDING DEVICES (ACDs) FOR

PARENTERAL NUTRITION COMPOUNDING

ACDs for the preparation of parenteral nutrition admixtures are widely used by pharmacists in hospitals and other healthcare settings. They are designed to streamline the labor-intensive processes involved in the compounding of these multiple-component formulations by automatically delivering the individual nutritional components in a predetermined sequence under computerized control. Parenteral nutrition admixtures often contain 20 or more individual additives representing as many as 50 or more individual components (e.g., 15 to 20 crystalline amino acids, dextrose monohydrate, and lipids; 10 to 12 electrolyte salts; 5 to 7 trace minerals; and 12 vitamins). Thus, ACDs can provide improved accuracy and precision of the compounding process over the traditional manual compounding methods.

Accuracy

The accuracy of an ACD can be determined in various ways to ensure that the correct quantities of nutrients, electrolytes, or other nutritional components are delivered to the final infusion container. Initially, the ACD is tested for its volume and weight accuracy. For volume accuracy, a suitable volume of Sterile Water for Injection, USP, which represents a typical additive volume (e.g., 40 mL for small-volume range of 1 to 100 mL, 300 mL for large-volume range of 100 to 1000 mL), is programmed into the ACD and delivered to the appropriate volumetric container. The compounding personnel should then consult *Volumetric Apparatus* ⟨31⟩ for appropriate parameters to assess the volumetric performance of the ACD. For gravimetric accuracy, the balance used in conjunction with the ACD is tested using various weight sizes that represent the amounts typically used to deliver the various additives. Compounding personnel should consult *Weights and Balances* ⟨41⟩ for acceptable tolerances of the weights used. In addition, the same volume of *Sterile Water for Injection* used to assess volumetric accuracy is then weighed on the balance used in conjunction with the ACD. For example, if 40 mL of water was used in the volumetric assessment, its corresponding weight should be about 40 g (assuming the relative density of water is 1.0). In addition, during the use of the ACD, certain additives, such as potassium chloride (corrected for density differences), can also be tested in the same manner as with an in-process test.

Finally, additional tests of accuracy may be employed that determine the content of certain ingredients in the final volume of the parenteral nutrition admixture. Generally, pharmacy departments do not have the capability to routinely perform chemical analyses such as analyses of dextrose or electrolyte concentrations. Consequently, hospital or institutional laboratories may be called upon to perform these quality assurance tests. However, the methods in such laboratories are often designed for biological, not pharmaceutical, systems. Thus, their testing procedures shall be verified to meet the *USP* requirements stated in the individual monograph for the component being tested. For example, under *Dextrose Injection*, the following is stated: It contains not less than 95.0% and not more than 105.0% of the labeled amount of $C_6H_{12}O_6 \cdot H_2O$. The hospital or institutional chemistry laboratories must validate their methods to apply to this range and correct for their typical measurement of anhydrous dextrose versus dextrose monohydrate. Similar ranges and issues exist, for example, for injections of calcium gluconate, magnesium sulfate, and potassium chloride. The critical point is the use of *USP* references and possible laboratory procedural differences.

Precision

The intermediate precision of the ACD can be determined on the basis of the day-to-day variations in performance of the accuracy measures. Thus, compounding personnel shall keep a daily record of the above-described accuracy assessments and review the results over time. This review shall occur at least at weekly intervals to avoid potentially clinically significant cumulative

errors over time. This is especially true for additives with a narrow therapeutic index, such as potassium chloride.

FINISHED PREPARATION RELEASE CHECKS AND TESTS

The following quality metrics shall be performed for all CSPs before they are dispensed or administered.

Inspection of Solution Dosage Forms and Review of Compounding Procedures

All CSPs that are intended to be solutions shall be visually examined for the presence of particulate matter and not administered or dispensed when such matter is observed. The prescription orders, written compounding procedure, preparation records, and expended materials used to make CSPs at all contamination risk levels are 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.

PHYSICAL INSPECTION

Finished CSPs are individually inspected in accordance with written procedures after compounding. If not distributed promptly, these CSPs are individually inspected just prior to leaving the storage area. Those CSPs that are not immediately distributed are stored in an appropriate location as described in the written procedures. Immediately after compounding, and as a condition of release, each CSP unit, where possible, should be inspected against lighted white or black background or both for evidence of visible particulates or other foreign matter. Prerelease inspection also includes container–closure integrity and any other apparent visual defect. CSPs with observed defects should be immediately discarded or marked and segregated from acceptable products in a manner that prevents their administration. When CSPs are not distributed promptly after preparation, a predistribution inspection is conducted to ensure that a CSP with defects, such as precipitation, cloudiness, and leakage, which may develop between the time of release and the time of distribution, is not released.

Compounding Accuracy Checks

Written procedures for double-checking compounding accuracy shall be followed for every CSP during preparation and immediately prior to release. The double-check system should meet state regulations and include label accuracy and accuracy of the addition of all drug products or ingredients used to prepare the finished product and their volumes or quantities. The used additive containers and, for those additives for which the entire container was not expended, the syringes used to measure the additive should be quarantined with the final products until the final product check is completed. Compounding personnel shall visually confirm that ingredients measured in syringes match the written order being compounded. Preferably, a person other than the compounder can verify that correct volumes of correct ingredients were measured to make each CSP. For example, compounding personnel would pull the syringe plunger back to the volume measured.

When practical, the accuracy of measurements is confirmed by weighing a volume of the measured fluid, then calculating that volume by dividing the weight by the accurate value of the density, or specific gravity, of the measured fluid. Correct density or specific gravity values programmed in ACDs, which measure by weight using the quotient of the programmed volume divided by the density or specific gravity, shall be confirmed to be accurate before and after delivering volumes of the liquids assigned to each channel or port. These volume accuracy checks and the following additional safety and accuracy checks in this section shall be included in the SOP manual of the CSP facility.

Sterility Testing

All high-risk level CSPs that are prepared in groups of more than 25 identical individual single-

dose packages (e.g., ampuls, bags, syringes, vials) or in multiple-dose vials (MDVs) for administration to multiple patients or that are exposed longer than 12 hours at 2° to 8° and longer than 6 hours at warmer than 8° before they are sterilized shall meet the sterility test (see *Sterility Tests* ⟨71⟩) before they are dispensed or administered. The *Membrane Filtration* method is the method of choice where feasible (e.g., components are compatible with the membrane). A method not described in the *USP* may be used if verification results demonstrate that the alternative is at least as effective and reliable as the *USP Membrane Filtration* method or the *USP Direct Inoculation of the Culture Medium* method where the *Membrane Filtration* method is not feasible.

When high-risk level CSPs are dispensed before receiving the results of their sterility tests, there shall be a written procedure requiring daily observation of the incubating test specimens and immediate recall of the dispensed CSPs when there is any evidence of microbial growth in the test specimens. In addition, the patient and the physician of the patient to whom a potentially contaminated CSP was administered are notified of the potential risk. Positive sterility test results should prompt a rapid and systematic investigation of aseptic technique, environmental control, and other sterility assurance controls to identify sources of contamination and correct problems in the methods or processes.

Bacterial Endotoxin (Pyrogen) Testing

All high-risk level CSPs, except those for inhalation and ophthalmic administration, that are prepared in groups of more than 25 identical individual single-dose packages (e.g., ampuls, bags, syringes, vials) or in MDVs for administration to multiple patients or that are exposed longer than 12 hours at 2° to 8° and longer than 6 hours at warmer than 8° before they are sterilized shall be tested to ensure that they do not contain excessive bacterial endotoxins (see *Bacterial Endotoxins Test* ⟨85⟩ and *Pyrogen Test* ⟨151⟩). In the absence of a bacterial endotoxins limit in the official monograph or other CSP formula source, the CSP shall not exceed the amount of USP Endotoxin Units (per hour per kilogram of body weight or square meters of body surface area) specified in *Bacterial Endotoxins Test* ⟨85⟩ referenced above for the appropriate route of administration.

Identity and Strength Verification of Ingredients

Compounding facilities shall have at least the following written procedures for verifying the correct identity and quality of CSPs before they are dispensed and administered:

1. That labels of CSPs bear correct names and amounts or concentrations of ingredients, the total volume, the BUD, the appropriate route(s) of administration, the storage conditions, and other information for safe use.
2. That there are correct identities, purities, and amounts of ingredients by comparing the original written order with the written compounding record for the CSP.
3. That correct fill volumes in CSPs and correct quantities of filled units of the CSPs were obtained. When the strength of finished CSPs cannot be confirmed to be accurate, based on the above three inspections, the CSPs shall be assayed by methods that are specific for the active ingredients.

STORAGE AND BEYOND-USE DATING

BUDs for compounded preparations are usually assigned on the basis of professional experience, which should include careful interpretation of appropriate information sources for the same or similar formulations (see *Stability Criteria and Beyond-Use Dating* under *Pharmaceutical Compounding—Nonsterile Preparations* ⟨795⟩). BUDs for CSPs are rarely based on preparation-specific chemical assay results, which are used with the Arrhenius equation to determine expiration dates (see *General Notices and Requirements*) for manufactured products. The majority of CSPs are aqueous solutions in which hydrolysis of dissolved ingredients is the most common chemical

degradation reaction. The extent of hydrolysis and other heat-catalyzed degradation reactions at any particular time point in the life of a CSP represents the thermodynamic sum of exposure temperatures and durations. Such lifetime stability exposure is represented in the mean kinetic temperature calculation (see *Pharmaceutical Calculations in Prescription Compounding* ⟨1160⟩). Drug hydrolysis rates increase exponentially with arithmetic temperature increase; thus, exposure of a beta-lactam antibiotic solution for 1 day at controlled room temperature (see *General Notices and Requirements*) will have an equivalent effect on the extent of hydrolysis of approximately 3 to 5 days in cold temperatures (see *General Notices and Requirements*).

Personnel who prepare, dispense, and administer CSPs shall store them strictly in accordance with the conditions stated on the label of ingredient products and finished CSPs. When CSPs are known to have been exposed to temperatures warmer than the warmest labeled limit or to temperatures exceeding 40° (see *General Notices and Requirements*) for more than 4 hours, such CSPs should be discarded unless direct assay data or appropriate documentation confirms their continued stability.

Determining Beyond-Use Dates

BUDs and expiration dates are not the same (see *General Notices and Requirements*). Expiration dates for the chemical and stability of manufactured sterile products are determined from results of rigorous analytical and performance testing, and they are specific for a particular formulation in its container and at stated exposure conditions of illumination and temperature. When CSPs deviate from conditions in the approved labeling of manufactured products contained in CSPs, compounding personnel may consult the manufacturer of particular products for advice on assigning BUDs based on chemical and physical stability parameters. BUDs for CSPs that are prepared strictly in accordance with manufacturers' product labeling shall be those specified in that labeling or from appropriate literature sources or direct testing. BUDs for CSPs that lack justification from either appropriate literature sources or by direct testing evidence shall be assigned as described in *Stability Criteria and Beyond-Use Dating* under *Pharmaceutical Compounding—Nonsterile Preparations* ⟨795⟩.

In addition, compounding personnel may refer to applicable publications to obtain relevant stability, compatibility, and degradation information regarding the drug or its congeners. When assigning a beyond-use date, compounding personnel should consult and apply drug-specific and general stability documentation and literature where available, and they should consider the nature of the drug and its degradation mechanism, the container in which it is packaged, the expected storage conditions, and the intended duration of therapy (see *Expiration Date and Beyond-Use Date* under *Labeling* in the *General Notices and Requirements*). Stability information must be carefully interpreted in relation to the actual compounded formulation and conditions for storage and use. Predictions based on other evidence, such as publications, charts, and tables, would result in theoretical BUDs. Theoretically predicted beyond-use dating introduces varying degrees of assumptions and, hence, a likelihood of error or at least inaccuracy. The degree of error or inaccuracy would be dependent on the extent of differences between the CSPs' characteristics (e.g., composition, concentration of ingredients, fill volume, container type and material) and the characteristics of the products from which stability data or information is to be extrapolated. The greater the doubt of the accuracy of theoretically predicted beyond-use dating, the greater the need to determine dating periods experimentally. Theoretically predicted beyond-use dating periods should be carefully considered for CSPs prepared from nonsterile bulk active ingredients having therapeutic activity, especially where these CSPs are expected to be compounded routinely. When CSPs will be distributed to and administered in residential locations other than healthcare facilities, the effect of potentially uncontrolled and unmonitored temperature condi-

tions shall be considered when assigning BUDs. It must be ascertained that CSPs will not be exposed to warm temperatures (see *General Notices and Requirements*) unless the compounding facility has evidence to justify stability of CSPs during such exposure.

It should be recognized that the truly valid evidence of stability for predicting beyond-use dating can be obtained only through product-specific experimental studies. Semiquantitative procedures such as thin-layer chromatography (TLC) may be acceptable for many CSPs. However, quantitative stability-indicating assays such as high-performance liquid chromatographic (HPLC) assays would be more appropriate for certain CSPs. Examples include CSPs with a narrow therapeutic index, where close monitoring or dose titration is required to ensure therapeutic effectiveness and to avoid toxicity; where a theoretically established beyond-use dating period is supported by only marginal evidence; or where a significant margin of safety cannot be verified for the proposed beyond-use dating period. In short, because beyond-use dating periods established from product-specific data acquired from the appropriate instrumental analyses are clearly more reliable than those predicted theoretically, the former approach is strongly urged to support dating periods exceeding 30 days.

To ensure consistent practices in determining and assigning BUDs, the compounding facility should have written policies and procedures governing the determination of the BUDs for all compounded products. When attempting to predict a theoretical BUD, a compounded or an admixed preparation should be considered as a unique system that has physical and chemical properties and stability characteristics that differ from its components. For example, antioxidant, buffering, or antimicrobial properties of a sterile vial for injection (SVI) might be lost upon its dilution, with the potential of seriously compromising the chemical stability of the SVI's active ingredient or the physical or microbiological stability of the SVI formulation in general. Thus, the properties stabilized in the SVI formulation usually cannot be expected to be carried over to the compounded or admixed preparation. Preparation-specific, experimentally determined stability data evaluation protocols are preferable to published stability information. Compounding personnel should consult general information chapter *Pharmaceutical Stability* ⟨1150⟩ for the appropriate stability parameters to be considered when initiating or evaluating a prep-aration-specific stability study.

Compounding personnel who assign BUDs to CSPs when lacking direct chemical assay results must critically interpret and evaluate the most appropriate available information sources to determine a conservative and safe BUD. The SOP manual of the compounding facility and each specific CSP formula record shall describe the general basis used to assign the BUD and storage conditions.

When manufactured MDVs (see *Multiple-Dose Container* under *Preservation, Packaging, Storage,* and *Labeling* in the *General Notices and Requirements*) of sterile ingredients are used in CSPs, the stoppers of the MDVs are inspected for physical integrity and disinfected by wiping with a sterile 70% IPA swab before each penetration with a sterile withdrawal device. When contaminants or abnormal properties are suspected or observed in MDVs, such MDVs shall be discarded. The BUD after initially entering or opening (e.g., needle puncturing) multiple-dose containers is 28 days (see *Antimicrobial Effectiveness Testing* ⟨51⟩) unless otherwise specified by the manufacturer.

Proprietary Bag and Vial Systems

The sterility storage and stability beyond-use times for attached and activated (where activated is defined as allowing contact of the previously separate diluent and drug contents) container pairs of drug products for intravascular administration (e.g., ADD-Vantage®, Mini Bag Plus®) shall be applied as indicated by the manufacturer. In other words, follow manufacturers' instructions for handling and storing ADD-Vantage®, Mini Bag Plus®, Add A Vial®, Add-Ease® products, and any others.

Monitoring Controlled Storage Areas

To ensure that product potency is retained through the manufacturer's labeled expiration date, compounding personnel shall monitor the drug storage areas within the compounding facility. Controlled temperature areas in compounding facilities include controlled room temperature, 20° to 25° with mean kinetic temperature 25°; controlled cold temperature, 2° to 8° with mean kinetic temperature 8°; cold temperature, 2° to 8°; freezing temperature, −25° and −10° (see *General Notices and Requirements)* if needed to achieve freezing, and the media-specific temperature range for microbial culture media. A controlled temperature area shall be monitored at least once daily and the results documented on a temperature log. Additionally, compounding personnel shall note the storage temperature when placing the product into or removing the product from the storage unit in order to monitor any temperature aberrations. Suitable temperature recording devices may include a calibrated continuous recording device or a National Institute of Standards and Technology (NIST) calibrated thermometer that has adequate accuracy and sensitivity for the intended purpose, and it shall be properly calibrated at suitable intervals. If the compounding facility uses a continuous temperature recording device, compounding personnel shall verify at least once daily that the recording device itself is functioning properly.

The temperature-sensing mechanisms shall be suitably placed in the controlled temperature storage space to reflect accurately its true temperature. In addition, the compounding facility shall adhere to appropriate procedures of all controlled storage spaces to ensure that such spaces are not subject to significantly prolonged temperature fluctuations as may occur, for example, by leaving a refrigerator door open too long.

MAINTAINING STERILITY, PURITY, AND STABILITY OF DISPENSED AND DISTRIBUTED CSPs

This section summarizes the responsibilities of compounding facilities for maintaining quality and control of CSPs that are dispensed and administered within their parent healthcare organizations.

Compounding personnel shall ensure proper storage and security of CSPs prepared by or dispensed from the compounding facility until either their BUDs are reached or they are administered to patients. In fulfilling this general responsibility, the compounding facility is responsible for the proper packaging, handling, transport, and storage of CSPs prepared by or dispensed from it, including the appropriate education, training, and supervision of compounding personnel assigned to these functions. The compounding facility should assist in the education and training of noncompounding personnel responsible for carrying out any aspect of these functions.

Establishing, maintaining, and ensuring compliance with comprehensive written policies and procedures encompassing these responsibilities is a further responsibility of the compounding facility. Where noncompounding personnel are assigned tasks involving any of these responsibilities, the policies and procedures encompassing those tasks should be developed by compounding supervisors. The quality and control activities related to distribution of CSPs are summarized in the following five subsections. Activities or concerns that should be addressed as the compounding facility fulfills these responsibilities are as follows.

Packaging, Handling, and Transport

Inappropriate processes or techniques involved with packaging, handling, and transport can adversely affect quality and package integrity of CSPs. Although compounding personnel routinely perform many of the tasks associated with these functions, some tasks, such as transport, handling, and placement into storage, may be fulfilled by noncompounding personnel who are not under the

direct administrative control of the compounding facility. Under these circumstances, appropriate SOPs shall be established by the compounding facility with the involvement of other departments or services whose personnel are responsible for carrying out those CSP-related functions for which the compounding facility has a direct interest. The performance of the noncompounding personnel is monitored for compliance to established policies and procedures.

The critical requirements that are unique to CSPs and that are necessary to ensure CSP quality and packaging integrity shall be addressed in SOPs. For example, techniques should be specified to prevent the depression of syringe plungers or dislodging of syringe tips during handling and transport. Additionally, disconnection of system components (e.g., where CSPs are dispensed with administration sets attached to them) shall be prevented through the BUD of the CSP. Foam padding or inserts are particularly useful where CSPs are transported by pneumatic tube systems. Regardless of the methods used, the compounding facility must evaluate their effectiveness and the reliability of the intended protection. Evaluation should be continuous—for example, through a surveillance system, including a system of problem reporting to the compounding facility.

Inappropriate transport and handling can adversely affect the quality of certain CSPs having unique stability concerns. For example, the physical shaking that might occur during pneumatic tube transport or undue exposure to heat or light must be addressed on a preparation-specific basis. Alternative transport modes or special packaging measures might be needed for the proper assurance of quality of these CSPs. The use of tamper-evident closures and seals on CSP ports can add an additional measure of security to ensure product integrity regardless of the transport method used.

Chemotoxic and other hazardous CSPs require safeguards to maintain the integrity of the CSP and to minimize the exposure potential of these products to the environment and to personnel who may come in contact with them. Transportation by pneumatic tube should be discouraged because of potential breakage and contamination. Special requirements associated with the packaging, transport, and handling of these agents include the prevention of accidental exposures or spills and the training of personnel in the event of an exposure or spill. Examples of special requirements of these agents also include exposure-reducing strategies such as the use of Luer lock syringes and connections, syringe caps, the capping of container ports, sealed plastic bags, impact-resistant containers, and cautionary labeling.

Use and Storage

The compounding facility is responsible for ensuring that CSPs in the patient-care setting maintain their quality until administered. The immediate labeling of the CSP container will display prominently and understandably the requirements for proper storage and expiration dating. Delivery and patient-care-setting personnel shall be properly trained to deliver the CSP to the appropriate storage location. Outdated and unused CSPs shall be returned to the compounding facility for disposition.

SOPs must exist to ensure that storage conditions in the patient-care setting are suitable for the CSP-specific storage requirements. Procedures include daily monitoring and documentation of drug storage refrigerators to ensure temperatures between 2° and 8° and the monthly inspection of all drug storage locations by compounding personnel. Inspections shall confirm compliance with appropriate storage conditions, separation of drugs and food, proper use of MDVs, and the avoidance of using single-dose products as MDVs. CSPs, as well as all other drug products, shall be stored in the patient-care area in such a way as to secure them from unauthorized personnel, visitors, and patients.

Readying for Administration

Procedures essential for generally ensuring quality, especially sterility assurance, when readying a CSP for its subsequent administration include proper hand washing, aseptic technique, site care,

and change of administration sets. Additional procedures may also be essential for certain CSPs, devices, or techniques. Examples where such special procedures are needed include in-line filtration, the operation of automated infusion control devices, and the replenishment of CSPs into the reservoirs of implantable or portable infusion pumps. When CSPs are likely to be exposed to warmer than 30° for more than 1 hour during their administration to patients, the maintenance of their sterility and stability should be confirmed from either relevant and reliable sources or direct testing.

Redispensed CSPs

The compounding facility shall have the sole authority to determine when unopened, returned CSPs may be redispensed. Returned CSPs may be redispensed only when personnel responsible for sterile compounding can ensure that such CSPs are sterile, pure, and stable (contain labeled strength of ingredients). The following may provide such assurance: the CSPs were maintained under continuous refrigeration and protected from light, if required, and no evidence of tampering or any readying for use outside the compounding facility exists. Assignment of new storage times and BUDs that exceed the original dates for returned CSPs is permitted only when there is supporting evidence from sterility testing and quantitative assay of ingredients. Thus, initial preparation and thaw times should be documented and reliable measures should have been taken to prevent and detect tampering. Compliance with all procedures associated with maintaining product quality is essential. The CSPs shall not be redispensed if there is not adequate assurance that preparation quality and packaging integrity (including the connections of devices, where applicable) were continuously maintained between the time the CSPs left and the time they were returned. Additionally, CSPs shall not be redispensed if redispensing cannot be supported by the originally assigned BUD.

Education and Training

The assurance of CSPs' quality and packaging integrity is highly dependent on the proper adherence of all personnel to the pertinent SOPs. Compounding personnel shall design, implement, and maintain a formal education, training, and competency assessment program that encompasses all the functions and tasks addressed in the foregoing sections and all personnel to whom such functions and tasks are assigned. This program includes the assessment and documentation of procedural breaches, administration mishaps, side effects, allergic reactions, and complications associated with dosage or administration, such as extravasation. This program should be coordinated with the institution's adverse-events and incident reporting programs.

Packing and Transporting CSPs

The following sections describe how to maintain sterility and stability of CSPs until they are delivered to patient care locations for administration.

PACKING CSPs FOR TRANSIT

When CSPs are distributed to locations outside the premises in which they are compounded, compounding personnel select packing containers and materials that are expected to maintain physical integrity, sterility, and stability of CSPs during transit. Packing is selected that simultaneously protects CSPs from damage, leakage, contamination, and degradation, and protects personnel who transport packed CSPs from harm. The SOP manual of the compounding facility specifically describes appropriate packing containers and insulating and stuffing materials, based on information from product specifications, vendors, and experience of compounding personnel. Written instructions that clearly explain how to safely open containers of packed CSPs are provided to patients and other recipients.

TRANSIT OF CSPs

Compounding facilities that ship CSPs to locations outside their own premises shall select modes of transport that are expected to deliver properly packed CSPs in undamaged, sterile, and stable condition to recipients.

Compounding personnel should ascertain that temperatures of CSPs during transit by the selected mode will not exceed the warmest temperature specified on the storage temperature range on CSP labels. It is recommended that compounding personnel communicate directly with the couriers to learn shipping durations and exposure conditions that CSPs may encounter.

Compounding personnel shall include specific handling and exposure instructions on the exteriors of containers packed with CSPs to be transported and obtain reasonable assurance of compliance therewith from transporters. Compounding personnel shall periodically review the delivery performance of couriers to ascertain that CSPs are being efficiently and properly transported.

Storage in Locations Outside Compounding Facilities

Compounding facilities that ship CSPs to patients and other recipients outside their own premises shall ascertain or provide, whichever is appropriate, the following assurances:

1. Labels and accessory labeling for CSPs include clearly readable BUDs, storage instructions, and disposal instructions for out-of-date units.
2. Each patient or other recipient is able to store the CSPs properly, including the use of a properly functioning refrigerator and freezer if CSPs are labeled for such storage.

PATIENT OR CAREGIVER TRAINING

A formal training program is provided as a means to ensure understanding and compliance with the many special and complex responsibilities placed on the patient or caregiver for the storage, handling, and administration of CSPs. The instructional objectives for the training program include all home care responsibilities expected of the patient or caregiver and is specified in terms of patient or caregiver competencies.

Upon the conclusion of the training program, the patient or caregiver should, correctly and consistently, be able to do the following:

1. Describe the therapy involved, including the disease or condition for which the CSPs are prescribed, goals of therapy, expected therapeutic outcome, and potential side effects of the CSPs.
2. Inspect all drug products, CSPs, devices, equipment, and supplies on receipt to ensure that proper temperatures were maintained during transport and that goods received show no evidence of deterioration or defects.
3. Handle, store, and monitor all drug products, CSPs, and related supplies and equipment in the home, including all special requirements related to same.
4. Visually inspect all drug products, CSPs, devices, and other items the patient or caregiver is required to use immediately prior to administration in a manner to ensure that all items are acceptable for use. For example, CSPs must be free from leakage, container cracks, particulates, precipitate, haziness, discoloration, or other deviations from the normal expected appearance, and the immediate packages of sterile devices must be completely sealed, with no evidence of loss of package integrity.
5. Check labels immediately prior to administration to ensure the right drug, dose, patient, and time of administration.
6. Clean the in-home preparation area, scrub hands, use proper aseptic technique, and manipulate all containers, equipment, apparatus, devices, and supplies used in conjunction with administration.
7. Employ all techniques and precautions associated with CSP administration; for example, preparing supplies and equipment, handling of devices, priming the tubing, and discontinuing an infusion.

8. Care for catheters, change dressings, and maintain site patency as indicated.
9. Monitor for and detect occurrences of therapeutic complications such as infection, phlebitis, electrolyte imbalance, and catheter misplacement.
10. Respond immediately to emergency or critical situations such as catheter breakage or displacement, tubing disconnection, clot formation, flow blockage, and equipment malfunction.
11. Know when to seek and how to obtain professional emergency services or professional advice.
12. Handle, contain, and dispose of wastes, such as needles, syringes, devices, biohazardous spills or residuals, and infectious substances.

Training programs include a hands-on demonstration and practice with actual items that the patient or caregiver is expected to use, such as CSP containers, devices, and equipment. The patient or caregiver practices aseptic and injection technique under the direct observation of a health professional.

The compounding facility, in conjunction with nursing or medical personnel, is responsible for ensuring initially and on an ongoing basis that the patient or caregiver understands, has mastered, and is capable of and willing to comply with all of these home care responsibilities. This is achieved through a formal, written assessment program. All specified competencies in the patient or caregiver training program are formally assessed. The patient or caregiver is expected to demonstrate to appropriate healthcare personnel mastery of assigned activities before being allowed to administer CSPs unsupervised by a health professional.

Printed material such as checklists or instructions provided during training may serve as continuing post-training reinforcement of learning or as reminders of specific patient or caregiver responsibilities. Post-training verbal counseling can also be used periodically, as appropriate, to reinforce training and to ensure continuing correct and complete fulfillment of responsibilities.

PATIENT MONITORING AND ADVERSE EVENTS REPORTING

Compounding facilities shall clinically monitor patients treated with CSPs according to the regulations and guidelines of their respective state healthcare practitioner licensure boards or of accepted standards of practice. Compounding facilities shall provide patients and other recipients of CSPs with a way to address their questions and report any concerns that they may have with CSPs and their administration devices.

The SOP manuals of compounding facilities shall describe specific instructions for receiving, acknowledging, and dating receipts, and for recording, or filing, and evaluating reports of adverse events and of the quality of preparation claimed to be associated with CSPs. Reports of adverse events with CSPs shall be reviewed promptly and thoroughly by compounding supervisors to correct and prevent future occurrences. Compounding personnel are encouraged to participate in adverse event reporting and product defects programs of the FDA and USP.

QUALITY ASSURANCE (QA) PROGRAM

A provider of CSPs shall have in place a formal QA program intended to provide a mechanism for monitoring, evaluating, correcting, and improving the activities and processes described in this chapter. Emphasis in the QA program is placed on maintaining and improving the quality of systems and the provision of patient care. In addition, the QA program ensures that any plan aimed at correcting identified problems also includes appropriate follow-up to make certain that effective corrective actions were performed.[13]

Characteristics of a QA program include the following:

1. Formalization in writing;
2. Consideration of all aspects of the preparations and dispensing of products as described

[13]The use of additional resources, such as the Accreditation Manual for Home Care from the Joint Commission on Accreditation of Healthcare Organizations, may prove helpful in the development of a QA plan.

in this chapter, including environmental testing and verification results;

3. Description of specific monitoring and evaluation activities;
4. Specification of how results are to be reported and evaluated;
5. Identification of appropriate follow-up mechanisms when action limits or thresholds are exceeded; and
6. Delineation of the individuals responsible for each aspect of the QA program.

In developing a specific plan, focus is on establishing objective, measurable indicators for monitoring activities and processes that are deemed high risk, high volume, or problem prone. In general, the selection of indicators and the effectiveness of the overall QA program is reassessed on an annual basis.

ABBREVIATIONS AND ACRONYMS

ACD	automated compounding device
ACPH	air changes per hour
ALARA	as low as reasonably achievable
ASHRAE	American Society of Heating, Refrigerating and Air-Conditioning Engineers
BI	biological indicator
BSC	biological safety cabinet
BUD	beyond-use date
CACI	compounding aseptic containment isolator
CAI	compounding aseptic isolator
CDC	Centers for Disease Control and Prevention
CETA	Controlled Environment Testing Association
cfu	colony-forming unit(s)
CSP	compounded sterile preparation
CSTD	closed-system vial-transfer device
DCA	direct compounding area
ECV	endotoxin challenge vial
EU	Endotoxin Unit
FDA	Food and Drug Administration
HEPA	high efficiency particulate air
HICPAC	Healthcare Infection Control Practices Advisory Committee
HVAC	heating, ventilation, and air conditioning
IPA	isopropyl alcohol
ISO	International Organization for Standardization
LAFW	laminar airflow workbench
MDVs	multiple-dose vials
MMWR	Morbidity and Mortality Weekly Report
NIOSH	National Institute for Occupational Safety and Health
NIST	National Institute of Standards and Technology
PEC	primary engineering control
PET	positron emission tomography
PPE	personnel protective equipment
psi	pounds per square inch
QA	quality assurance
SOP	standard operating procedure
SVI	sterile vial for injection
TSA	trypticase soy agar
USP	United States Pharmacopeia

APPENDICES

Appendix I. Principal Competencies, Conditions, Practices, and Quality Assurances That Are Required († "shall") and Recommended (‡ "should") in USP Chapter ⟨797⟩

NOTE—This tabular appendix selectively abstracts and condenses the full text of ⟨797⟩ for rapid reference only. Compounding personnel are responsible for reading, understanding and complying with the full text and all official USP terminology, content, and conditions therein.

INTRODUCTION

‡ Chapter purpose is to prevent harm and death to patients treated with CSPs.

† Chapter pertains to preparation, storage, and transportation, but not administration, of CSPs.

† Personnel and facilities to which ⟨797⟩ applies; therefore, for whom and which it may be enforced by regulatory and accreditation authorities.

† Types of preparations designated to be CSPs according to their physical forms, and their sites and routes of administration to patients.

† Compounding personnel must be meticulously conscientious to preclude contact contamination of CSPs both within and outside ISO Class 5 areas.

ORGANIZATION

† All compounding personnel shall be responsible for understanding fundamental practices and precautions within USP ⟨797⟩, for developing and implementing appropriate procedures, and for continually evaluating these procedures and the quality of final CSPs to prevent harm.

DEFINITIONS

† Twenty-eight terms are defined and integral to complying with USP ⟨797⟩.

RESPONSIBILITY OF COMPOUNDING PERSONNEL

† Practices and quality assurances required to prepare, store, and transport CSPs that are sterile, and acceptably accurate, pure, and stable.

CSP MICROBIAL CONTAMINATION RISK LEVELS

† Proper training and evaluation of personnel, proper cleansing and garbing of personnel, proper cleaning and disinfecting of compounding work environments, and proper maintenance and monitoring of controlled environmental locations (all of which are detailed in their respective sections).

Low-Risk Level CSPs

† Aseptic manipulations within an ISO Class 5 environment using three or fewer sterile products and entries into any container.

† In absence of passing sterility test, store not more than 48 hours at controlled room temperature, 14 days at cold temperature, and 45 days in solid frozen state at –25° to – 10° or colder.

† Media-fill test at least annually by compounding personnel.

Low-Risk Level CSPs with 12-Hour or Less BUD

† Fully comply with all four specific criteria.

‡ Sinks should not be located adjacent to the ISO Class 5 primary engineering control.

‡ Sinks should be separated from the immediate area of the ISO Class 5 primary engineering control device.

Medium-Risk Level CSPs

† Aseptic manipulations within an ISO Class 5 environment using prolonged and complex mixing and transfer, more than three sterile products and entries into any container, and pooling ingredients from multiple sterile products to prepare multiple CSPs.

† In absence of passing sterility test, store not more than 30 hours at controlled room temperature, 9 days at cold temperature, and 45 days in solid frozen state at –25° to –10° or colder.

† Media-fill test at least annually by compounding personnel.

High-Risk Level CSPs

† Confirmed presence of nonsterile ingredients and devices, or confirmed or suspected exposure of sterile ingredients for more than one hour to air quality inferior to ISO Class 5 before final sterilization.

† Sterilization method verified to achieve sterility for the quantity and type of containers.

† Meet allowable limits for bacterial endotoxins.

† Maintain acceptable strength and purity of ingredients and integrity of containers after sterilization.

† In absence of passing sterility test, store not more than 24 hours at controlled room temperature, 3 days at cold temperature, and 45 days in solid frozen state at –25° to –10° or colder.

† Media-fill test at least semiannually by compounding personnel.

Appendix I. Principal Competencies, Conditions, Practices, and Quality Assurances That Are Required († "shall") and Recommended (‡ "should") in USP Chapter ⟨797⟩

PERSONNEL TRAINING AND EVALUATION IN ASEPTIC MANIPULATIONS SKILLS

† Pass didactic, practical skill assessment and media-fill testing initially, followed by an annual assessment for a low- and medium-risk level compounding and semi-annual assessment for high-risk level compounding.

† Compounding personnel who fail written tests, or whose media-fill test vials result in gross microbial colonization, shall be immediately reinstructed and re-evaluated by expert compounding personnel to ensure correction of all aseptic practice deficiencies.

IMMEDIATE-USE CSPs

† Fully comply with all six specified criteria.

SINGLE-DOSE AND MULTIPLE-DOSE CONTAINERS

† Beyond-use date 28 days, unless specified otherwise by the manufacturer, for closure sealed multiple-dose containers after initial opening or entry.

† Beyond-use time of 6 hours, unless specified otherwise by the manufacturer, for closure sealed single-dose containers in ISO Class 5 or cleaner air after initial opening or entry.

† Beyond-use time of 1 hour for closure sealed single-dose containers after being opened or entered in worse than ISO Class 5 air.

† Storage of opened single-dose ampuls is not permitted.

HAZARDOUS DRUGS AS CSPs

† Appropriate personnel protective equipment.

† Appropriate primary engineering controls (BSCs and CACIs) are used for concurrent personnel protection and exposure of critical sites.

† Hazardous drugs shall be stored separately from other inventory in a manner to prevent contamination and personnel exposure.

† At least 0.01 inch water column negative pressure and 12 air changes per hour in non-cleanrooms in which CACIs are located.

† Hazardous drugs shall be handled with caution at all times using appropriate chemotherapy gloves during receiving, distribution, stocking, inventorying, preparing for administration, and disposal.

† Hazardous drugs shall be prepared in an ISO Class 5 environment with protective engineering controls in place, and following aseptic practices specified for the appropriate contamination risk levels.

† Access to drug preparation areas shall be limited to authorized personnel.

† A pressure indicator shall be installed that can readily monitor room pressurization, which is documented daily.

† Annual documentation of full training of personnel regarding storage, handling, and disposal of hazardous drugs.

† When used, a CSTD shall be used in an ISO Class 5 primary engineering control device.

† At least 0.01 inch water column negative pressure is required for compounding of hazardous drugs.

‡ Negative-pressure buffer area is not required for low-volume compounding operations when CSTD is used in BSC or CACI.

† Compounding personnel of reproductive capability shall confirm in writing that they understand the risks of handling hazardous drugs.

† Disposal of all hazardous drug wastes shall comply with all applicable federal and state regulations.

‡ Total external exhaust of primary engineering controls.

‡ Assay of surface wipe samples every 6 months.

RADIOPHARMACEUTICALS AS CSPs

† Positron Emission Tomography is according to USP chapter ⟨823⟩.

† Appropriate primary engineering controls and radioactivity containment and shielding.

† Radiopharmaceuticals compounded from sterile components, in closed sterile containers, with volume of 100 mL or less for a single-dose injection or not more than 30 mL taken from a multiple-dose container shall be designated as and conform to the standards for low-risk level CSPs.

† Radiopharmaceutical vials, designed for multi-use, compounded with technetium-99m, exposed to ISO Class 5 environment and punctured by needles with no direct contact contamination may be used up to the time indicated by manufacturers recommendations.

† Location of primary engineering controls permitted in ISO Class 8 controlled environment.

† Technetium-99m/Molybdenum-99 generators used according to manufacturer, state, and federal requirements.

† Radiopharmaceuticals prepared as low-risk level CSPs with 12-hour or less BUD shall be prepared in a segregated compounding area.

† Materials and garb exposed in patient-care and treatment area shall not cross a line of demarcation into the segregated compounding area.

† Technetium-99m/Molybdenum-99 generators must be eluted in ISO Class 8 conditions.

† Segregated compounding area will be designated with a line of demarcation

‡ Storage and transport of properly shielded vials of radiopharmaceutical CSPs may occur in a limited access ambient environment without a specific ISO class designation.

Appendix I. Principal Competencies, Conditions, Practices, and Quality Assurances That Are Required († "shall") and Recommended (‡ "should") in USP Chapter ⟨797⟩

ALLERGEN EXTRACTS AS CSPs

† Allergen extracts as CSPs are not subject to the personnel, environmental, and storage requirements for all CSP Microbial Contamination Risk Levels when certain criteria are met.

VERIFICATION OF COMPOUNDING ACCURACY AND STERILITY

† Review labels and document correct measurements, aseptic manipulations, and sterilization procedures to confirm correct identity, purity, and strength of ingredients in, and sterility of, CSPs.

‡ Assay finished CSPs to confirm correct identity and, or, strength of ingredients.

‡ Sterility test finished CSPs.

Sterilization Methods

† Verify that methods achieve sterility while maintaining appropriate strength, purity, quality, and packaging integrity.

‡ Prove effectiveness by USP chapter ⟨71⟩, equivalent, or superior sterility testing.

Sterilization of High-Risk Level CSPs by Filtration

† Nominal 0.2-µm pore size sterile membranes that are chemically and physically compatible with the CSP.

† Complete rapidly without filter replacement.

† Subject filter to manufacturers recommended integrity test (e.g., bubble point test) after filtering CSPs.

Sterilization of High-Risk Level CSPs by Steam

† Test to verify the mass of containers to be sterilized will be sterile after the selected exposure duration in the particular autoclave.

† Ensure live steam contacts all ingredients and surfaces to be sterilized.

† Pass solutions through a 1.2-µm or smaller nominal pore size filter into final containers to remove particulates before sterilization.

† Heated filtered air shall be evenly distributed throughout the chamber by a blower device.

† Dry heat shall only be used for those materials that cannot be sterilized by steam, when the moisture would either damage or be impermeable to the materials.

† Sufficient space shall be left between materials to allow for good circulation of the hot air.

† The description of dry heat sterilization conditions and duration for specific CSPs shall be included in written documentation in the compounding facility. The effectiveness of dry heat sterilization shall be verified using appropriate biological indicators and other confirmation.

‡ The oven should be equipped with a system for controlling temperature and exposure period.

Depyrogenation by Dry Heat

† Dry heat depyrogenation shall be used to render glassware or containers, such as vials free from pyrogens as well as viable microbes.

† The description of the dry heat depyrogenation cycle and duration for specific load items shall be included in written documentation in the compounding facility.

† The effectiveness of the dry heat depyrogenation cycle shall be verified using endotoxin challenge vials (ECVs).

‡ The bacterial endotoxin test should be performed on the ECVs to verify the cycle is capable of achieving a 3 log reduction in endotoxin.

ENVIRONMENTAL QUALITY AND CONTROL

Exposure of Critical Sites

† ISO Class 5 or better air.

† Preclude direct contact (e.g., touch and secretions) contamination.

ISO Class 5 Air Sources, Buffer Areas, and Ante-Areas

† A buffer area is an area that provides at least ISO Class 7 air quality.

† New representations of facility layouts.

† Each compounding facility shall ensure that each source of ISO Class 5 environment for exposure of critical sites and sterilization by filtration is properly located, operated, maintained, monitored, and verified.

† Placement of devices (e.g., computers and printers) and objects (e.g., carts and cabinets) can be placed in buffer areas and shall be verified by testing or monitoring.

Viable and Nonviable Environmental Sampling (ES) Testing

† Environmental sampling shall occur as part a comprehensive quality management program and shall occur minimally when several conditions exist.

‡ The ES program should provide information to staff and leadership to demonstrate that the engineering controls are maintaining an environment within the compounding area that consistently maintains acceptably low viable and nonviable particle levels.

Environmental Nonviable Particle Testing Program

† Certification and testing of primary (LAFWs, BSCs, CAIs and CACIs) and secondary engineering controls (buffer and ante areas) shall be performed by a qualified individual no less than every six months and whenever the device or room is relocated, altered, or major service to the facility is performed. Certification procedures such as those outlined in the CETA Certification Guide for Sterile Compounding Facilities (CAG-003-2006) shall be used.

Appendix I. Principal Competencies, Conditions, Practices, and Quality Assurances That Are Required († "shall") and Recommended (‡ "should") in USP Chapter ⟨797⟩

Total Particle Counts

† Certification that each ISO classified area (e.g., ISO Class 5, 7 and 8) is within established guidelines shall be performed no less than every 6 months and whenever the LAFW, BSC, CAI, or CACI is relocated or the physical structure of the buffer room or ante-area has been altered.

† Testing shall be performed by qualified operators using current, state-of-the-art electronic equipment with results meeting ISO Class 5, 7, or 8 depending on the requirements of the area.

† All certification records shall be maintained and reviewed by supervising personnel or other designated employee to ensure that the controlled environments comply with the proper air cleanliness, room pressures, and air changes per hour.

Pressure Differential Monitoring

† A pressure gauge or velocity meter shall be installed to monitor the pressure differential or airflow between the buffer area and ante-area and the ante-area and the general environment outside the compounding area.

† The results shall be reviewed and documented on a log at least every work shift (minimum frequency shall be at least daily) or by a continuous recording device.

† The pressure between the ISO Class 7 and general pharmacy area shall not be less than 5 Pa (0.02 inch water column (w.c.).

† In facilities where low- and medium-risk level CSPs are prepared, differential airflow shall maintain a minimum velocity of 0.2 meter/second (40 fpm) between buffer area and ante-area.

Environmental Viable Airborne Particle Testing Program—Sampling Plan

† An appropriate environmental sampling plan shall be developed for airborne viable particles based on a risk assessment of compounding activities performed.

† Selected sampling sites shall include locations within each ISO Class 5 environment and in the ISO Class 7 and 8 areas, and the segregated compounding areas at greatest risk of contamination (e.g., work areas near the ISO Class 5 environment, counters near doors, pass-through boxes).

† The plan shall include sample location, method of collection, frequency of sampling, volume of air sampled, and time of day as related to activity in the compounding area and action levels.

‡ It is recommended that compounding personnel refer to USP Chapter *Microbiological Evaluation of Clean Rooms and Other Controlled Environments* ⟨*1116*⟩ and the CDC Guidelines for Environmental Infection Control in Healthcare Facilities-2003 for more information.

Growth Media

† A general microbiological growth medium such as Soybean–Casein Digest Medium (also known as trypticase soy broth (TSB) or agar (TSA)) shall be used to support the growth of bacteria.

† Malt extract agar (MEA) or some other media that supports the growth of fungi shall be used in high-risk level compounding environments.

† Media used for surface sampling shall be supplemented with additives to neutralize the effects of disinfecting agents (e.g., TSA with lecithin and polysorbate 80).

Viable Air Sampling

† Evaluation of airborne microorganisms using volumetric collection methods in the controlled air environments shall be performed by properly trained individuals for all compounding risk levels.

† Impaction shall be the preferred method of volumetric air sampling.

† For low-, medium-, and high-risk level compounding, air sampling shall be performed at locations that are prone to contamination during compounding activities and during other activities like staging, labeling, gowning, and cleaning.

† Locations shall include zones of air backwash turbulence within laminar airflow workbench and other areas where air backwash turbulence may enter the compounding area.

† For low-risk level CSPs with 12-hour or less BUD, air sampling shall be performed at locations inside the ISO Class 5 environment and other areas that are in close proximity to the ISO class 5 environment, during the certification of the primary engineering control.

‡ Consideration should be given to the overall effect the chosen sampling method will have on the unidirectional airflow within a compounding environment.

Air Sampling Devices

† The instructions in the manufacturers user manual for verification and use of electric air samplers that actively collect volumes of air for evaluation shall be followed.

† A sufficient volume of air (400–1000 liters) shall be tested at each location in order to maximize sensitivity.

‡ It is recommended that compounding personnel also refer to USP Chapter ⟨1116⟩ that can provide more information on the use of volumetric air samplers and volume of air that should be sampled to detect environmental bioburden excursions.

Air Sampling Frequency and Process

† Air sampling shall be performed at least semiannually (i.e. every 6 months), as part of the re-certification of facilities and equipment for area where primary engineering controls are located.

† A sufficient volume of air shall be sampled and the manufacturers guidelines for use of the electronic air sampling equipment followed.

‡ Any facility construction or equipment servicing may require the need to perform air sampling during these events.

Appendix I. Principal Competencies, Conditions, Practices, and Quality Assurances That Are Required († "shall") and Recommended (‡ "should") in USP Chapter ⟨797⟩

Incubation Period

† The microbial growth media plates used to collect environmental sampling are recovered, covers secured (e.g., taped), inverted, and incubated at a temperature and for a time period conducive to multiplication of microorganisms.

† The number of discrete colonies of microorganisms shall be counted and reported as colony-forming units (cfu) and documented on an environmental monitoring form. Counts from air monitoring need to be transformed into cfu/cubic meter of air and evaluated for adverse trends.

‡ TSA should be incubated at 35° ± 2 ° for 2–3 days.

‡ MEA or other suitable fungal media should be incubated at 28° ± 2 ° for 5–7 days.

Action Levels, Documentation and Data Evaluation

† Sampling data shall be collected and reviewed on a periodic basis as a means of evaluating the overall control of the compounding environment.

† Competent microbiology personnel shall be consulted if an environmental sampling consistently shows elevated levels of microbial growth.

† An investigation into the source of the environmental contamination shall be conducted.

‡ Any cfu count that exceeds its respective action level should prompt a re-evaluation of the adequacy of personnel work practices, cleaning procedures, operational procedures, and air filtration efficiency within the aseptic compounding location.

‡ Table titled, Recommended Action Levels for Microbial Contamination should only be used as a guideline

Facility Design and Environmental Controls

† Compounding facilities are physically designed and environmentally controlled to minimize airborne contamination from contacting critical sites.

† Compounding facilities shall provide a comfortable and well-lighted working environment, which typically includes a temperature of 20° or cooler to maintain comfortable conditions for compounding personnel when attired in the required aseptic compounding garb.

† Primary engineering controls provide unidirectional (i.e., laminar) HEPA air at a velocity sufficient to prevent airborne particles from contacting critical sites.

† In situ air pattern analysis via smoke studies shall be conducted at the critical area to demonstrate unidirectional airflow and sweeping action over and away from the product under dynamic conditions.

† Policies and procedures for maintaining and working within the primary engineering control area shall be written and followed. The policies and procedures will be determined by the scope and risk levels of the aseptic compounding activities used during the preparation of the CSPs.

† The principles of HEPA-filtered unidirectional airflow in the work environment shall be understood and practiced in the compounding process in order to achieve the desired environmental conditions.

† Clean rooms for nonhazardous and nonradioactive CSPs are supplied with HEPA that enters from ceilings with return vents low on walls, and provide not less than 30 air changes per hour.

† Buffer areas maintain 0.02- to 0.05-inch water column positive pressure, and do not contain sinks or drains.

† Air velocity from buffer rooms or zones to ante-areas is at least 40 feet/minute.

† The primary engineering controls shall be placed within a buffer area in such a manner as to avoid conditions that could adversely affect their operation.

† The primary engineering controls shall be placed out of the traffic flow and in a manner to avoid disruption from the HVAC system and room cross-drafts.

† HEPA-filtered supply air shall be introduced at the ceiling.

† All HEPA filters shall be efficiency tested using the most penetrating particle size and shall be leak tested at the factory and then leak tested again in situ after installation.

† Activities and tasks carried out within the buffer area shall be limited to only those necessary when working within a controlled environment.

† Only the furniture, equipment, supplies, and other material required for the compounding activities to be performed shall be brought into the room.

† Surfaces and essential furniture in buffer rooms or zones and clean rooms shall be nonporous, smooth, nonshedding, impermeable, cleanable, and resistant to disinfectants.

† The surfaces of ceilings, walls, floors, fixtures, shelving, counters, and cabinets in the buffer area shall be smooth, impervious, free from cracks and crevices, and nonshedding, thereby promoting cleanability and minimizing spaces in which microorganisms and other contaminants may accumulate.

† The surfaces shall be resistant to damage by disinfectant agents.

† Junctures of ceilings to walls shall be coved or caulked to avoid cracks and crevices where dirt can accumulate.

† Ceiling tiles shall be caulked around each perimeter to seal them to the support frame.

† The exterior lens surface of ceiling lighting fixtures shall be smooth, mounted flush, and sealed.

† Any other penetrations through the ceiling or walls shall be sealed.

† The buffer area shall not contain sources of water (sinks) or floor drains. Work surfaces shall be constructed of smooth, impervious materials, such as stainless steel or molded plastic, so that they are easily cleaned and disinfected.

Appendix I. Principal Competencies, Conditions, Practices, and Quality Assurances That Are Required († "shall") and Recommended (‡ "should") in USP Chapter ⟨797⟩ *(Continued)*

† Carts shall be of stainless steel wire, nonporous plastic, or sheet metal construction with good quality, cleanable casters to promote mobility.

† Storage shelving, counters, and cabinets shall be smooth, impervious, free from cracks and crevices, nonshedding, cleanable, and disinfectable.

† Their number, design, and manner of installation the itmes above shall promote effective cleaning and disinfection.

‡ If ceilings consist of inlaid panels, the panels should be impregnated with a polymer to render them impervious and hydrophobic.

‡ Dust-collecting overhangs, such as ceiling utility pipes, or ledges, such as windowsills, should be avoided.

‡ Air returns should be mounted low on the wall creating a general top-down dilution of room air with HEPA-filtered make-up air.

Placement Of Primary Engineering Controls Within Iso Class 7 Buffer Areas

† Primary engineering controls for nonhazardous and nonradioactive CSPs are located in buffer areas, except for CAIs that are proven to maintain ISO Class 5 air when particle counts are sampled 6 to 12 inches upstream of critical site exposure areas during performance of normal inward and outward transfer of materials, and compounding manipulations when such CAIs are located in air quality worse than ISO Class 7.

† Presterilization procedures for high-risk level CSPs, such as weighing and mixing, shall be completed in no worse than an ISO Class 8 environment.

† Primary engineering controls shall be located out of traffic patterns and away from room air currents that could disrupt the intended airflow patterns.

† When isolators are used for sterile compounding, the recovery time to achieve ISO Class 5 air quality shall be documented and internal procedures developed to ensure that adequate recovery time is allowed after material transfer before and during compounding operations.

† When compounding activities require the manipulation of a patients blood-derived or other biological material (e.g., radiolabeling a patients or a donors white blood cells), the manipulations shall be clearly separated from routine material-handling procedures and equipment used in CSP preparation activities, and they shall be controlled by specific standard operating procedures in order to avoid any cross-contamination.

† Food, drinks, and items exposed in patient care areas, and unpacking of bulk supplies and personnel cleansing and garbing are prohibited from buffer areas or rooms.

† Demarcation designation between buffer areas or rooms and ante-areas.

† Antiseptic hand cleansing and sterile gloves in buffer areas or rooms.

‡ Packaged compounding supplies and components, such as needles, syringes, tubing sets, and small- and large-volume parenterals, should be uncartoned and wiped down with a disinfectant that does not leave a residue (e.g., sterile 70% IPA) when possible in an ante-area, of ISO Class 8 air quality, before being passed into the buffer areas.

Cleaning and Disinfecting the Sterile Compounding Areas

† Trained personnel write detailed procedures including cleansers, disinfectants, and non-shedding wipe and mop materials.

† Cleaning and disinfecting surfaces in the LAFWs, BSCs, CAIs, and CACIs shall be cleaned and disinfected frequently including at the beginning of each work shift, before each batch preparation is started, every 30 minutes during continuous compounding periods of individual CSPs, when there are spills, and when surface contamination is known or suspected from procedural breaches.

† Trained compounding personnel are responsible for developing, implementing, and practicing the procedures for cleaning and disinfecting the DCAs written in the SOPs.

† Cleaning and disinfecting shall occur before compounding is performed. Items shall be removed from all areas to be cleaned and surfaces shall be cleaned by removing loose material and residue from spills, e.g., water-soluble solid residues are removed with Sterile Water (for Injection or Irrigation) and low-shedding wipes. This shall be followed by wiping with a residue-free disinfecting agent, such as sterile 70% IPA, which is allowed to dry before compounding begins.

† Work surfaces in ISO Class 7 and 8 areas and segregated compounding areas are cleaned at least daily.

† Dust and debris shall be removed when necessary from storage sites for compounding ingredients and supplies, using a method that does not degrade the ISO Class 7 or 8 air quality.

† Floors in ISO Class 7 and 8 areas are cleaned daily when no compounding occurs.

† IPA (70% isopropyl alcohol) remains on surfaces to be disinfected for at least 30 seconds before such are used to prepare CSPs.

† Emptied shelving, walls, and ceilings in ante-areas are cleaned and disinfected at least monthly.

† Mopping shall be performed by trained personnel using approved agents and procedures described in the written SOPs.

† Cleaning and disinfecting agents, their schedules of use and methods of application shall be in accordance with written SOPs and followed by custodial and/or compounding personnel.

† All cleaning materials, such as wipers, sponges, and mops, shall be nonshedding, preferably composed of synthetic micro fibers, and dedicated to use in the buffer area, or ante-area, and segregated compounding areas and shall not be removed from these areas except for disposal.

† If cleaning materials are reused (e.g., mops), procedures shall be developed (based on manufacturer recommendations) that ensure that the effectiveness of the cleaning device is maintained and repeated use does not add to the bioburden of the area being cleaned.

† Supplies and equipment removed from shipping cartons shall be wiped with a suitable disinfecting agent (e.g., sterile 70% IPA) delivered from a spray bottle or other suitable delivery method.

† After the disinfectant is sprayed or wiped on a surface to be disinfected, the disinfectant shall be allowed to dry, and during this time the item shall not be used for compounding purposes.

Appendix I. Principal Competencies, Conditions, Practices, and Quality Assurances That Are Required († "shall") and Recommended (‡ "should") in USP Chapter ⟨797⟩ *(Continued)*

† Sterile 70% IPA wetted gauze pads or other particle-generating material shall not be used to disinfect the sterile entry points of packages and devices.

Personnel Cleansing And Garbing

† Personnel shall also be thoroughly competent and highly motivated to perform flawless aseptic manipulations with ingredients, devices, and components of CSPs.

† Personnel with rashes, sunburn, weeping sores, conjunctivitis, active respiratory infection, and cosmetics are prohibited from preparing CSPs.

† Compounding personnel remove personal outer garments; cosmetics; artificial nails; hand, wrist, and body jewelry that can interfere with the fit of gowns and gloves; and visible body piercing above the neck.

† Order of compounding garb and cleansing in ante-area: shoes or shoe covers, head and facial hair covers, face mask, fingernail cleansing, hand and forearm washing and drying; non-shedding gown.

† Order of cleansing and gloving in buffer room or area: hand cleansing with a persistently active alcohol-based product with persistent activity, allow hands to dry; don sterile gloves.

† Routinely disinfect gloves with sterile 70% IPA after contacting nonsterile objects.

† Inspect gloves for holes and replace when breaches are detected.

† Personnel repeat proper procedures after they are exposed to direct contact contamination or worse than ISO Class 8 air.

† These requirements are exempted only for immediate use CSPs and CAIs for which manufacturers provide written documentation based on validated testing that such personnel practices are not required to maintain sterility in CSPs.

Personnel Training And Competency Evaluation Of Garbing, Aseptic Work Practices And Cleaning/Disinfection Procedures

† Personnel who prepare CSPs shall be trained conscientiously and skillfully by expert personnel, multi-media instructional sources, and professional publications in the theoretical principles and practical skills of garbing procedures, aseptic work practices, achieving and maintaining ISO Class 5 environmental conditions, and cleaning and disinfection procedures.

† This training shall be completed and documented before any compounding personnel begin to prepare CSPs.

† Compounding personnel shall complete didactic training, pass written competence assessments, undergo skill assessment using observational audit tools, and media-fill testing.

† Media-fill testing of aseptic work skills shall be performed initially before beginning to prepare CSPs and at least annually thereafter for low- and medium-risk level compounding; and semiannually for high-risk level compounding.

† Compounding personnel who fail written tests, observational audits, or whose media-fill test vials have one or more units showing visible microbial contamination, shall be reinstructed and re-evaluated by expert compounding personnel to ensure correction of all aseptic work practice deficiencies.

† Compounding personnel shall pass all evaluations prior to resuming compounding of sterile preparations.

† Compounding personnel must demonstrate proficiency of proper hand hygiene, garbing, and consistent cleaning procedures in addition to didactic evaluation and aseptic media fill.

† Cleaning and disinfecting procedures performed by other support personnel shall be thoroughly trained in proper hand hygiene, and garbing, cleaning, and disinfection procedures by a qualified aseptic compounding expert.

† Support personnel shall routinely undergo performance evaluation of proper hand hygiene, garbing, and all applicable cleaning and disinfecting procedures conducted by a qualified aseptic compounding expert.

Competency Evaluation of Garbing and Aseptic Work Practices

† Compounding personnel shall be evaluated initially prior to beginning compounding CSPs and whenever an aseptic media fill is performed using a Sample Form for Assessing Hand Hygiene and Garbing Related Practices of Compounding Personnel and the personnel glove fingertip sampling procedures

Aseptic Work Practice Assessment and Evaluation via Personnel Glove Fingertip Sampling

† Monitoring of compounding personnel glove finger tips shall be performed for all CSP risk level compounding.

† Glove fingertip sampling shall be used to evaluate the competency of personnel in performing hand hygiene and garbing procedures in addition to educating compounding personnel on proper work practices.

† All personnel shall demonstrate competency in proper hand hygiene and garbing procedures in addition to aseptic work practices.

† Sterile contact agar plates shall be used to sample the gloved fingertips of compounding personnel after garbing to assess garbing competency and after completing the media-fill preparation.

† Gloves shall not be disinfected with sterile 70% IPA immediately prior to sampling.

Garbing and Gloving Competency Evaluation

† Compounding personnel shall be visually observed during the process of performing hand hygiene and garbing procedures.

† The visual observation shall be documented on a Sample Form for Assessing Hand Hygiene and Garbing Related Practices of Compounding Personnel and maintained to provide a permanent record of and long-term assessment of personnel competency.

Gloved Fingertip Sampling

† Immediately after the compounder completes the hand hygiene and garbing procedure, the evaluator shall collect a gloved fingertip and thumb sample from both hands of the compounder onto appropriate agar plates by lightly pressing each finger tip into the agar.

† The plates shall be incubated for the appropriate incubation period and at the appropriate temperature.

† All employees shall successfully complete an initial competency evaluation and gloved fingertip/thumb sampling procedure (0 cfu) no less than three times before initially being allowed to compound CSPs for human use.

Appendix I. Principal Competencies, Conditions, Practices, and Quality Assurances That Are Required († "shall") and Recommended (‡ "should") in USP Chapter ⟨797⟩ *(Continued)*

† After completing the initial gowning and gloving competency evaluation, re-evaluation of all compounding personnel shall occur at least annually for low- and medium-risk level CSPs and semiannually for high-risk level CSPs before being allowed to continue compounding CSPs.

† Gloves shall not be disinfected with sterile 70% IPA prior to testing.

† The sampled gloves shall be immediately discarded and proper hand hygiene performed after sampling. The nutrient agar plates shall be incubated as stated below.

† The cfu action level for gloved hands shall be based on the total number of cfu on both gloves and not per hand.

‡ Results should be reported separately as number of cfu per employee per hand (left hand, right hand).

Incubation Period

† At the end of the designated sampling period, the agar plates are recovered, covers secured, inverted and incubated at a temperature and for a time period conducive to multiplication of microorganisms. Trypticase soy agar (TSA) with lecithin and polysorbate 80 shall be incubated at 35°± 2° for 2–3 days.

Aseptic Manipulation Competency Evaluation

† All compounding personnel shall have their aseptic technique and related practice competency evaluated initially during the media-fill test procedure and subsequent annual or semiannual media-fill test procedures on the Sample Form for Assessing Aseptic Technique and Related Practices of Compounding Personnel.

Media-Fill Test Procedure

† The skill of personnel to aseptically prepare CSPs shall be evaluated using sterile fluid bacterial culture media-fill verification.

† Media-filled vials shall be incubated within a range of 35° ± 2° for 14 days.

Surface Cleaning and Disinfection Sampling and Assessment

† Surface sampling shall be performed in all ISO classified areas on a periodic basis and can be accomplished using contact plates and/or swabs and shall be done at the conclusion of compounding

† Locations to be sampled shall be defined in a sample plan or on a form.

Cleaning and Disinfecting Competency Evaluation

† Compounding personnel and other personnel responsible for cleaning shall be visually observed during the process of performing cleaning and disinfecting procedures during initial personnel training on cleaning procedures, changes in cleaning staff and at the completion of any Media-Fill Test Procedure.

† Visual observation shall be documented on a Sample Form for Assessing Cleaning and Disinfection Procedures and maintained to provide a permanent record of, and long-term assessment of, personnel competency.

Surface Collection Methods

† Immediately after sampling a surface with the contact plate, the sampled area shall be thoroughly wiped with a non-shedding wipe soaked in sterile 70% IPA.

‡ Results should be reported as cfu per unit of surface area.

Action Levels, Documentation, and Data Evaluation

† Environmental sampling data shall be collected and reviewed on a routine basis as a means of evaluating the overall control of the compounding environment.

† If an activity consistently shows elevated levels of microbial growth, competent microbiology personnel shall be consulted.

† An investigation into the source of the contamination shall be conducted.

† When gloved fingertip sample results exceeds action levels after proper incubation, a review of hand hygiene and garbing procedures as well as glove and surface disinfection procedures and work practices shall be performed and documented.

‡ Any cfu count that exceeds its respective action level should prompt a re-evaluation of the adequacy of personnel work practices, cleaning procedures, operational procedures, and air filtration efficiency within the aseptic compounding location.

SUGGESTED STANDARD OPERATING PROCEDURES

† All facilities are required to have these, and they must include at least the items enumerated in this section.

FINISHED PREPARATION RELEASE CHECKS AND TESTS

Inspection of Solution Dosage Forms and Review of Compounding Procedures

† Review procedures and documents to ensure sterility, purity, correct identities and amounts of ingredients, and stability.

† Visually inspect for abnormal particulate matter and color, and intact containers and seals.

Sterility Testing

† High-risk level CSPs prepared in batches of more than 25 identical containers, or exposed longer than 12 hours at 2° to 8° and 6 hours at warmer than 8° before being sterilized.

Bacterial Endotoxin (Pyrogen) Testing

† High-risk level CSPs, excluding those for inhalation and ophthalmic administration, prepared in batches of more than 25 identical containers, or exposed longer than 12 hours at 2° to 8° and 6 hours at warmer than 8° before being sterilized.

Identity and Strength Verification of Ingredients

† Written procedures to verify correct identity, quality, amounts, and purities of ingredients used in CSPs.

Appendix I. Principal Competencies, Conditions, Practices, and Quality Assurances That Are Required († "shall") and Recommended (‡ "should") in USP Chapter ⟨797⟩ *(Continued)*

†Written procedures to ensure labels of CSPs contain correct names and amounts or concentrations of ingredients, total volumes, beyond-use dates, storage conditions, and route(s) of administration.

STORAGE AND BEYOND-USE DATING

Determining Beyond-Use Dates

† Use the general criteria in USP ⟨795⟩ in the absence of direct stability-indicating assays or authoritative literature that supports longer durations.

MAINTAINING STERILITY, PURITY, AND STABILITY OF DISPENSED AND DISTRIBUTED CSPs

† Written procedures for proper packaging, storage, and transportation conditions to maintain sterility, quality, purity, and strength of CSPs.

Redispensed CSPs

† When sterility, and acceptable purity, strength, and quality can be ensured.

† Assignment of sterility storage times and stability beyond-use dates that occur later than those of originally dispensed CSPs must be based on results of sterility testing and quantitative assay of ingredients.

Packaging And Transporting CSPs

† Packaging maintains physical integrity, sterility, stability, and purity of CSPs.

† Modes of transport that maintain appropriate temperatures and prevent damage to CSPs.

PATIENT OR CAREGIVER TRAINING

† Multiple component formal training program to ensure patients and caregivers understand the proper storage, handling, use, and disposal of CSPs.

PATIENT MONITORING AND ADVERSE EVENTS REPORTING

† Written standard procedures describe means for patients to ask questions and report concerns and adverse events with CSPs, and for compounding supervisors to correct and prevent future problems.

‡ Adverse events and defects with CSPs reported to FDA's MedWatch and USP's MEDMARX programs.

Appendix II

		Microbial Inactivation[2]						Important Chemical & Physical Properties							
Chemical Category of Disinfectant	Concentration Used	Bacteria	Lipophilic viruses	Hydrophilic viruses	M.tuberculosis	Mycotic agents (fungi)	Bacterial spores	Shelf life >1 week	Corrosive or deleterious effects	Non-evaporable residue	Inactivated by organic matter	Skin irritant	Eye irritant	Respiratory irritant	Systemic toxicity
Isopropyl alcohol	60-95%	+	+	±	+	+	-	+	±	-	+	±	+	-	+
Accelerated Hydrogen peroxide[4]	0.5%	+	+	+	+	+	-	+	-	-	±	-	-	-	-
Quaternary Ammonium (eg, dodecyl dimethyl ammonium chloride)	0.4-1.6% aq	+	+	±	±	+	-	+	-	+	+	+	+	-	+
Phenolics	0.4-1.6% aq	+	+	±	+	+	-	+	-	+	±	+	+	-	+
Chlorine (e.g., sodium hypochlorite)	100-5000 ppm	+	+	+	+	+	+	+	±	-	+	+	+	+	+
Iodophors (e.g., povidone-iodine)	30-50 ppm	+	+	±	±	±	-	+	±	+	+	±	+	-	+

[1]Modified from World Health Organization, Laboratory Bio Safety Manual 1983 and Rutala WA, "Antisepsis, disinfection and sterilization in the hospital and related institutions," *Manual of Clinical Microbiology,* American Society for Microbiology, Washington DC, 1995, pages 227-245.

[2]Inactivation of the most common microorganisms (i.e., bacteria) occurs with a contact time of >1 minute; inactivation of spores requires longer contact times (e.g., 5-10 minutes for 5,000ppm chlorine solution against *C. difficile* spores). Reference: Perez J, Springthorpe VS, Sattar SA, Activity of selected oxidizing microbicides against the spores of *Clostridium difficile*: Relevance to environmental control, American ***Journal of Infection Control,* August 2005, pages 320-325.**

[3]*Accelerated* hydrogen peroxide is a new generation of hydrogen peroxide-based germicides in which the potency and performance of the active ingredient have been enhanced and accelerated through the use of appropriate acids and detergents.

Key to abbreviations and symbols: aq = diluted with water; ppm = parts per million; + = yes; - = no; ± = variable results.

Appendix III. Sample Form for Assessing Hand Hygiene and Garbing Related Practices of Compounding Personnel

Printed name and position/title of person assessed: _____
Name of facility or location: _____

Hand Hygiene and Garbing Practices: The qualified evaluator will mark (×) each space for which the person being assessed has acceptably completed the described activity, prints N/A if the activity is not applicable to the assessment session or N/O if the activity was not observed.*

_____ Presents in a clean appropriate attire and manner.
_____ Wears no cosmetics or jewelry (watches, rings, earrings, etc. piercing jewelry included) upon entry into ante-areas.
_____ Brings no food or drinks into or stored in the ante-areas or buffer areas.
_____ Is aware of the line of demarcation separating clean and dirty sides and observes required activities.
_____ Dons shoe covers or designated clean-area shoes one at a time, placing the covered or designated shoe on clean side of the line of demarcation, as appropriate.
_____ Dons beard cover if necessary.
_____ Dons head cover assuring that all hair is covered.
_____ Dons face mask to cover bridge of nose down to include chin.
_____ Performs hand hygiene procedure by wetting hands and forearms and washing using soap and warm water for at least 30 seconds.
_____ Dries hands and forearms using lint-free towel or hand dryer.
_____ Selects the appropriate sized gown examining for any holes, tears, or other defects.
_____ Dons gown and ensures full closure.
_____ Disinfects hands again using a waterless alcohol-based surgical hand scrub with persistent activity and allows hands to dry thoroughly. before donning sterile gloves
_____ Dons appropriate sized sterile gloves ensuring that there is a tight fit with no excess glove material at the fingertips.
_____ Examines gloves ensuring that there are no defects, holes, or tears.
_____ While engaging in sterile compounding activities, routinely disinfects gloves with sterile 70% IPA prior to work in the direct compounding area (DCA) and after touching items or surfaces that may contaminate gloves.
_____ Removes PPE on the clean side of the ante-area.
_____ Removes gloves and performs hand hygiene.
_____ Removes gown and discards it, or hangs it on hook if it is to be reused within the same work day.
_____ Removes and discards mask, head cover, and beard cover (if used).
_____ Removes shoe covers or shoe one at a time, ensuring that uncovered foot is placed on the dirty side of the line of demarcation and performs hand hygiene again. (Removes and discards shoe covers every time the compounding area is exited).

* **The person assessed is immediately informed of all unacceptable activities (i.e., spaces lacking a Check marks, N/A, or N/O) and shown and informed of specific corrections.**

Signature of Person Assessed	Printed Name	Date
Signature of Qualified Evaluator	Printed Name	Date

Appendix IV. Sample Form for Assessing Aseptic Technique and Related Practices of Compounding Personnel

Printed name and position/title of person assessed: _____

Name of facility or location: _____

Aseptic Technique, Safety, and Quality Assurance Practices: The qualified evaluator will mark (×) each space for which the person being assessed has acceptably completed the described activity, prints N/A if the activity is not applicable to the assessment session or N/O if the activity was not observed.*

_____ Completes the Hand Hygiene and Garbing Competency Assessment Form.
_____ Performs proper hand hygiene, garbing, and gloving procedures according to SOPs.
_____ Disinfects ISO Class 5 device surfaces with an appropriate agent.
_____ Disinfects components/vials with an appropriate agent prior to placing into ISO Class 5 work area.
_____ Introduces only essential materials in a proper arrangement in the ISO Class 5 work area.
_____ Does not interrupt, impede, or divert flow of first-air to critical sites.
_____ Ensures syringes, needles, and tubing remain in their individual packaging and are only opened in ISO Class 5 work area
_____ Performs manipulations only in the appropriate DCA of the ISO Class 5 device.
_____ Does not expose critical sites to contact contamination or worse than ISO Class 5 air.
_____ Disinfects stoppers, injection ports, and ampul necks by wiping with sterile 70% IPA and allows sufficient time to dry.
_____ Affixes needles to syringes without contact contamination.
_____ Punctures vial stoppers and spikes infusion ports without contact contamination.
_____ Labels preparation(s) correctly.
_____ Disinfects sterile gloves routinely by wiping with sterile 70% IPA during prolonged compounding manipulations.
_____ Cleans, sets up, and calibrates automated compounding device (e.g., "TPN compounder") according to manufacturer's instructions.
_____ Disposes of sharps and waste according to institutional policy or recognized guidelines.

* **The person assessed is immediately informed of all unacceptable activities (i.e., spaces lacking a Check marks, N/A, or N/O) and shown and informed of specific corrections.**

_____	_____	_____
Signature of Person Assessed	Printed Name	Date
_____	_____	_____
Signature of Qualified Evaluator	Printed Name	Date

Appendix V. Sample Form for Assessing Cleaning and Disinfection Procedures

Printed name and position/title of person assessed: _____

Name of facility or location: _____

Cleaning and Disinfection Practices: The qualified evaluator will mark (×) each space for which the person being assessed has acceptably completed the described activity, prints N/A if the activity is not applicable to the assessment session or N/O if the activity was not observed.*

Daily Tasks:

_____ Prepares correct concentration of disinfectant solution according to manufacturer's instructions.

_____ Uses appropriately labeled container for the type of surface to be cleaned (floor, wall, production bins, etc.).

_____ Documents disinfectant solution preparation.

_____ Follows garbing procedures when performing any cleaning activities.

_____ At the beginning of each shift, cleans all ISO Class 5 devices prior to compounding in the following order: walls, IV bar, automated compounders, and work surface.

_____ Uses a lint free wipe soaked with sterile 70% IPA or other approved disinfectant solution and allows to dry completely.

_____ Removes all compounder components and cleans all ISO Class 5 areas as stated above at the end of each shift.

_____ Cleans all counters and easily cleanable work surfaces.

_____ Mops floors, using the mop labeled "floors", starting at the wall opposite the room entry door; mops floor surface in even strokes toward the operator. Moves carts as needed to clean entire floor surface. Use of a microfiber cleaning system is an acceptable alternative to mops.

_____ In the ante-area, cleans sink and all contact surfaces; cleans floor with a disinfectant solution or uses microfiber cleaning system.

Monthly Tasks:

_____ Performs monthly cleaning on a designated day. Prepares a disinfectant solution as stated in daily tasks that is appropriate for the surfaces to be cleaned.

_____ Cleans buffer area and ante-area ceiling, walls, and storage shelving with a disinfectant solution and a mop or uses a microfiber cleaning system.

_____ Once ISO Class 5 area is clean, cleans compounding room ceiling, followed by walls and ending with the floor. Uses appropriate labeled mops or microfiber cleaning system.

_____ Cleans all buffer area totes and storage shelves by removing contents and using a germicidal detergent soaked lint free wipe, cleans the inside surfaces of the tote and then the entire exterior surfaces of the tote. Allows totes to dry. Prior to replacing contents into tote, wipes tote with sterile 70% IPA to remove disinfectant residue. Uses new wipe as needed.

_____ Cleans all buffer area carts by removing contents and using germicidal detergent soaked lint free wipe, cleans all carts starting with the top shelf and top of post, working down to wheels. Cleans the under side of shelves in a similar manner. Uses a new wipe for each cart. Allows to dry. Wipes carts with sterile 70% IPA wetted lint-free wipe to remove any disinfectant residue. Uses new wipe as needed.

_____ Cleans buffer area chairs, the interior and exterior of trash bins, and storage bins using disinfectant solution soaked lint free wipe.

_____ Documents all cleaning activities as to who performed such activities with date and time noted.

* **The person assessed is immediately informed of all unacceptable activities (i.e., spaces lacking a Check marks, N/A, or N/O) and shown and informed of specific corrections.**

Signature of Person Assessed	Printed Name	Date
Signature of Qualified Evaluator	Printed Name	Date

(Official June 1, 2008)

Midazolam storage and preparation instructions

USP Chapter 797 sets the following BUDs on high-risk compounded preparations: 1) 24 hours at room temperature; 2) 3 days at cold temperature (refrigerated); and 3) 45 days frozen. Once thawed at room temperature, the preparation must be used within 24 hours and cannot be refrozen to extend that time. If thawed in refrigerator it must be used within 3 days.

Items you will need:

1. Four 5 ml midazolam 50mg/ml vials
2. Gloves
3. Alcohol swabs
4. Four 50 ml bags of normal saline 0.9%
5. Four 50 ml/cc syringes

Preparation:

1. Remove 4 vials of midazolam from the freezer and place in refrigerator 24 hours prior to use as to allow to thaw.

2. On day of use prepare the four 50ml bags of normal saline 0.9% by removing them from the outer package. Remove an alcohol wipe from the package and swipe the injection port twice with intent and friction. Repeat with an additional alcohol pad on the second bag of normal saline.

3. On the day of use, retrieve the necessary vials of Midazolam from the refrigerator and remove the blue seal from the top of each vial of midazolam.

4. Remove an alcohol wipe from the package and swipe each medication vial stopper with intent and friction with two swipes. A new alcohol wipe should be used for each vial.

5. Obtain four 50ml/cc syringes

6. Open one syringe package using aseptic technique by peeling the paper packaging at the syringe tip end until you are able to grasp the syringe outer barrel. You may then drop the packaging onto the counter. Move the syringe between your dominant ring finger and middle finger, taking special care not to contaminate the syringe tip or the area of the plunger that extends into the barrel by touching them to any surface or fingers.

7. Retrieve the needle package with your non-dominant hand. Open the needle package using aseptic technique by peeling the paper packaging at the needle hub end until you are able to grasp the outer cap. Take special care not to contaminate the needle hub by touching it to any surface or fingers. Drop the needle packaging onto the counter.

8. Using aseptic technique, connect the needle to the syringe tip. If any of the connection points are contaminated, you must obtain new supplies and start over.

9. Take the outer protective cap off the needle and place the cap onto the counter, taking care not to contaminate the point of the needle.
10. These instructions list drawing the midazolam first followed by saline but the order can be reversed and the saline may be drawn first followed by the midazolam.
11. Secure the first medication vial with your non-dominant hand and insert the needle into the soft, rubber portion of the vial.
12. While holding the vial and the syringe together, invert them and bring them to eye-level. Take special care not to contaminate the syringe tip and the needle.
13. Withdraw 5 ml from the first vial of midazolam by drawing back slowly on the syringe plunger until 5 ml is obtained, making sure that the needle tip is below the solution level at all times. There is overfill in each vial, so you may see a small amount of liquid leftover.
14. Withdraw the needle from the vial, taking care not to contaminate the needle tip. Set the vial down on the counter while holding the needle and syringe upright in the air.
15. Inspect the syringe now filled with midazolam, inspect to ensure you see no particles or discoloring (should be clear liquid and without debris).
16. With the current syringe, take one of the bags of normal saline and puncture the injection port with the syringe taking care not contaminate the tip of the needle. Do not inject the midazolam into the bag of normal saline. Draw out enough normal saline to achieve a final solution volume of 50ml/cc.
17. Remove the syringe from the bag and assess the syringe for air bubbles and the appropriate volume. If air bubbles are present, gently tap the syringe with your finger or a pen to release the air bubbles and then eject the air. Adjust needle tip to below the level of the fluid and withdraw more fluid until the desired volume is reached.
18. Replace the outer needle cap carefully by scooping the needle into the cap. And lay the syringe on the counter. The prepared syringe will have 5mg/ml midazolam in 50ml solution for a total dose of 250mg of midazolam.
19. Repeat steps 6-17 for the remaining vials until the desired quantity of solution is obtained.
20. Dispose of any wrappers or packages in the garbage. If the medication vial contains any unused medications, dispose of the medication fluid according to institutional policies. Dispose of the empty medication vial in the sharps container, according to institutional policies. Needles may be removed from syringe and disposed of in sharps containers. Syringes may be disposed of in the garbage or according to institutional policies.

Potassium Chloride preparation instructions

Items you will need:

1. Two 60ml vials of 15% Potassium Chloride Solution (2 mEq/ml equivalent)
2. Gloves
3. Alcohol swabs
4. Two 60 ml syringes

Preparation:

1. Remove 2 vials of potassium chloride from the freezer and place in refrigerator 24 hours prior to use as to allow to thaw.

2. On the day of use, retrieve the necessary vials of Potassium Chloride from the refrigerator and remove the red or silver seal from the top of the vial of potassium.

3. Remove an alcohol wipe from the package and swipe the medication vial stopper with intent and friction with two swipes.

4. Obtain two 60ml syringes

5. Open one syringe package using aseptic technique by peeling the paper packaging at the syringe tip end until you are able to grasp the syringe outer barrel. You may then drop the packaging onto the counter. Move the syringe between your dominant ring finger and middle finger, taking special care not to contaminate the syringe tip or the area of the plunger that extends into the barrel by touching them to any surface or fingers.

6. Retrieve the needle package with your non-dominant hand. Open the needle package using aseptic technique by peeling the paper packaging at the needle hub end until you are able to grasp the outer cap. Take special care not to contaminate the needle hub by touching it to any surface or fingers. Drop the needle packaging onto the counter.
7. Using aseptic technique, connect the needle to the syringe tip. If any of the connection points are contaminated, you must obtain new supplies and start over.
8. Take the outer protective cap off the needle and place the cap onto the counter, taking care not to contaminate the point of the needle.
9. Secure the first medication vial with your non-dominant hand and insert the needle into the soft, rubber portion of the vial.

10. While holding the vial and the syringe together, invert them and bring them to eye-level. Take special care not to contaminate the syringe tip and the needle.

11. Withdraw 60 ml of potassium chloride from the vial. There is overfill in the vial, so you may see a small amount of liquid leftover.

12. Withdraw the needle from the vial, taking care not to contaminate the needle tip. Set the vial down on the counter while holding the needle and syringe upright in the air.

13. Replace the outer needle cap carefully by scooping the needle into the cap.

14. Inspect the syringe now filled with potassium chloride, inspect to ensure you see no particles or discoloring (should be clear liquid and without debris). Set aside.

15. Repeat process with an additional new, unused syringe.

16. The prepared syringes will have 2mEq/ml Potassium Chloride.

17. Dispose of any wrappers or packages in the garbage. If the medication vial contains any unused medications, dispose of the medication fluid according to institutional policies. Dispose of the empty medication vial in the sharps container, according to institutional policies. Needles may be removed from syringe and disposed of in sharps containers. Syringes may be disposed of in the garbage or according to institutional policies.

[redacted]

From: [redacted]
Sent: Wednesday, May 11, 2022 1:00 PM
To: [redacted]
Subject: FW: Reprieve
Attachments: Statement_4.21.docx

From: [redacted]
Sent: Thursday, April 21, 2022 5:57 PM
To: [redacted]
Subject: Fwd: Reprieve

Sent from my iPhone

Begin forwarded message:

From: [redacted]
Date: April 21, 2022 at 5:46:09 PM CDT
To: [redacted]
Subject: Reprieve

[redacted]

The attached is going statewide any minute. This is the approved statement for all inquiry on this issue. Please feel free to send folks to our office when they follow up.

Sent from my iPhone

FOR IMMEDIATE RELEASE
April 21, 2022

CONTACT: [redacted]

Statement on Oscar Smith Temporary Reprieve

NASHVILLE, Tenn. – Today, Tennessee Governor Bill Lee released the following statement:

"Due to an oversight in preparation for lethal injection, the scheduled execution of Oscar Smith will not move forward tonight. I am granting a temporary reprieve while we address Tennessee Department of Correction protocol. Further details will be released when they are available."

###

[redacted]

From: [redacted]
Sent: Wednesday, May 11, 2022 1:01 PM
To: [redacted]
Subject: FW: Oscar Smith Reprieve
Attachments: 2022 04 21 Reprieve.pdf

From: [redacted]
Sent: Thursday, April 21, 2022 5:33 PM
To: [redacted]
Cc: [redacted]
Subject: Oscar Smith Reprieve

[redacted]

Please find the attached document.

Respectfully,

[redacted]

THE STATE OF

TENNESSEE

EXECUTIVE CHAMBER

REPRIEVE

Pursuant to the authority vested in me by Article III, Section 6 of the Constitution of the State of Tennessee, I, Bill Lee, Governor of the State of Tennessee, do hereby grant to Oscar Franklin Smith a reprieve from execution of the sentence of death imposed upon him by the Criminal Court for Davidson County in 1990 and scheduled to be carried out on April 21, 2022. *State v. Smith*, No. M2016-01869-SC-R11-PD (Tenn. Nov. 3, 2021). This reprieve shall continue in effect until June 1, 2022.

IN TESTIMONY WHEREOF, I have hereunto set my hand and caused the Great Seal of the State to be affixed at Nashville, Tennessee on this 21st day of April, 2022.

Bill Lee

GOVERNOR

Tre Hargett

SECRETARY OF STATE

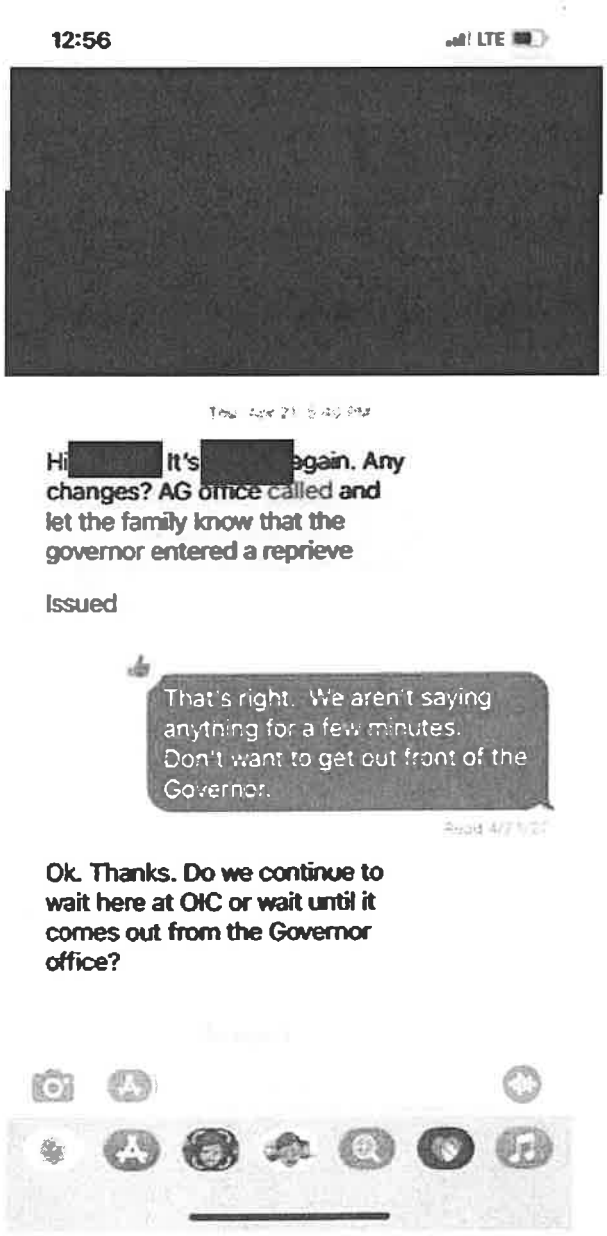
Thu, Apr 21, 6:31 PM

Do we need to maintain the chemicals in the event of a challenge?

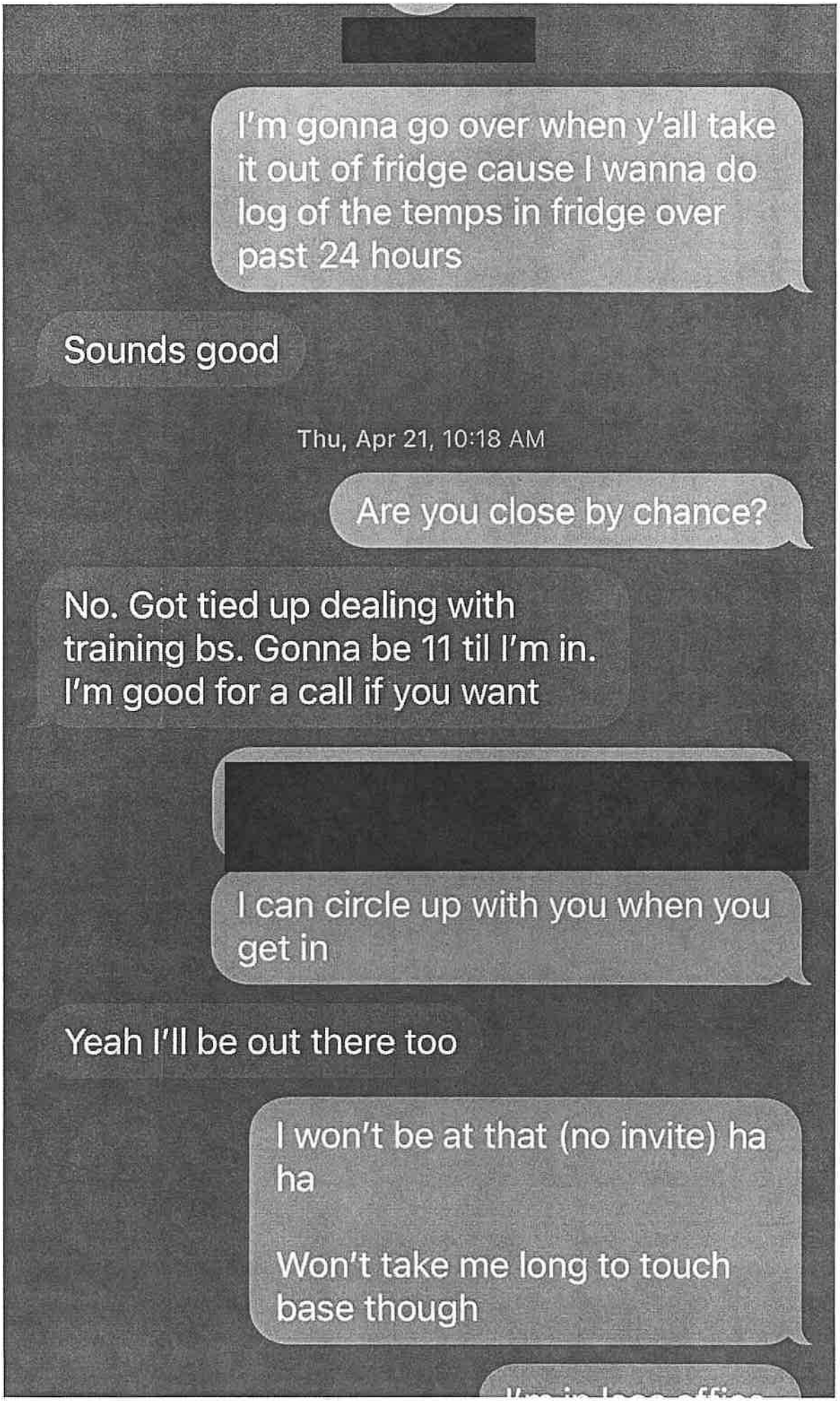

[redacted]
Thu, Apr 21, 7:48 PM
Just checking on you and your team.
Thanks for checking. Team is good [redacted] is here working through some last minute issues with the AG's office.
Let me know if you need anything from me.
Thanks!

[redacted]

From: [redacted]
Sent: Wednesday, May 11, 2022 12:57 PM
To: [redacted]
Subject: Screenshot 2022-05-11 at 12.56.17 PM



Sent from my iPhone


[redacted]
I'm gonna go over when y'all take it out of fridge cause I wanna do log of the temps in fridge over past 24 hours
Sounds good
Thu, Apr 21, 10:18 AM
Are you close by chance?
No. Got tied up dealing with training bs. Gonna be 11 til I'm in. I'm good for a call if you want
[redacted]
I can circle up with you when you get in
Yeah I'll be out there too
I won't be at that (no invite) ha ha
Won't take me long to touch base though

[redacted]

training bs. Gonna be 11 til I'm in.
I'm good for a call if you want

[redacted]

I can circle up with you when you get in

Yeah I'll be out there too

I won't be at that (no invite) ha ha

Won't take me long to touch base though

I'm i[redacted]

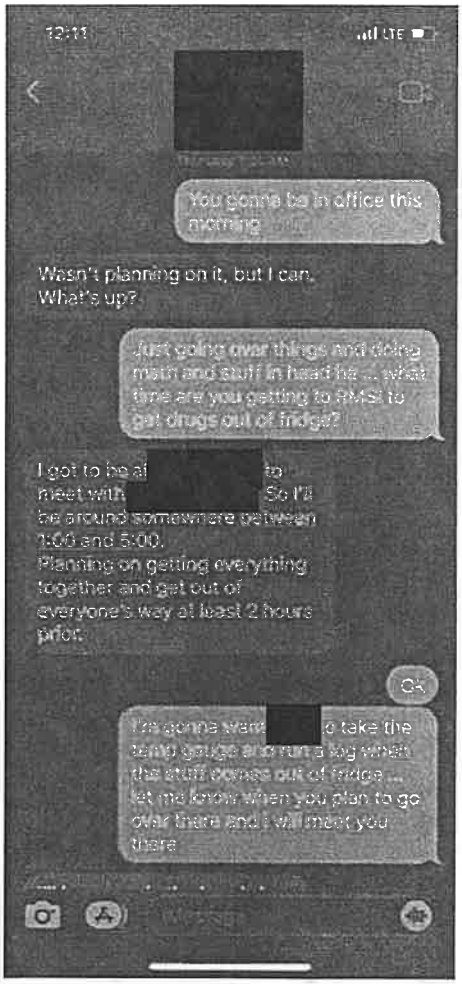
Thu, Apr 21, 1:09 PM

4:30 it is

Thanks

Thu, Apr 21, 6:36 PM

We are preserving everything so don't throw anything away or alter any stuff


12:11
LTE
[redacted]
You gonna be in office this morning
Wasn't planning on it, but I can. What's up?
Just going over things and doing math and stuff in head he ... what time are you getting to RMSI to get drugs out of fridge?
I got to be at [redacted] to meet with [redacted] So I'll be around somewhere between 1:00 and 5:00. Planning on getting everything together and get out of everyone's way at least 2 hours prior.
Ok
I'm gonna want [redacted] to take the temp gauge and run a log when the stuff comes out of fridge ... let me know when you plan to go over there and I will meet you there

[redacted]

Awesome thanks

Thursday 12:48 PM

Start getting things ready at 4:30

Ok I will be there

10-4

Want me to meet y'all at [redacted]

Yelp. Call when you a there or close

Thursday 4:30 PM

On the way over meet you at the [redacted]

In parking lot

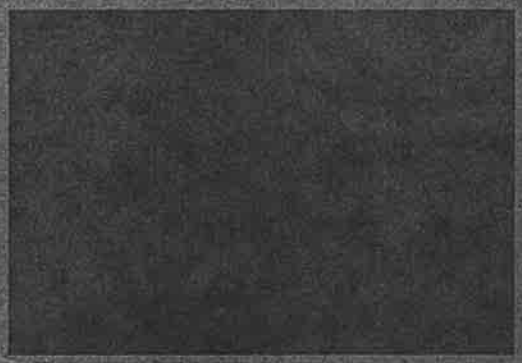
We are at the [redacted]

Read Thursday

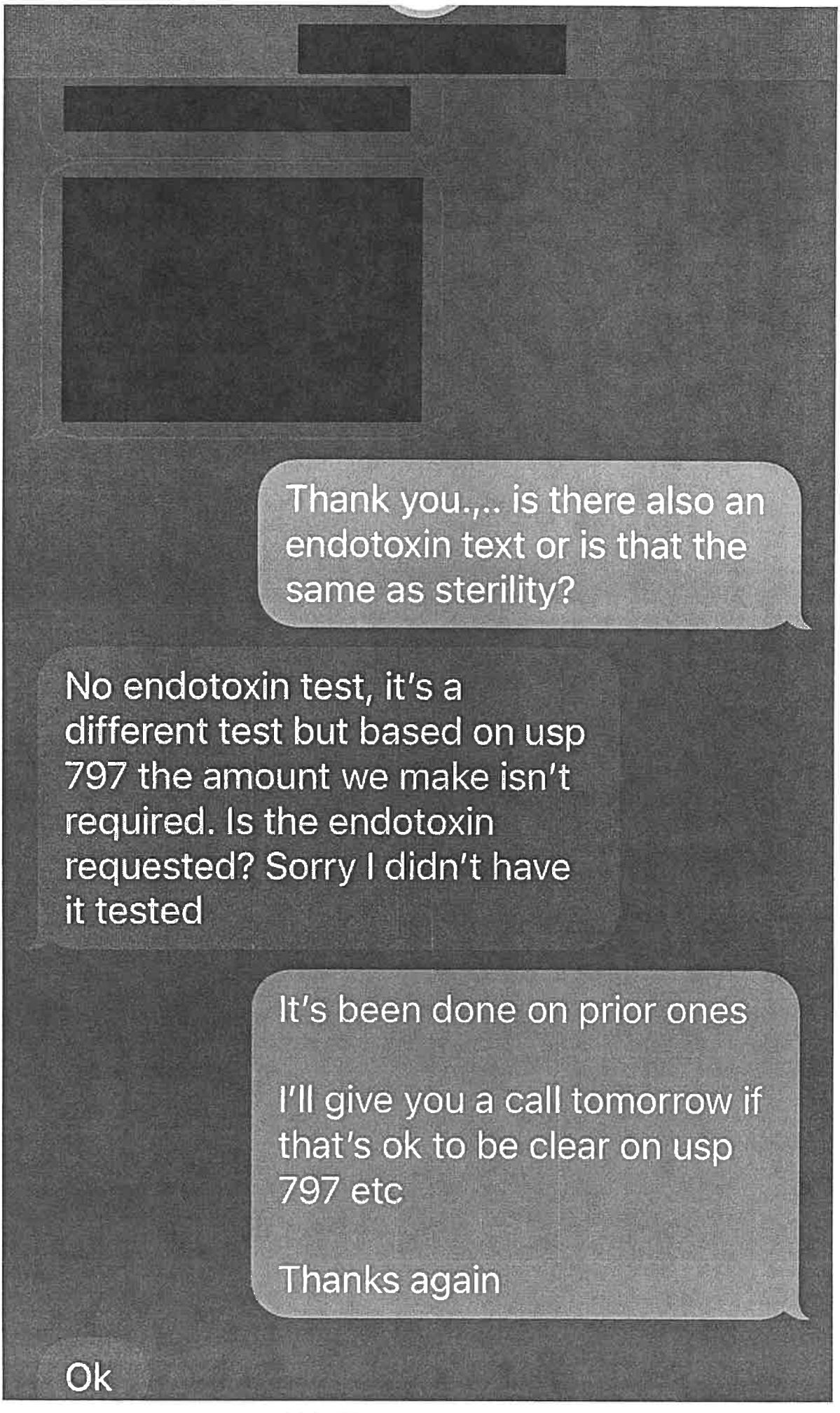
[redacted]

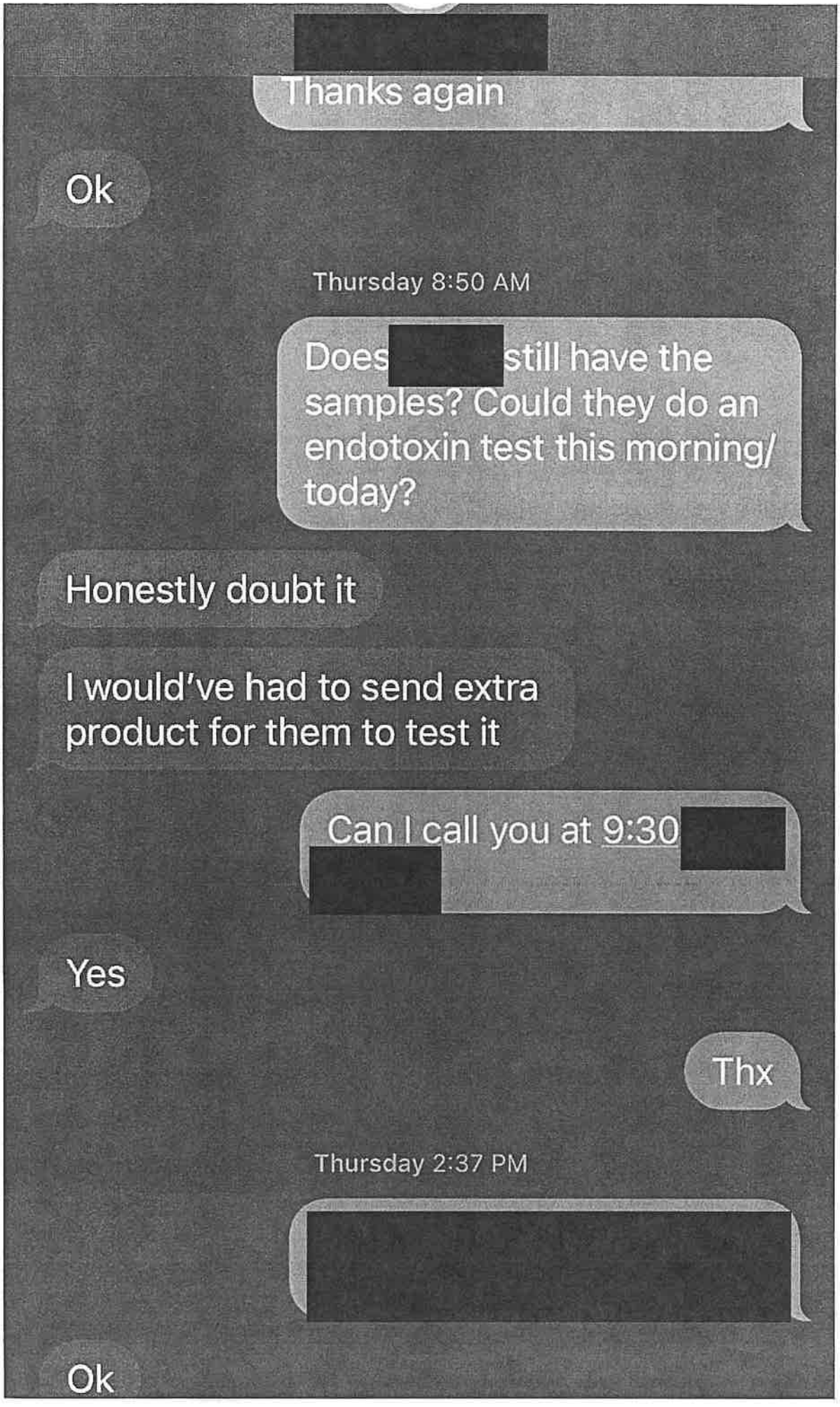
Wed, Apr 20, 7:54 PM

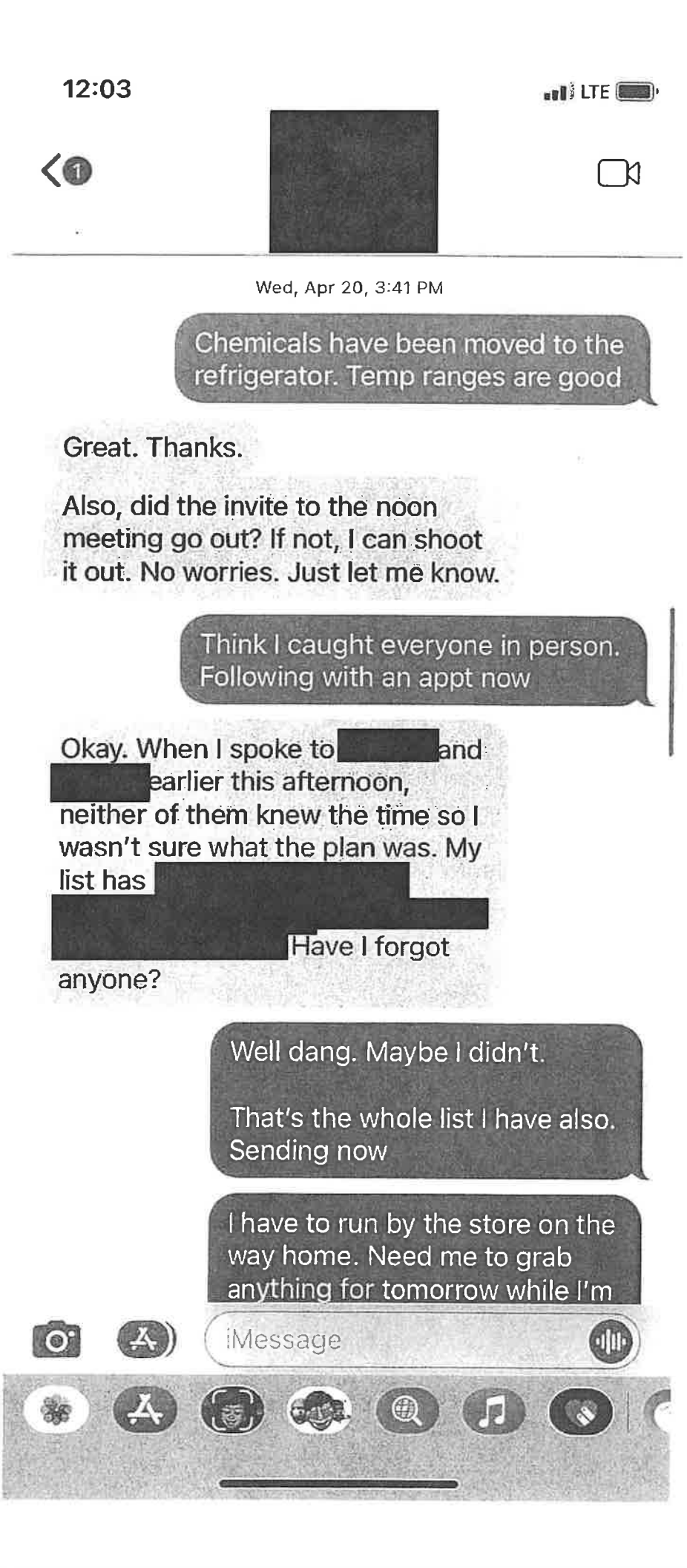
Can you send me the lab reports on the Midazolam and KCL?



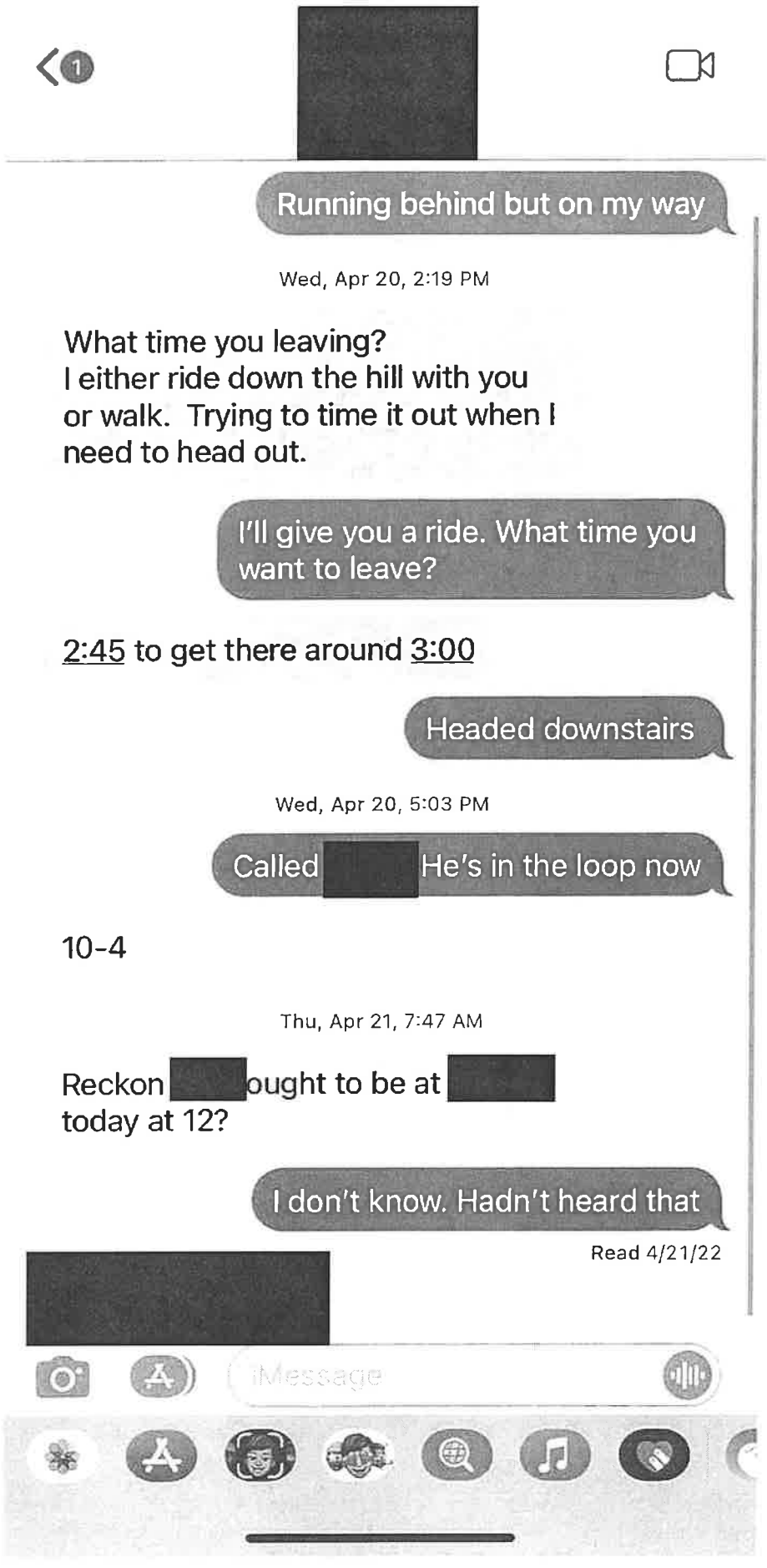
Thank you.,.. is there also an endotoxin text or is that the same as sterility?


Thank you.,.. is there also an endotoxin text or is that the same as sterility?
No endotoxin test, it's a different test but based on usp 797 the amount we make isn't required. Is the endotoxin requested? Sorry I didn't have it tested
It's been done on prior ones
I'll give you a call tomorrow if that's ok to be clear on usp 797 etc
Thanks again
Ok


[redacted]
Thanks again
Ok
Thursday 8:50 AM
Does [redacted] still have the samples? Could they do an endotoxin test this morning/ today?
Honestly doubt it
I would've had to send extra product for them to test it
Can I call you at 9:30 [redacted]
Yes
Thx
Thursday 2:37 PM
[redacted]
Ok


12:03
LTE
[redacted]
Wed, Apr 20, 3:41 PM
Chemicals have been moved to the refrigerator. Temp ranges are good
Great. Thanks.
Also, did the invite to the noon meeting go out? If not, I can shoot it out. No worries. Just let me know.
Think I caught everyone in person. Following with an appt now
Okay. When I spoke to [redacted] and [redacted] earlier this afternoon, neither of them knew the time so I wasn't sure what the plan was. My list has [redacted] Have I forgot anyone?
Well dang. Maybe I didn't.
That's the whole list I have also. Sending now
I have to run by the store on the way home. Need me to grab anything for tomorrow while I'm
iMessage


12:04
LTE
[redacted]
Well dang. Maybe I didn't.
That's the whole list I have also. Sending now
I have to run by the store on the way home. Need me to grab anything for tomorrow while I'm there?
Thanks. I think I am good.
Thu, Apr 21, 5:51 PM
I seen that [redacted] told you we are standing down but in case you didn't I'm letting you know.
Good lands. Not I seen! I said I assume!
[redacted] didn't. But [redacted] was outside the room. We are stopping setup now
I will be back in a few minutes.
10-4. Is [redacted] coming back?
I am
Fri, Apr 22, 11:55 AM
iMessage


12:01
LTE
[redacted]
Running behind but on my way
Wed, Apr 20, 2:19 PM
What time you leaving?
I either ride down the hill with you
or walk. Trying to time it out when I
need to head out.
I'll give you a ride. What time you
want to leave?
2:45 to get there around 3:00
Headed downstairs
Wed, Apr 20, 5:03 PM
Called [redacted] He's in the loop now
10-4
Thu, Apr 21, 7:47 AM
Reckon [redacted] ought to be at [redacted]
today at 12?
I don't know. Hadn't heard that
Read 4/21/22
[redacted]
iMessage

[redacted]

Inventory & Use for Specific Chemical

Printed 5/11/2022

Page 1 Between 1/1/2000 and 05/11/2022

MIDAZOLAM BP CIV (4)

							Balance	Chk'd
3/7/2018 14:35								
IN:	Mfg: [redacted]	Inv.#:	Lot#: [redacted]			1 (GM, ML, UNITS	1	
	Package size	1 x	1 Inv. date:	3/7/2018	Exp. date:	1/31/2021 Whlsr: [redacted]		
5/8/2018 9:03								
IN:	Mfg: [redacted]	Inv.#:	Lot#: [redacted]			50 (GM, ML, UNITS	51	
	Package size	50 x	1 Inv. date:	5/8/2018	Exp. date:	1/31/2021 Whlsr: [redacted]		
1/2/2020 16:30								
IN:	Mfg: [redacted]	Inv.#:	Lot#: [redacted]			100 (GM, ML, UNITS	151	
	Package size	50 x	2 Inv. date:	1/2/2020	Exp. date:	10/31/2023 Whlsr: [redacted]		
5/8/2018								
OUT:	Made:	90 MIDAZOLAM 50 MG/ML INJECTION SOLUTION (3)				Qty used:	4.5 GM	
	Log Lot#: [redacted]	Lot#: [redacted]		Mfg: [redacted]		Whlsr: [redacted]	146.5	
7/20/2018								
OUT:	Made:	55 MIDAZOLAM 50 MG/ML INJECTION SOLUTION (3)				Qty used:	2.75 GM	
	Log Lot#: [redacted]	Lot#: [redacted]		Mfg: [redacted]		Whlsr: [redacted]	143.8	
10/25/2018								
OUT:	Made:	30 MIDAZOLAM 50 MG/ML INJECTION SOLUTION (3)				Qty used:	1.5 GM	
	Log Lot#: [redacted]	Lot#: [redacted]		Mfg: [redacted]		Whlsr: [redacted]	142.25	

OUT: Made:
Log Lot#: [redacted]
60 MIDAZOLAM 50 MG/ML INJECTION SOLUTION (3)
Lot#: [redacted] Mfg: [redacted]
Qty used: 3 GM
Whlsr: [redacted] 139.25
(GM, ML, or UNITS)

OUT: Made:
Log Lot#: [redacted]
85 MIDAZOLAM 50 MG/ML INJECTION SOLUTION (3)
Lot#: [redacted] Mfg: [redacted]
Qty used: 4.25 GM
Whlsr: [redacted] 135
11/18/2019
(GM, ML, or UNITS)

OUT: Made:
Log Lot#: [redacted]
85 MIDAZOLAM 50 MG/ML INJECTION SOLUTION (3)
Lot#: [redacted] Mfg: [redacted]
Qty used: 4.25 GM
Whlsr: [redacted] 130.75
(GM, ML, or UNITS)

Log Lot#: [redacted]
Lot#: [redacted] Mfg: [redacted]
Whlsr: [redacted] (GM, ML, or UNITS)
1/3/2020
(GM, ML, or UNITS)

OUT: Made:
Log Lot#: [redacted]
85 MIDAZOLAM 50 MG/ML INJECTION SOLUTION (3)
Lot#: [redacted] Mfg: [redacted]
Qty used: 4.25 GM
Whlsr: [redacted] (GM, ML, or UNITS)
11/10/2020
126.5

OUT: Made:
Log Lot#: [redacted]
85 MIDAZOLAM 50 MG/ML INJECTION SOLUTION (3)
Lot#: [redacted] Mfg: [redacted]
Qty used: 4.25 GM
Whlsr: [redacted] (GM, ML, or UNITS)
3/17/2022

OUT: Made:
Log Lot#: [redacted]
85 MIDAZOLAM 50 MG/ML INJECTION SOLUTION (3)
Lot#: [redacted] Mfg: [redacted]
Qty used: 4.25 GM
Whlsr: [redacted] (GM, ML, or UNITS)
3/29/2022

OUT: Made:
Log Lot#: [redacted]
85 MIDAZOLAM 50 MG/ML INJECTION SOLUTION (3)
Lot#: [redacted] Mfg: [redacted]
Qty used: 4.25 GM
Whlsr: [redacted] (GM, ML, or UNITS)
4/5/2022

OUT: Made:
Log Lot#: [redacted]
85 MIDAZOLAM 50 MG/ML INJECTION SOLUTION (3)
Lot#: [redacted] Mfg: [redacted]
Qty used: 4.25 GM
Whlsr: [redacted] (GM, ML, or UNITS)

1/31/2021 Removal of expired inventory:
IN: Mfg: [redacted] Inv.#: Lot#: [redacted] 1 (GM, ML, UNITS -1
Package size 1 x 1 Inv. date: 3/7/2018 Exp. date: 1/31/2021 Whlsr: [redacted]
5/8/2018 9:03

IN: Mfg: [redacted] Inv.#: Lot#: [redacted] 50 (GM, ML, UNITS -51

Package size 50 x 1 Inv. date: 5/8/2018 Exp. date: 1/31/2021 Whlsr: [redacted]

(GM, ML, or UNITS)

Remaining 58.5

Inventory & Use for Specific Chemi [redacted]

Printed 5/11/2022

Page 1 Between 1/1/2000 and 5/11/2022

POTASSIUM CHLORIDE USP GRANULAR GRANULES (L)

########

IN: Mfg: [redacted] Inv.#: [redacted]

Package size 1000 x 2

########

IN: Mfg: [redacted] Inv.#:

Package size 1000 x 3

########

IN: Mfg: [redacted] Inv.#:

Package size 454 x 1

7/8/2019

OUT: Made: 20 POTASSIUM CHLORIDE 4MEQ/ML SOLUTION ()

Log Lot#: [redacted] Lot#: [redacted]

7/15/2019

OUT: Made: 140 POTASSIUM CHLORIDE 4MEQ/ML SOLUTION ()

Log Lot#: [redacted] Lot#: [redacted]

7/16/2019

OUT: Made: 520 POTASSIUM CHLORIDE 4MEQ/ML SOLUTION ()

Log Lot#: [redacted] Lot#: [redacted]

OUT: Made: 560 POTASSIUM CHLORIDE 4MEQ/ML SOLUTION ()
Log Lot#: [redacted] Lot#: [redacted]

OUT: Made: 650 POTASSIUM CHLORIDE 4MEQ/ML SOLUTION ()
Log Lot#: [redacted] Lot#: [redacted]
7/23/2019

OUT: Made: 60 POTASSIUM CHLORIDE 4MEQ/ML SOLUTION ()
Log Lot#: [redacted] Lot#: [redacted]

OUT: Made: 325 POTASSIUM CHLORIDE 4MEQ/ML SOLUTION ()
Log Lot#: [redacted] Lot#: [redacted]
7/24/2019

OUT: Made: 325 POTASSIUM CHLORIDE 4MEQ/ML SOLUTION ()
Log Lot#: [redacted] Lot#:

OUT: Made: 380 POTASSIUM CHLORIDE 4MEQ/ML SOLUTION ()
Log Lot#: [redacted] Lot#:
7/29/2019

OUT: Made: 380 POTASSIUM CHLORIDE 4MEQ/ML SOLUTION ()
Log Lot#: [redacted] Lot#:
7/31/2019

OUT: Made: 380 POTASSIUM CHLORIDE 4MEQ/ML SOLUTION ()
Log Lot#: [redacted] Lot#:
7/31/2019

OUT: Made: 70 POTASSIUM CHLORIDE 4MEQ/ML SOLUTION ()
Log Lot#: [redacted] Lot#:
8/5/2019

OUT: Made: 270 POTASSIUM CHLORIDE 15% INJECTION SOLUTION CONCENTRA Qty used:
Log Lot#: [redacted] Lot#: [redacted]
11/6/2019

OUT: Made: 580 POTASSIUM CHLORIDE 15% INJECTION SOLUTION CONCENTRA Qty used:

Log Lot#: [redacted] Lot#: [redacted]

OUT: Made: 580 POTASSIUM CHLORIDE 15% INJECTION SOLUTION CONCENTRA Qty used:

Log Lot#: Lot#: [redacted]

OUT: Made: 760 POTASSIUM CHLORIDE 15% INJECTION SOLUTION CONCENTRA Qty used:

Log Lot#: Lot#: [redacted]

11/27/2019

OUT: Made: 700 POTASSIUM CHLORIDE 15% INJECTION SOLUTION CONCENTRA Qty used:

Log Lot#: Lot#: [redacted]

1/10/2020

OUT: Made: 700 POTASSIUM CHLORIDE 15% INJECTION SOLUTION CONCENTRA Qty used:

Log Lot#: Lot#: [redacted]

7/9/2020

OUT: Made: 700 POTASSIUM CHLORIDE 15% INJECTION SOLUTION CONCENTRA Qty used:

Log Lot#: Lot#: [redacted]

7/14/2020

OUT: Made: 700 POTASSIUM CHLORIDE 15% INJECTION SOLUTION CONCENTRA Qty used:

Log Lot#: Lot#: [redacted]

11/10/2020

OUT: Made: 700 POTASSIUM CHLORIDE 15% INJECTION SOLUTION CONCENTRA Qty used:

Log Lot#: Lot#: [redacted]

Removal of inventory for expiration:

OUT: Mfg: [redacted] Inv.#:

Package size 1000 x [redacted] 2

#########

OUT Mfg: [redacted] Inv.#:

Package size 1000 x 3

10/11/2021

IN: Mfg: [redacted] Inv.#:

Package size 500 x 2

3/17/2022

OUT: Made: 700 POTASSIUM CHLORIDE 15% INJECTION SOLUTION CONCENTRA Qty used:

Log Lot#: [redacted] Lot#: [redacted]

Balance Chk'd

Lot#: [redacted] 2000 (GM, ML, UNITS 2000

Inv. date: 2/15/2019 Exp. date: 3/1/2021 Whlsr: [redacted] (GM, ML, or UNITS)

Lot#: [redacted] 3000 (GM, ML, UNITS 5000

Inv. date: 6/27/2019 Exp. date: 3/30/2021 Whlsr: [redacted]

(GM, ML, or UNITS)

Lot#: [redacted] 454 (GM, ML, UNITS 5454

Inv. date: 7/29/2019 Exp. date: 11/13/2021 Whlsr: [redacted]

(GM, ML, or UNITS)

Qty used: 3.12 GM 5450.88

Mfg: [redacted] Whlsr: [redacted]

(GM, ML, or UNITS)

5429.04

Qty used: 21.84 GM

Mfg: [redacted] Whlsr: [redacted] (GM, ML, or UNITS)

Qty used: 81.12 GM 5347.92

Mfg: [redacted] Whlsr: [redacted]

(GM, ML, or UNITS) 7/17/2019

Qty used 87.36 GM 5260.56

Mfg: [redacted] Whlsr: [redacted] (GM, ML, or UNITS) 7/23/2019

Qty used 195 GM 5065.56

Mfg: [redacted] Whlsr: [redacted] (GM, ML, or UNITS)

Qty used 17.88 GM 5047.68

Mfg: [redacted] Whlsr: [redacted] (GM, ML, or UNITS) 7/24/2019

Qty used 97.5 GM 4950.18

Mfg: [redacted] Whlsr: [redacted] (GM, ML, or UNITS)

Qty used 97.5 GM 4852.68

Mfg: [redacted] Whlsr: [redacted] (GM, ML, or UNITS) 7/26/2019

Qty used 114 GM 4738.68

Mfg: [redacted] Whlsr: [redacted] (GM, ML, or UNITS)

Qty used 114 GM 4624.68

Mfg: [redacted] Whlsr: [redacted] (GM, ML, or UNITS)

Qty used 113.24 GM 4511.44

Mfg: [redacted] Whlsr: [redacted] (GM, ML, or UNITS)

Qty used 20.86 GM 4490.58

Mfg: [redacted] Whlsr: [redacted] (GM, ML, or UNITS)

40.5 GM 4450.08

Mfg: [redacted] Whlsr: [redacted] (GM, ML, or UNITS)

87 GM 4363.08

Mfg [redacted] Whlsr: [redacted]

(GM, ML, or UNITS) 11/11/2019

87 GM 4276.08

Mfg [redacted] Whlsr: [redacted]

(GM, ML, or UNITS) 11/18/2019

114 GM

Mfg [redacted] Whlsr: [redacted]

(GM, ML, or UNITS)

105 GM 4057.08

Mfg [redacted] Whlsr: [redacted] (GM, ML, or UNITS)

105 GM 3952.08

Mfg [redacted] Whlsr: [redacted] (GM, ML, or UNITS)

105 GM 3847.08

Mfg [redacted] Whlsr: [redacted]

(GM, ML, or UNITS)

3742.08

105 GM

Mfg [redacted] Whlsr: [redacted]

(GM, ML, or UNITS)

105 GM 3637.08

Mfg [redacted] Whlsr: [redacted]

Lot#: [redacted] 2000 (GM, ML, UNITS -2000

Inv. date: 2/15/2019 Exp. date: 3/1/2021 Whlsr: [redacted] (GM, ML, or UNITS)

Lot#: [redacted] 3000 (GM, ML, UNITS -3000

Inv. date 6/27/2019 Exp. date: 3/30/2021 Whlsr: [redacted]

Lot#: [redacted] 1000 (GM, ML, UNITS)

Inv. date 10/11/2021 Exp. date. 7/31/2023 Whlsr: [redacted] (GM, ML, or UNITS)

105 GM

Mfg: [redacted]

895

Whlsr: [redacted]

(GM, ML, or UNITS)

(GM, ML, or UNITS)

Remaining Inv 895

Introduction

Which sterile compounds does your pharmacy prepare? How can you expand your sterile compounding service? How can you improve your sterile compounding service?

United States Pharmacopeial (USP) Chapter <797>, Pharmaceutical Compounding: Sterile Preparations sets the standards that apply to all practice settings where sterile preparations are made, stored and transported.[1,2,3] It is the responsibility of pharmacy staff working with sterile compounds to be familiar with these standards. Many state boards enforce the standards set in Chapter <797> and they are used as accreditation criteria by some organizations.

USP <797> was last revised in 2008. A new chapter <797>, along with updates to chapter <795>, was published in the USP-NF on June 1, 2019. USP received appeals on certain provisions in these chapters and granted those appeals. Therefore, the chapters have been remanded back to the Compounding Expert Committee. Until a new chapter is finalized, the existing chapter <797>, which became official in 2008, is currently the official and enforceable standard.[4]

There are a lot of potential risks with sterile compounds. Compounders must pay close attention to the details of their aseptic processes to be sure they are meeting all standards to produce a quality, sterile preparation.[1,5]

Sterile compounds meet specific needs for patients. They can provide specialized treatments to patients, allow outpatients to receive medications often reserved for inpatients, provide preparations that may be unavailable (e.g., backordered), or medications that have been discontinued by manufacturers for non-safety reasons (e.g., for financial reasons, a manufacturer stops making a rarely used product).[6]

Sterile preparations must be free from microbial contamination as well as any other contaminants, like crystals, particles, or other foreign matter. All types of injections and ophthalmic preparations must be sterile.

Examples of preparations that can be made with sterile compounding:[6,7]

- Cardioplegic solutions
- Chelation therapy
- Chemotherapy
- Diagnostic preparations (e.g., methylene blue)
- Dialysis solutions
- Hormones
- Immunotherapy: low dose allergens, custom allergen extracts
- Injectable preparations for intravenous, subcutaneous, intramuscular, etc use
- Intracavernosal injections (e.g., trimix and bimix injections with phentolamine and papaverine)
- Intrathecal pump reservoirs
- Mesotherapy
- Ophthalmic drops and injections
- Prefilled syringes (e.g., narcotic patient-controlled analgesia (PCA) syringes)
- Veterinary medicines

Vitamins, minerals, and amino acids (e.g., riboflavin, vitamin B12)

Policies and Procedures for Sterile Compounding

It is important to have established, well-defined policies and procedures in your pharmacy to guide sterile compounding.[8] These policies and procedures will help to maintain the quality, sterility, and consistency of preparations, as well as help prevent errors in the preparations produced.[7,8]

Compounding documentation is essential. Master formulation records detail procedures to be followed including name, strength and dosage form, ingredients, amounts of ingredients, type and size of container-closure system(s) to use when compounding preparations, and much more. Compounding records are also required documentation and there should be one for each sterile preparation that is made. Compounding records should include details specific to making that particular sterile preparation, such as the date the preparation was made, total quantity made, beyond-use date, lot numbers of ingredients used, etc.[8]

Policies and procedures must comply with state regulations and should comply with USP Chapter <797> standards, although not all states have fully adopted these standards.[8]

Does your pharmacy have policies and procedures in place for sterile compounded preparations? What information is included in your policies and procedures? What is your process for adding and updating existing policies?

Schedule regular reviews of these procedures. Revise them as needed to correct any weaknesses you discover in your daily workflow and audits or to address any problems that may have occurred in your pharmacy.

As much as possible, compounding processes should be automated, to include barcode verification, IV robotics, IV workflow software and any other automated compounding devices that may be available to meet your pharmacy's needs.[8]All routine maintenance, calibration, and certification should be current and documented for all equipment used. Be sure to use all current service releases for software after proper installation and testing.[8]

Pharmaceutical Calculations

What calculations do you use in your daily practice? What resource do you use to find information on pharmaceutical calculations? Which calculations do you use for sterile preparations? What is your pharmacy's policy for checking calculations?

Correct calculations are a vital part of sterile compounding. They can include conversion from one measurement to another, accurate/correct decimal points, calculations of dilutions, or alligation

calculations. There are many electronic methods and programs for pharmaceutical calculations that will help you, but you need to have an understanding of the calculations to ensure that the final answers make sense to you and are ultimately correct.[9]

Over 30% of claims to liability insurance from compounded preparations were attributed to calculation errors.[10]

From 1993 to 1998, 13% of the fatal medication errors from FDA's Adverse Event Reporting System were a result of dose calculation errors.[10]

There are sometimes different ways to approach calculations for a pharmaceutical formulation. Use the most logical method with the least number of steps possible. Establish your master formulation record so that each preparation you make includes the most appropriate calculation.

Calculations should be independently double-checked by another trained sterile compounder if possible. Be sure this verification happens prior to beginning any preparation to prevent errors and waste. From start to finish, staff should be thoughtful of the preparation, including the calculations, always making sure the numbers and process are logical. One way to do this is to 'eye-ball' the calculation or to estimate, by rounding, in order to figure out an approximate answer to see if you're on track.

Systems of Measure

You are likely familiar with mg and mL, but what do you remember about drams, scruples, or grains as units of measurement? Do you see these measurements used in your practice? Where do you look to find conversion information on these older measurements?

There are four different systems of measure that are used in various pharmaceutical calculations:[11]

- International System of Units (SI) or metric system
- Avoirdupois system
- Apothecary system
- Household

The International System of Units (SI), also called the metric system, is a decimal system that uses gram (weight), meter (length), and liter (volume). This system is the official standard and is preferred for all pharmacy calculations.

The avoirdupois system is for weight only (i.e., no measures of volumes within this system). It is commonly used in the U.S. (e.g., in grocery stores). It is used in measuring bulk medications (pounds, ounces, grains). Of note, the dram and scruple do not exist in this system.

The apothecary system is a traditional system of measurement that uses drams and minims for liquids, and grains for solids. These measures are occasionally found in prescriptions. This system was developed to allow fine weighing of medications. It includes pounds, ounces, drams, scruples, and grains as measures of weight. And gallons, pints, fluid ounces, fluid drams, and minims as measures of volume.

The household system includes teaspoon, tablespoon, cup, pint, and quart.

Grains are equal in the apothecary and avoirdupois systems.

However, the weight of the ounce and pound in each of these systems is different.

Avoirdupois: 7000 grains = 16 ounces = 1 pound

Apothecary: 5760 grains = 12 ounces = 1 pound

Significant Numbers

When performing pharmaceutical calculations, be sure to keep all digits until your calculation is complete. Do not round any numbers until the end of your calculation. Numbers are accurate to the second last digit, including any zeros after your decimal.[9]

29.8 = 29.8 +/- 0.05 mL (accurate to the nearest 0.1 mL)

29.80 = 29.81 +/- 0.005 mL (accurate to the nearest 0.01 mL)

29.800 = 29.801 +/- 0.0005 mL (accurate to the nearest 0.001 mL) – most accurate

The number of decimal places in your final answer should always be the same as the component with the fewest decimals, so 1.11 + 3.2 = 4.3 and 3.448 x 12 = 41.

Dose Calculations

Dose calculations are required for some medications such as chemotherapy, and are common in pediatrics. You'll see orders placed for these patients with units such as mg/kg or mg/m^2. Or you'll receive an order in mg from a provider and, using the patient's weight, you'll need to calculate the mg/kg dose so you can check for the appropriateness of the dose in the final compounded preparation.

Body Surface Area (BSA) =

Square Root of [height (inches) x weight (pounds)/3131]

OR

Square Root of [height (cm) x weight (kg)/3600]

Average adult weight is considered to be 70 kg

Average adult Body Surface Area (BSA) is considered to be 1.73 m^2

Expression of the Active Ingredient

The amount of active ingredient in a preparation can be expressed in several different ways:[11]

- amount per individual dosage form (e.g., mg in a capsule)
- concentration per dosing volume (e.g., mg/mL)
- percent
- ratio strength
- parts per million

Percent

Percentage is the number of active parts per 100 parts and can be expressed in several ways:[11]

- Volume percent (v/v) = volume of solute/volume of solution x100%; i.e. the amount of mL in 100 mL of final preparation.
- Weight percent (w/w) = weight of solute/weight of solution x100%; i.e. the amount of g in 100 g of final preparation.
- Weight in volume percent (w/v) = weight of solute/volume of solution x100%; i.e. the amount of g in 100 mL of final preparation.

Percentages can be converted to decimal fractions by dividing the number by 100, so 23% = 23/100 = 0.23.[11]

Solutions commonly used in compounding sterile preparations indicate the percentage in their name.

D5W = Dextrose 5% in water

D10W = Dextrose 10% in water

NS = 0.9% sodium chloride = 0.9% NaCl = normal saline
½ NS = 0.45% sodium chloride = 0.45% NaCl = ½ normal saline

Ratios

Ratio strength is the expression of concentration in terms of parts of active ingredient related to parts of the whole.[11] So, 1:2 is interpreted as one part drug in 2 parts total mixture.

D5W is expressed as dextrose 5%, or a ratio of 1:20, because 5 out of 100 simplifies to 1:20.

A **proportion** is an expression of two equal ratios in order to solve for one unknown variable. If you know 3 of the 4 terms, you are able to solve for the fourth. These calculations are often used to determine the volume of a dose from a premade solution.

Your calculation is set up so the units cancel, leaving you with only the units of your answer. This can be a check to ensure you have your equation set up correctly.

If you have 40 mg/2 mL, how much volume (mL) do you need for a dose of 300 mg?

$\frac{40\text{ mg}}{2\text{ mL}} = \frac{300\text{ mg}}{X}$ (40 mg)(X) = (2 mL)(300 mg) $x = \frac{(2\text{ mL})(300\text{ mg})}{40\text{ mg}}$ x = 15 mL

Can also be expressed as 300 mg x $\frac{2\text{ mL}}{40\text{ mg}}$ = 15 mL

Parts per million

This is a ratio strength used for very dilute concentrations. The denominator is set to one million, so parts per million (ppm) represents the number of parts of solute (active ingredient) in 10^6(1,000,000)parts of solution.[11]

Dilution and Concentration

Sometimes a manufactured product must be concentrated or diluted for administration. For example, you may have a 1 mL vial of gentamicin with a concentration of 10 mg/mL that needs to be diluted to 1 mg/mL

so a 4 mg dose can be accurately measured and administered to an infant.[11]

Your 1 mL vial contains 10 mg (i.e., a concentration of 10 mg/mL). Assuming that you'll use this entire vial to make a batch, you'll need to calculate how much final volume you'll need if your final concentration is 1 mg/mL:

1 mg= 10 mg x = 10 mL (total volume of the preparation)

1 mL x mL

Then, take away the volume of the drug (10 mg = 1 mL) from your final volume (10 mL):

10 mL – 1 mL (drug) = 9 mL diluent needed

Your mixture will contain 1 mL of drug and 9 mL of diluent for a total of 10 mL with a final concentration of 1 mg/mL.

To calculate the volume of your ordered dose:

1 mg= 4 mg x = 4 mL of solution will contain 4 mg of drug

1 mL x mL

Reconstitution of drugs when further dilution is required

You may have a special dilution you prepare for certain populations, such as neonates, that is not in the instructions on the vial or the product insert. Always follow the product label or product insert for the dilution amounts and final concentration FIRST, then dilute further if needed.

For example, you have ceftriaxone 1,000 mg vial which requires reconstitution. The product insert states to add 9.6 mL of sterile water for injection which yields a concentration of 100 mg/mL for a total of 10 mL inside the vial.

However, for neonatal patients a typical concentration of 20 mg/mL is administered. Therefore the 100 mg/mL concentration in the 1,000 mg vial must be further diluted to yield a concentration of 20 mg/mL to draw up the neonate patient's dose.

To prepare 50 mL of 20 mg/mL ceftriaxone you will calculate as follows:

20 mg/mL = x/50 mL = 1,000 mg

Therefore adding 10 mL of 100 mg/mL = 1,000 mg to an exact volume of 40 mL of NaCl will

equal 20 mg/mL

1,000 mg/50 mL (10 mL of ceftriaxone + 40 mL of NaCl) = 20 mg/mL

Alligation

What is alligation? Have you had to mix two different solutions to create a third concentration that has been ordered? What is your policy for double-checking pharmaceutical calculations?

It is sometimes necessary to mix two different percentage strength solutions to create the desired/prescribed concentration. Alligation is a quick method to determine proportions of different strengths in order to yield a desired strength or concentration. You determine the proportions you need of each component, then you are able to calculate exactly how much of each you need for your final preparation.

Example:

You need a final dextrose concentration of 7.5%. In stock, you have dextrose 5% and dextrose 50%. How much of each solution do you need to create 250 mL of 7.5% dextrose solution?

Higher strength – desired strength = parts of the lower strength needed.

50 – 7.5 = 42.5 parts of the lower strength needed

Desired strength – lower strength = parts of the higher strength needed.

7.5 – 5 = 2.5 parts of the higher strength needed

42.5 parts + 2.5 parts = 45 parts

Total volume is 250 mL so 1 part = 250/45 = 5.556 mL

D5W: 42.5 parts x 5.556 mL = 236.13 mL plus

D50W: 2.5 parts x 5.556 mL = 13.89 mL

for a total of 250 mL of 7.5% dextrose in water.

You can check the grams of dextrose in each concentration of dextrose mixed to ensure the final solution is correct.

Final volume of 250 mL D7.5W:

$\frac{7.5 \text{ g of dextrose}}{100 \text{ mL water}} = \frac{x}{250 \text{ mL}}$ x = 18.75 g of dextrose needed in your final preparation

13.89 mL of D50W = 13.89 x 50% = 6.95 g of dextrose

236.13 mL of D5W = 236.13 x 5% = 11.8 g of dextrose

6.95 + 11.8 = 18.75 g of dextrose provided by your two components

Molarity, Molality, Normal Concentrations

Molarity, the molar concentration, M, of a solution is the number of moles of the solute contained in one L of solution. A mmol is one-thousandth of a mole. Sodium chloride has a molecular weight of 58.5 g, so 58.5 g of NaCl makes 1 mole of sodium chloride and 1 mmol is 58.5 mg of NaCl.

Molality, the molal concentration, m, is the number of moles of the solute contained in one kg of solvent.

Normality, the normal concentration, N, of a solution expresses the number of equivalents (Eq) of solute contained in 1 L of solution (or number of milliequivalents [mEq] in 1 mL).

Milliequivalents

When electrolytes, such as potassium, magnesium, or sodium are administered to patients, they are usually ordered in terms of milliequivalents. An electrolyte is a compound that dissociates into ions in solution.[13]The valance of an ion determines how many other ions it must combine with to form a stable

compound. An equivalent weight is the measure of the chemical activity of the electrolyte and is determined by the atomic weight and the valance. A milliequivalent (mEq) is one-thousandth of the equivalent weight and is usually expressed in mg.

$$mEq = mg \times \frac{valance}{atomic\ weight}$$

Question:

Sodium has an atomic weight of 23 and a valance of 1. How many mEq are in 115 mg of sodium?

The correct answer is 5 mEq.

Millimoles and Milliosmoles

mole = the molecular weight of a substance in grams

mmol = the molecular weight of a substance in mg

Potassium has an atomic weight of 39.1 grams. Therefore 1 mmol = 39.1 mg.

Osmotic concentration is a measure of the total number of particles in solution and is expressed in mOsmol (milliosmoles) per L of solution. The number of particles is the total of all anions and cations.

$$mOsmol/L = \frac{weight\ of\ substance\ (g/L) \times number\ of\ species \times 1000}{molecular\ weight\ (g)}$$

An isotonic (also called iso-osmotic) solution has the same osmotic pressure as the body fluid it is to be mixed in. This allows the solution to be better tolerated by the patient. Hyper- or hypo-tonic solutions can cause discomfort and pain to the patient.

Isotonic solutions are needed for ophthalmic, subcutaneous, parenteral, nasal, and sometimes rectally-administered preparations. Sodium chloride 0.9% solution is isotonic. You can find lists of sodium chloride equivalents in textbooks such as Remington's Pharmaceutical Sciences to help you calculate the final amounts for ingredients you'll need to make your final solutions isotonic.

Flow Rates in IV Sets

What questions do you get regarding the calculation of flow rates for IV infusions? How do you estimate a flow rate prior to calculating to check your final answer? What is your pharmacy's policy on how pharmaceutical calculations should be double checked?

To calculate the amount and/or volume of drug a patient will receive over a certain period of time, you must calculate the flow rate. This ensures the patient receives the amount of medication in the time frame the provider has ordered.

Examples:

1. 25,000 units of heparin in 250 mL D5W ordered to infuse at 1000 units per hour. What is the infusion rate in mL per hour?

Concentration of IV = total amount of drug = 25,000 units heparin = 100 units per mL heparin

total volume 250 mL of D5W

IV rate = dose desired = 1,000 units per hour = 10 mL per hour

concentration of IV solution 100 units per mL

2. Physician's order is for 5 mg/minute, your IV solution is 2 mg/mL.

What rate does the nurse infuse the solution per the provider's order?

5 mg x 1 mL = 2.5 mL per minute

1 minute 2 mg

Note that the equation is set up so that the mg units cancel themselves out and you are left with the appropriate mL/minute units in your answer.

This calculation helps you determine that 2.5 mL of your solution contains 5 mg, the amount that needs to be administered per minute.

Aliquots

If an ingredient amount is smaller than you can accurately measure with the equipment you have, you will need to use aliquots.

The standard pharmacy balance has a sensitivity requirement of 6 mg.

The maximum acceptable error in measurement is 5%.

Therefore, the least weighable amount on the standard balance is 120 mg.

Note that electronic balances can sometimes accurately weigh smaller amounts. Check the user manuals to find out the least weighable amount on these balances in your pharmacy.

1. Weigh your active ingredient. This needs to be a minimum of the least weighable amount for your balance.
2. Dilute that amount with a compatible, inert material.
3. Mix well.
4. Weigh out the amount of the mixture that contains the total amount of active ingredient you need. Again, this weight must be greater than the least weighable amount for your balance.

You can also measure small quantities by diluting your active ingredient in a solution.

1. Weigh your active ingredient. This needs to be a minimum of the least weighable amount for your balance.
2. Dilute that amount with a liquid that will dissolve your active ingredient and be compatible with your final mixture.
3. Mix well.
4. Measure out the amount of the solution that contains the total amount of active ingredient you need. This must be greater than the least measurable amount for your device (syringe, graduated cylinder, etc).

Specific Gravity

One mL of water at 25 degrees Celsius weighs approximately 1 gram.

A compound's specific gravity is based on the ratio of its weight at 25 degrees C to that of the weight of an equal volume of water at the same temperature.[9]

Specific Gravity(SG) = weight of substance/weight of an equal volume of water

There are no units on SG as they cancel each other out.[11]

What is the SG of 100 mL of D50W if the weight is 117g?

$\frac{117g}{100\ g\ \text{(weight of 100 mL of water)}}$ = 1.17 is the SG of the dextrose

If the SG of a solution is 0.75, what is the weight of 50 mL?

g = g of an equal weight of water x SG

x = 50 g x 0.75

x = 37.5 g

Final Verification

There are many different methods for checking that compounded sterile preparations are prepared correctly. Different methods will be appropriate for different preparations and your pharmacy's master formulation record should dictate how each preparation needs to be verified.

A visual check by a qualified person must be performed to verify accuracy of diluents and drugs, including volumes and concentrations.[8]Some preparations will require pre-preparation visual confirmation of the amount of each ingredient PRIOR to the addition to the final container. Most pharmacies do this for chemotherapy, parenteral nutrition, pediatric and neonatal preparations, preparations using multidose vials of high-alert meds (such as insulin, concentrated electrolytes, heparin), and for preparations administered via high-risk routes like intrathecal (IT), epidural, or intraocular.

Verification via "proxy methods" like Syringe Pull-Back Method should be avoided and never used in the preparation of chemotherapy, complex medications, pediatric, neonatal, or high-alert medications and should not be used without the actual, original source containers (medication and diluent). Never use the practice of handwriting the amount of additive as the sole verification method.

The pharmacist is responsible to ensure the accuracy and completeness of the final compounded sterile preparation. This final check should be comprehensive and must verify:[7]

- The right formulation was chosen for the prescription.
- All of the ingredients, adjuvants, and equipment were selected appropriately.

- Calculations are correct.
- Measurements were performed accurately with the right equipment.
- The final amount is consistent with what was expected.
- The physical characteristics (color, clarity, etc) are as expected.
- Physical tests have been performed when indicated and the results are appropriate.
- Documentation is appropriate and complete, including all legal requirements, both on the label and in the compounding record. You should record lot numbers, volumes used, expiry dates, etc.
- Packaging is suitable for patient use and the container selected will protect the preparation until at least the "discard after" or "beyond-use" date.
- All processes were followed.
- The preparation is labeled with explicit storage and administration instructions.
- Check the preparation against the prescription order.

Always refer to the federal and state regulations to ensure your pharmacy labels comply. If you are practicing in Canada, the National Association of Pharmacy Regulatory Authorities (NAPRA) has developed recommendations for labeling and packaging compounded preparations for patient-specific prescriptions.[12]

Pharmacies can do specific testing on their compounded sterile preparations for sterility, stability, pH, etc to ensure preparations are safe and consistent.[7,13] These can either be done within your pharmacy or by an external testing lab. The pharmacist's final check needs to include an analysis of the results of any testing.

Any errors or near-miss, potential errors that are identified should be documented and reported via your pharmacy's process for corrective and preventive action. Serious incidents must be reported per federal and state requirements. It is recommended that they are also reported to ISMP Med Error Reporting System, where they are then forwarded to FDA MedWatch for learning purposes. Internal and external information on medication errors should be reviewed and then used to improve your practices and procedures.

Patient Education

How many examples can you think of where your patients were incorrectly using their medications? How many errors do you think your patients make that you never hear about?

Sterile compounded prescriptions offer an excellent opportunity for patient education. Use this opportunity to help share information on how to correctly store, prepare, and administer the medication.[13]

The patient is the last person in the medication use process and the pharmacist is often the last healthcare professional to interact with the patient before medication is administered.[14] This unique opportunity and interaction can have a significant impact on how a patient takes their medications and help to prevent medication errors before they happen.[14]

Consider these three factors and how they influence the outcomes of patient counseling and error-prevention efforts:[14]

1. direct patient education
2. patient and healthcare literacy
3. patient adherence

Direct Patient Education

What resources are used in your pharmacy to provide patients with education regarding sterile preparations? How often do you give patients written information?

Compounded sterile preparations are often more complex in their patient teaching than other prescriptions.

Written information is common, given with up to 87% of prescriptions. But, only 35% of pharmacists make reference to this material if they speak to the patient and only 8% actually review it with the patient.[14] And then, up to 75% of patients throw out the medication leaflets that are included with the prescription without reading them at all. Don't assume your patients read the information you give them. Pharmacists should still talk to patients about any written information given to them. This results in direct instruction and can also reinforce the written information so they are aware of its content and can refer back to it later.[14]

Patient Literacy

What questions can be asked to ensure patients are able to understand their medication therapies and how to use them? What clues have you seen with your patients that might indicate they have a low level of literacy? What reading level is your pharmacy's written patient information?

Only half of patients take their medications as directed.[14] There are lots of reasons and contributing factors that you can watch for. Patients can be too embarrassed or ashamed that they don't understand, won't ask questions, and often pretend to understand.[14]Even bright, educated patients can have a hard time understanding their health problems, the proper management of the disease and their role in maintaining their health. This understanding is sometimes referred to as healthcare literacy.

It is important to realize that you cannot judge a patient's understanding by how they appear, how they are dressed, their ethnic background, how they speak, etc. A patient's level of healthcare literacy can be much lower than many healthcare professionals realize due to things like an inability to read or a lack of understanding and ability to act on healthcare information.

Can you think of examples in your pharmacy of medications being used incorrectly? What are some ways you can help prevent these errors for your patients?

Examples of medications used incorrectly:

- An elderly woman who takes her ophthalmic drops orally rather than putting them into her eyes.
- Parents confuse different syringes for their chronically ill child.
- A patient doesn't take his medications often enough because he can't afford the monthly costs.

Almost 40% of patients with chronic illness are functionally illiterate.[14]

Almost 25% of Americans read below a fifth-grade level.[14]

[redacted]

It can be impossible to know if a patient is able to read and at what level. Low literacy is not obvious. Poor reading skills are reported in some of the most poised and articulate patients you may see.[14] You'll need to be sure to screen the medical literature you distribute for its reading level. It's not uncommon for some information to be at a tenth-grade reading level. Your material should be at a fifth-grade reading level.

Patient Adherence

Up to 76% of patients take medications differently than they are prescribed.[15] Nonadherence is reported to account for up to 33% of hospital admissions.[16] Nonadherence can include things like not having a prescription filled or refilled, missing doses, taking the wrong dose, stopping medications, administering medications incorrectly or at the wrong time, taking someone else's medication, or being financially unable to buy medications.

Risk factors for nonadherence:

- cost
- taking more than one medication (polypharmacy)
- chronic conditions with complex regimens that result in bothersome adverse effects
- taking a drug more than once daily
- having a condition that doesn't have overt symptoms or physical impairment such as hypertension or diabetes
- decreased mental acuity due to advanced age, increased confusion, lack of family or caregiver support, decreased coordination and dexterity, or impaired vision

Consider the above factors when you develop and provide patient education for compounded sterile preparations.[14]Pharmacists are in a unique position and need to be fully focused when counseling patients, offering multiple options for patient learning, and watching very closely for any subtle signs that there may be a lack of understanding.

What information do you give your patients about the correct storage of sterile preparations? What details do you give them about storing their refrigerated and room-temperature medications?

Patients must be educated on how to maintain the stability of compounded sterile preparations after they leave your pharmacy. Use auxiliary labeling whenever possible to help alert patients about how to store their medications appropriately. Pharmacists should also verbally give patients storage information and tell patients if there are ways they can tell that the preparation might be unstable or compromised, such as a change in color or visible particles.

Below are some storage examples that may apply to your preparations:

- Refrigerate – not on the door or too far back for the most consistent temperature.
- Room temperature – not left in the car or any area that is in direct sunlight or increased level of heat or humidity; a cool, dark place like a kitchen cupboard is often best.
- If, and when, the preparation needs to be removed from the fridge before administration.
- How long the preparation can be left out of the fridge – i.e., does it need to be transported cold with an ice pack if, for example, they will be away from home at administration time in one, four, or eight hours?

- Protect from light – give them specifics about what this means. It's a common term for pharmacists and technicians, but patients need more information, such as "any dark bag/protection should be left on while a medication is infusing." Define light; not only direct sunlight but ordinary daylight can affect some drugs.
- Original containers – instruct patients to never transfer their medication to another container. It can be helpful to define "sterile" for them and help them understand how their medications can become contaminated and lose their sterility.
- Outer secondary packaging – instruct patients to keep compounded medication in the outer container during storage to keep the outside of original container clean.

Many sterile preparations have routes of administration that are unfamiliar to patients, such as subcutaneous or intraocular. Pharmacists should offer instructions and demonstrations, if possible, to patients. It's helpful if the first administration of the drug can be given by a nurse or trained healthcare professional. This can give the patient an opportunity to learn how to do it themselves and to ask questions before they need to do it alone.

Be sure the patient knows who will administer the medication and where. Some of these preparations require special administration techniques, equipment, and monitoring and can only be given in a physician's office, a clinic, or another outpatient facility.

Nurses or caregivers who will be administering the compounded sterile preparation also need to be educated appropriately, including giving written information, on the administration techniques, proper storage, disposal, etc. Ensure they know how to contact the pharmacy if any questions arise regarding these preparations.

Conclusion

Compounded sterile preparations are very important to patients and any errors in their preparation and administration can have serious effects. Be sure your pharmacy has effective, current policies and procedures and master formulation records in place to guide all aspects of their preparation and dispensing. A well-trained staff, aware of all your policies and procedures will consistently produce safe, high quality compounded sterile preparations.

Additional Resources

- United States Pharmacopeia (USP) – Compounding Standards
- U.S. Food and Drug Administration – Human Drug Compounding

References

Click here to view References for this course.

QUESTION 1

What information should be included in your pharmacy's master formulation records for sterile compounds?

Select one:

a. Amounts of ingredients
b. Lot numbers of ingredients
c. Pharmacy's phone number
d. Total quantity made

QUESTION 2

Why are policies and procedures for sterile compounding important?

Select one:

a. To establish standards for all employees around sterile compounding.
b. To guarantee all sterile compounded preparations are sterile.
c. To provide records of sterile compounded preparations.
d. To prevent all errors in sterile compounded preparations.

QUESTION 3

Why is it important to have an understanding of pharmaceutical calculations?

Select one:

a. To prevent all errors
b. To prevent all fatal errors
c. Errors in pharmaceutical calculations are common
d. An automated calculator may not be available

QUESTION 4

You receive an order for ampicillin 320 mg intravenously every six hours for a patient who weighs 12.7 kg. What is the ordered dose in mg/kg/day?

Select one:

a. 50 mg/kg/day
b. 100 mg/kg/day

c. 150 mg/kg/day

d. 200 mg/kg/day

QUESTION 5

An order is sent to the pharmacy for 10 mg of gentamicin for a 4 kg infant. The stock solution of gentamicin is 40 mg/mL. What volume of this stock solution will provide the ordered dose?

Select one:

a. 0.1 mL

b. **0.25 mL**

c. 1.5 mL

d. 3 mL

QUESTION 6

You have an order for magnesium sulfate intravenous 4 g in 100 mL D5W over 30 minutes. How much magnesium sulfate 50% do you need to add to 100 mL D5W for this order?

Select one:

a. 1 mL

b. 2 mL

c. 6 mL

d. 8 mL

QUESTION 7

You have an order for magnesium sulfate intravenous 4 g in 100 mL D5W over 30 minutes. What is the hourly rate required for this order?

Select one:

a. 100 mL/hour

b. 150 mL/hour

c. 200 mL/hour

d. 250 mL/hour

QUESTION 8

How can written information be best used to enhance patient counseling?

Select one:

a. Written information is ineffective and should not be given to patients.

b. Several written handouts should be provided to ensure patients understand their medication.

c. All written information provided to patients should be at or below a ninth-grade reading level.

d. Any written information given to the patient should be reinforced with pharmacist counseling.

QUESTION 9

About how many Americans read below a fifth-grade level?

Select one:

a. 25%

b. 45%

c. 60%

d. 80%

QUESTION 10

Where is the best place to store a preparation labeled "Store at room temperature"?

Select one:

a. In the sunlight

b. In a cool, dark place

c. In the medicine cabinet in the bathroom

d. In the glove compartment of a car

[redacted]

References for Sterile Compounding: Managing the Process, 07.01.2021

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[redacted]

[redacted]

From: [redacted]
Sent: Thursday, April 21, 2022 4:13 PM
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Subject: Order setting date
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[redacted]

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From: [redacted]
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