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STERILE COMPOUNDING

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CHAPTER 17

STERILE COMPOUNDING

Section 1. Authority.

These rules are promulgated as authorized by the Act, and pursuant to the Wyoming Administrative Procedure Act, W.S. § 16-3-101, *et seq.* The effective date of this Chapter is January 1, 2012.

Section 2. Definitions.

(a) “Ante-Area” means an ISO Class 8 or better area where personnel hand hygiene and garbing procedures, staging of components, order entry, compounded sterile preparation labeling, and other high-particulate generating activities are performed. It is also a transition area where pressure relationships are constantly maintained so that air flows from clean to dirty areas.

(b) “Aseptic Processing” means processing of pharmaceutical products that involves the separate sterilization of the product and of the package, and the transfer of the product into the container and its closure under at least ISO Class 5 conditions.

(c) “Beyond-Use Date” (BUD) means a date after which a compounded sterile preparation shall not be used, stored, or transported. BUD is determined from the date or time the preparation is compounded.

(d) “Biological Safety Cabinet” means a ventilated cabinet for compounded sterile preparations, personnel, product, and environmental protection having:

- (i) an open front with inward airflow for personnel protection;
- (ii) downward High-Efficiency Particulate Air (HEPA)-filtered laminar airflow for product protection; and
- (iii) HEPA-filtered exhausted air for environmental protection.

(e) “Buffer Area” means a Clean Room or area in which the Primary Engineering Control is physically located. In this area, activities include the preparation and staging of components and supplies used to compound sterile products.

(f) “Clean Room” means a room with a minimum of an ISO Class 7 environment (ISO Class 8 environment for compounding radiopharmaceuticals):

- (i) in which the concentration of airborne particles is controlled;
- (ii) that is constructed and used in a manner to minimize the introduction, generation, and retention of particles inside the room;
- (iii) in which other relevant variables (e.g., temperature, humidity, and pressure) are controlled as necessary; and

(iv) in which microorganisms in the environment are monitored so that a microbial level for air, surface, and personnel gear is not exceeded for a specified cleanliness class.

(g) “Closed System Transfer Device (CSTD)” is a drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of Hazardous Drug or vapor concentrations outside the system.

(h) “Compounding Aseptic Containment Isolator” (CACI) means a closed system designed to provide personnel protection from exposure to undesirable levels of airborne drug throughout the compounding and transfer processes, and designed to provide an aseptic environment for compounding sterile preparations. Air is first passed through a microbial retentive filter (HEPA minimum) system. If volatile Hazardous Drugs are prepared, the exhaust air from the isolator should be appropriately removed by properly designed building ventilation.

(i) “Compounding Aseptic Isolator” (CAI) means a closed system specifically designed to maintain an aseptic compounding environment within the isolator. Air is first passed through a microbially retentive filter (HEPA minimum). Transfers are designed to minimize the entry of contamination and are accomplished through air locks, glove rings, or ports.

(j) “Critical Area” means any area in the Buffer Area where products or containers are exposed to the environment. It should be an ISO Class 5 environment.

(k) “CSP” means compounded sterile product.

(l) “Critical Site” means a location that includes any component or fluid pathway surfaces (such as injection ports) or openings (such as opened ampules or needle hubs) exposed and at risk of direct contact with air, moisture, or touch contamination.

(m) “Cytotoxic Drug” means a pharmaceutical product that has the capability of direct toxic action on living tissue that can result in severe leukopenia and thrombocytopenia, depression of the immune system, and the alteration of a host’s inflammatory response system.

(n) “Disinfectant” means an agent applied to inanimate objects that frees from infection and that destroys disease-causing pathogens or other harmful microorganisms but may not kill bacterial and fungal spores.

(o) “FDA” means the United States Food and Drug Administration, Department of Health and Human Services.

(p) “Hazardous Drugs” means studies in animals or humans indicate that exposures to them have a potential for causing cancer, developmental or reproductive toxicity, or harm to organs.

(q) “HEPA Filter” means a filter where air is forced through in a uniform flow and 99.97% of all particles three-tenths (0.3) microns or larger are removed.

(r) “Immediate-Use” compounded sterile preparations means those products used in situations where there is a need for emergency or immediate patient administration. Examples are cardiopulmonary resuscitation, emergency room treatment, preparation of diagnostic agents, or critical therapy where delays caused by using conditions described for Low-Risk Level subjects the patient to additional risk. Batch compounding or storage is not appropriate for Immediate-Use compounded sterile preparations.

(i) The compounding process involves simple transfer of not more than three (3) commercially manufactured packages of sterile nonhazardous products from the manufacturers’ original containers and not more than two (2) entries into any one container.

(ii) Unless required for the preparation, the compounding procedure is a continuous process not to exceed one (1) hour.

(iii) During preparation, aseptic technique is followed. If not immediately administered, the finished compounded sterile preparation is under continuous supervision to minimize the potential for contact with nonsterile surfaces, introduction of particulate matter, or biological fluids, mix-ups with other products, and direct contact of outside surfaces.

(iv) Administration begins not later than one (1) hour following the START of the preparation of the compounded sterile preparation.

(v) Unless immediately and completely administered by the person who prepared it, or immediate and complete administration is witnessed by the preparer, the compounded sterile preparation shall bear a label listing patient identification information, the names and amounts of all ingredients, the name or initials of the person who prepared the compounded sterile preparation, and the exact one (1) hour BUD and time.

(vi) If administration has not begun within one (1) hour following the start of preparing the compounded sterile preparation, it shall be promptly, properly, and safely discarded.

(s) “ISO (International Organization for Standardization) Classification of Particulate Matter in Room Air” means limits in particles of 0.5 micrometer and larger per cubic meter. Class Name and Particle Count:

ISO Class 3	35.2 m3
ISO Class 4	352 m3
ISO Class 5	3,520 m3
ISO Class 6	35,200 m3
ISO Class 7	352,000 m3
ISO Class 8	3,520,000 m3

(t) “Media-Fill Test” means using a microbiological growth medium to substitute for the actual drug product to simulate admixture compounding in determining the quality of a person’s technique.

(u) “Multiple-Dose Container” means more than one (1) dose is in the vial and it usually contains antimicrobial preservatives. The BUD for an opened or entered Multiple-Dose Container with antimicrobial preservatives is twenty-eight (28) days, unless otherwise specified by the manufacturer.

(v) “Negative Pressure Room” means a room that is at a lower pressure than the adjacent spaces and, therefore, the net flow of air is *into* the room.

(w) “Parenteral” means a sterile preparation of drugs for injection through one (1) or more layers of skin.

(x) “Positive Pressure Room” means a room that is at a higher pressure than the adjacent spaces and, therefore, the net airflow is *out of* the room.

(y) “Primary Engineering Control” (PEC) means a device or room that provides an ISO Class 5 environment for the exposure of Critical Sites when compounding sterile products. Such devices include, but may not be limited to, Laminar Airflow Workbenches (LAFWs), Biological Safety Cabinets (BSCs), Compounding Aseptic Isolators (CAIs), and Compounding Aseptic Containment Isolators (CACIs).

(z) “Quality Assurance” means, for purposes of these regulations, the set of activities used to ensure that the processes used in the preparation of sterile drug products lead to products that meet predetermined standards of quality.

(aa) “Quality Control” means, for the purposes of these regulations, the set of testing activities used to determine that the ingredients, components, and final sterile products meet predetermined requirements with respect to identity, purity, nonpyrogenicity, and sterility.

(bb) “Risk Levels” means, for the purposes of these regulations, the categories assigned according to the potential for microbial contaminations of compounded sterile preparations.

(i) Low-Risk Level means compounded sterile preparations under the following conditions:

(A) Compounded with aseptic manipulations entirely with ISO Class 5 or better air quality using only sterile ingredients, products, components, and devices;

(B) The compounding involves only transfer, measuring, and mixing using not more than three (3) commercially manufactured packages of sterile products and not more than two (2) entries into any one sterile container (not applicable to compounding Low-Risk Level CSP radiopharmaceuticals);

(C) Manipulations are limited to aseptically opening ampules, penetrating disinfected stoppers with sterile needles and syringes, and transferring sterile liquids into sterile administration devices or containers for storage;

(D) In the absence of passing a sterility test, the storage periods cannot exceed forty-eight (48) hours at controlled room temperature, for not more than fourteen (14) days at a refrigerated temperature, and for forty-five (45) days in solid frozen state, minus twenty-five degrees Centigrade (-25°C) or colder; minus ten degrees Fahrenheit (-10°F) or colder.

(E) Examples of Low-Risk Level compounding include single-volume transfers of sterile dosage forms from ampules, bottles, bags, and vials with sterile needles OR simple aseptic measuring and transferring with not more than three (3) packages of manufactured sterile products including an infusion or diluents solution. The solution content of ampules should be passed through a sterile filter to remove any particles.

(ii) Low-Risk Level with twelve (12) hour or less BUD means:

(A) PEC shall be certified and maintain ISO Class 5 for exposure of Critical Sites and shall be in a Segregated Compounding Area restricted to sterile compounding activities that minimize the risk of contamination;

(B) The location shall not have unsealed windows or doors that connect to the outdoors or in a location with high traffic flow, nor be adjacent to construction site, warehouse, or food preparation areas;

(C) Personnel shall follow the procedures in Sections 3 and 7 for personnel cleansing and garbing and additional requirements prior to compounding. Sinks shall not be located adjacent to the ISO Class 5;

(D) Specifications in Sections 3, 4, and 7 through 9 for cleaning and disinfecting, personnel training and competency evaluation, and environmental sampling shall be followed;

(E) Quality Assurance includes routine disinfection, air quality testing, visual confirmation that compounding personnel are properly gowned and garbed, review of all orders and packages of ingredients, and visual inspection of the compounded sterile preparation to ensure the absence of particulate matter or leakage, and thoroughness of labeling. Visual inspection of Low-Risk Level CSP radiopharmaceuticals will be limited, in accordance with radiation safety practices;

(F) Media-Fill Test procedure is performed annually by each person authorized to compound.

(iii) Medium-Risk Level means compounded sterile preparations are prepared aseptically under Low-Risk Level conditions and one or more the following conditions exists:

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

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

(C) The compounding process requires unusually long duration such as that required to complete dissolution;

(D) In the absence of passing a sterility test, the storage periods cannot exceed thirty (30) hours at controlled room temperature, for not more than nine (9) days at refrigerated temperature, and for forty-five (45) days in solid frozen state, minus twenty-five degrees Centigrade (-25°C) or colder; minus ten degrees Fahrenheit (-10°F) or colder.

(E) Examples of Medium-Risk Level compounded sterile preparations include total parenteral nutrient fluids using manual or automated devices, filling of reservoirs of injection and infusion devices with more than three sterile drug products, transfer of volumes from multiple ampules or vials into one or more final sterile containers.

(F) Quality Assurance procedures include all elements of Low-Risk Level compounded sterile preparations as well as a more challenging Media-Fill Test passed annually or more frequently.

(G) Media-Fill Tests are performed at least annually under stressful conditions encountered during compounding Medium-Risk Level CSPs.

(H) If the pharmacy performs sterility testing, the pharmacy will document results of tests, as described in their policies and procedures. If sterility is documented, the compounded product may be retained and used up to the limits established by authoritative sources for potency and stability.

(iv) “High-Risk Level” compounded sterile preparations means the end product is either contaminated or at a high risk to become contaminated, for example:

(A) Nonsterile ingredients are incorporated or a nonsterile device is employed before terminal sterilization;

(B) Exposure to air quality worse than ISO Class 5 for more than one (1) hour by the sterile contents, a lack of effective antimicrobial preservatives, or sterile surfaces of devices and containers;

(C) Personnel are improperly garbed and gloved;

(D) Nonsterile water-containing preparations are stored for more than six (6) hours before being sterilized;

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

(F) The storage periods cannot exceed twenty-four (24) hours at controlled room temperature; cannot exceed three (3) days at refrigerated temperature; and cannot exceed forty-five (45) days in solid frozen state, minus twenty-five degrees Centigrade (-25°C) or colder; minus ten degrees Fahrenheit (-10°F) or colder.

(G) All nonsterile measuring, mixing, and purifying devices are rinsed thoroughly with sterile pyrogen free water, then thoroughly drained or dried immediately before use for High-Risk Level compounding. All High-Risk Level solutions subjected to terminal sterilization are prefiltered by passing through a filter not larger than 1.2 microns. Sterilization of High-Risk Level solutions by filtration shall be performed with a sterile 0.2 micron or 0.22 micron nominal pore size filter entirely within an ISO Class 5 or superior air quality environment.

(H) Examples of High-Risk Level Conditions include: dissolving nonsterile bulk drug and nutrient powders to make solutions that will be terminally sterilized; exposing the ingredients or components to air quality worse than ISO Class 5 for more than one (1) hour; measuring and mixing in nonsterile devices; assuming, without appropriate evidence, that packages contain at least ninety-five percent (95%) by weight of their active chemical and have not been contaminated between uses.

(I) Quality Assurance procedures include all those for Low-Risk Level compounded sterile preparations and, in addition, a Media-Fill Test that represents High-Risk Level compounding semiannually by each person authorized to compound High-Risk Level compounded sterile preparations.

(cc) “Segregated Compounding Area” means a designated space, either a demarcated area or room, which is restricted to preparing Low-Risk Level compounded sterile preparations with twelve (12) hour or less BUD. The area must contain a device that provides Unidirectional Flow of ISO Class 5 air quality and shall be void of activities and materials that are extraneous to sterile compounding.

(dd) “Single-Dose Container” means a vial intended for a single parenteral use and is labeled as such. Opened or needle-punctured Single-Dose Containers such as bags, bottles, syringes, and vials shall be used within one (1) hour, if opened in worse than ISO Class 5 air quality, and any remaining contents must be discarded. Opened single-dose ampules shall not be stored for any time period. Single-dose vials exposed to ISO Class 5 or cleaner air may be used up to six (6) hours after initial needle puncture.

(ee) “Temperature” means, for the purposes of these regulations:

(i) “Frozen” means temperatures of minus twenty-five degrees Centigrade (-25°C to -10°C) or colder, minus 13 to plus 14 degrees Fahrenheit (-13 F to 14 F).

(ii) “Refrigerated” means temperatures of two to eight degrees Centigrade (2°C to 8°C), thirty-six to forty-six degrees Fahrenheit (36°F to 46°F).

(iii) “Room Temperature” means temperatures of twenty to twenty-five degrees Centigrade (20°C to 25°C), sixty-eight to seventy-seven degrees Fahrenheit (68°F to 77°F).

(ff) “Unidirectional Flow” means airflow moving in a single direction in a robust and uniform manner and at sufficient speed to reproducibly sweep particles away from the critical processing or testing area.

(gg) “USP” means the United States Pharmacopeia, an official public standards setting authority for all prescription and over-the-counter medicines and other health care products manufactured or sold in the United States. USP sets standards for the quality, purity, strength, and consistency of these products. USP is a non-governmental, not-for-profit public health organization.

(hh) “USP 797” means Chapter 797 in the United States Pharmacopeia-National Formulary book of public pharmacopeial standards specifically for pharmaceutical compounding of sterile preparations.

Section 3. Physical Layout and Environment.

(a) Compounding environment description.

(i) The compounding environment shall be contained in an area that is segregated from other pharmacy activities and limits access and activities to personnel, materials, and processes that are directly related to production of sterile compounded products, therefore, minimizing risk of particulate or microbial contamination. The compounding area shall be of sufficient size, lighting, and physical conditions (such as maintenance of temperature of 70 degrees Fahrenheit (70°F) or lower) to maximize the compounding accuracy and potential of compounding personnel.

(ii) The compounding area shall be constructed of smooth, impervious, non-particulate shedding materials that optimize the ability to routinely clean and disinfect surfaces. Ventilation should occur in a manner that allows the maintenance of appropriate ISO Class designations of each separate working area and should avoid disruption and cross-room currents.

(iii) The compounding area shall have walls, floors, and ceilings, along with fixtures, counters, shelves, and cabinets, that are smooth, impervious, free of cracks or crevices, non-shedding, and resistant to damage that could occur from routine disinfection with cleaning agents. Junctions between surfaces should be caulked or formed in a manner to avoid deep corners that cannot be reached and disinfected. Additional equipment/features, such as pass-throughs, refrigerators, lights, and vents shall be constructed to not become a vector for contamination of the work area.

(iv) The compounding area will not contain supplies other than those that are necessary for compounding and will not be considered a bulk storage area. All particle shedding packing will be removed and products cleaned before being brought into the compounding area.

(b) Low-Risk Level and Medium-Risk Level compounding areas.

(i) Ante-Area.

(A) The compounding work room shall contain an Ante-Area that conforms to ISO Class 8 conditions.

(B) The Ante-Area may contain a hands-free sink and closed soap system that allows use and movement to the next compounding area without recontamination of hands on extrinsic surfaces.

(C) The Ante-Area shall have area to support the gowning of compounding personnel.

(ii) Buffer Area.

(A) The compounding work room shall contain a Buffer Area that conforms to ISO Class 7 conditions. When compounding Low-Risk Level radiopharmaceutical CSPs, the compounding work room shall contain a Buffer Area that conforms to ISO Class 8 conditions.

(B) The Buffer Area shall be physically separated or have designated boundaries that separate it from the Ante-Area. The Buffer Area shall not be in a location with high traffic. The Buffer Area shall not be in a location with unsealed windows or doors that connect to the outdoors.

(C) Ventilation shall assure that contamination from the Ante-Area does not enter the Buffer Area through utilization of filtered Unidirectional Flow and principles of air displacement.

(D) The Buffer Area shall not contain sinks or drains and shall be void of all materials, equipment, and fixtures that are not directly involved in the current processing of compounded sterile preparations.

(E) The construction, arrangement, and ventilation of the Buffer Area shall not allow conditions that could adversely affect compounding, such as aberrant heating, cooling, door-drafts, and personnel traffic air currents.

(iii) Primary Engineering Control (PEC).

(A) The Buffer Area shall contain a Primary Engineering Control that conforms to ISO Class 5 conditions. This may be accomplished through utilization

of a laminar flow hood, Compounding Aseptic Isolator, Compounding Aseptic Containment Isolator, or an entire clean room that is filtered, ventilated, and constructed to maintain ISO Class 5 conditions during dynamic operating conditions.

(iv) Compounding Aseptic Isolators (CAIs).

(A) Compounding Aseptic Isolators shall be contained inside of an ISO Class 7 Buffer Area, unless the manufacturer of the unit can certify that its engineering controls will maintain ISO Class 5 conditions during dynamic operating conditions, such as personnel and product entry or transfer and throughout typical compounding duties.

(B) The compounding pharmacy that employs a Compounding Aseptic Isolator as a Buffer Area and Primary Engineering Control shall maintain documentation from the manufacturer.

(c) High-Risk Level additions.

(i) All conditions of Low-Risk Level and Medium-Risk Level compounding shall be maintained, and shall include the additional requirement that the Buffer Area shall have physical separation from the Ante-Area.

(d) Immediate Use and twelve (12) hour Beyond-Use Date (BUD).

(i) Compounding pharmacies may utilize a Primary Engineering Control in conditions that are less than ISO Class 7 quality, as long as the Primary Engineering Control is appropriately maintained, is segregated from other activities, personnel comply with all gowning and garbing procedures, and the compounded sterile preparation will be used immediately or within twelve (12) hours of compounding.

(ii) Personnel utilizing this form of compounding must be appropriately trained, with documentation in:

- (A) Personnel;
- (B) Equipment;
- (C) Product cleansing;
- (D) Gowning and garbing;
- (E) Utilization of the Primary Engineering Control;
- (F) Aseptic practices;

and be subject to all quality requirements of normal sterile compounding staff.

Section 4. Responsibility of Compounding Personnel.

(a) Professional compounding personnel are responsible for ensuring that, at a minimum:

(i) Proper aseptic technique is practiced at all times during sterile product compounding;

(ii) Compounded sterile preparations are appropriately and accurately prepared, identified, purified, sterilized, packaged, labeled, stored, dispensed, and distributed;

(iii) The compounding area is appropriately cleaned and maintained.

(b) Compounding supervisors (persons who supervise the compounding and dispensing of compounded sterile preparations) are responsible for ensuring that:

(i) Compounding personnel are appropriately educated to correctly perform compounding duties and ensure that correct compounding procedures and processes are used;

(ii) Compounding equipment is clean, accurate, appropriate and properly inspected and the compounding environment is properly maintained, isolated and inspected;

(iii) Ingredients have their correct identity, quality, and purity and opened or partially used containers are properly stored and inspected;

(iv) Proper and adequate sterilization methods are used;

(v) Completed compounded sterile preparations are appropriately packaged, labeled, and assigned an appropriate BUD, and evaluated for safety;

(vi) Deficiencies in compounding can be rapidly identified and corrected;

(vii) A written Quality Assurance program is established for monitoring, evaluating, correcting, and improving the activities, systems, and processes that support the preparation of compounded sterile preparations;

(viii) Policies and procedures are prepared and updated for the compounding, dispensing, delivery, administration, storage, and use of sterile pharmaceutical products appropriate for their facility.

Section 5. Personnel Training and Evaluation in Aseptic Manipulation Skills.

(a) Personnel who prepare compounded sterile preparations shall be trained in the theoretical principals and practical skills of Aseptic Processing and in achieving and maintaining ISO Class 5 environmental conditions before they begin to prepare compounded sterile preparations.

(i) This can be through any combination of written, audio, or video sources.

(ii) Personnel shall also pass written and Media-Fill Testing of aseptic technique before they begin to prepare compounded sterile preparations.

(iii) Results of all testing shall be recorded.

(b) Personnel shall also perform a didactic review and pass written and Media-Fill Testing of aseptic technique:

(i) annually for Low- and Medium-Risk Level compounding;

(ii) semiannually for High-Risk Level compounding.

(c) There shall be a process to retest and evaluate for personnel who fail testing processes.

(d) Results of all testing shall be recorded.

Section 6. Hazardous Drugs as CSPs.

(a) Physical Requirements.

(i) If the pharmacy practice site is engaged in the compounding of hazardous sterile products, they must ensure the safety of the personnel during the compounding and storage of the Hazardous Drugs.

(ii) Appropriate garbing must be used during receiving, distribution, stocking, inventorying, preparation for administration, and disposal of Hazardous Drugs.

(iii) Personnel shall be appropriately trained prior to initial handling and annually thereafter in the storage, handling, preparing, and disposing of Hazardous Drugs.

(iv) Such pharmacy will be designed and equipped for appropriate storage.

(A) Hazardous Drugs must be stored separately from other inventory and storage areas so identified.

(B) Access should be limited to appropriate personnel.

(v) Such pharmacy will have an appropriate area to prepare sterile Hazardous Drugs.

(A) All Hazardous Drugs shall be prepared in a CACI or in a BSC that is located in a negative pressure room. If a compounding facility prepares hazardous drugs in a sufficiently low volume (five [5] or less products per week), the use of two tiers of containment (e.g, a Closed System Transfer Device within a BSC) is acceptable.

(vi) Such pharmacy will have a procedure for disposal of materials containing hazardous residues in accordance with state and federal laws.

Section 7. Radiopharmaceuticals as CSPs.

(a). Standards for the production of Positron Emission Tomography (PET) drugs are addressed in USP Chapter <823> *Radiopharmaceuticals for Positron Emission Tomography - Compounding*, while USP Chapter <797> applies to the further handling, manipulation, or use of the product once it is released as a finished drug product from a production facility.

(i) For the purpose of this Section, the following shall be designated low-risk level radiopharmaceutical CSPs:

(A) Radiopharmaceuticals compounded from sterile components in closed sterile containers, using appropriately shielded vials and syringes in a properly functioning and certified ISO Class 5 PEC located in an ISO Class 8 or cleaner air environment.

(B) Compounded Radiopharmaceuticals with a volume of 100 mL or less for a single-dose injection or not more than 30 mL taken from a multiple-dose container.

(ii) Radiopharmaceuticals prepared as Low-Risk Level CSPs with 12-Hour or Less BUD shall be prepared in a properly designated and segregated compounding area.

(iii) 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 manufacturer recommendations or as established by stability testing.

(iv) Technetium-99m/molybdenum-99 generator systems shall be stored and operated under conditions recommended by the manufacturer and applicable state and federal regulations in an ISO Class 8 or cleaner air environment.

Section 8. Gowning and Garbing.

(a) Personal cleansing and gowning/garbing shall be as follows:

(i) Personnel shall not compound if they have open sores or infected wounds;

ii) Personnel shall not compound if they have an upper respiratory infection;

(iii) Upon entering a compounding area, personnel must remove outer garments (such as coats, hats, sweaters, bandanas, vests, and scarves), hand and other exposed jewelry, and any other unnecessary and potentially contaminated or particle shedding articles. If hand jewelry cannot be removed, then it must be thoroughly cleaned and covered with a sterile glove;

(iv) Hand cleansing and donning of personal protective equipment should proceed in a manner that goes from the dirtiest to the cleanest area: shoe covers, hair covers, facial hair covers, and face mask or eye shields (if working with caustic or irritant agents). Cleansing should be done in a no-touch sink using appropriate antibacterial detergent, starting at the hands and nails and progressing to the elbows. The process should take at least thirty (30) seconds. Hand and forearm drying should be done with non-shedding paper towels.

(A) At this point, personnel should don a non-shedding gown with sleeves that fit snugly around wrists. Lastly, sterile gloves should be donned. The gloves should form a continuous surface with the gown sleeves. Care should be exercised when progressing through the Ante-Area and Clean Room to not re-contaminate the gloves.

(B) Re-sanitizing of the gloves with sterile 70% IPA should occur routinely throughout the compounding process, or at any point that the gloves may have touched a non-sterile surface.

(v) If it is necessary to leave the compounding area, hand cleansing and replacement of all personal protective equipment except for the non-shedding gown shall occur. The gown must be left in the Ante-Area if it is to be reused during a shift (not to exceed twenty-four (24) hours).

(vi) If a Compounding Aseptic Isolator is used, gowning and garbing should occur in a manner consistent with the manufacturer's documented procedures. If no studies have been done and the manufacturer cannot assure maintenance of sterility and ISO Class 5 conditions outside of an ISO Class 7 space, the compounder must follow gowning and garbing procedures discussed above.

Section 9. Policy and Procedure.

(a) Pharmacies that engage in the practice of sterile compounding shall have a Policies and Procedures (P&P) manual that describes the common practices of the pharmacy. The P&P manual will be reviewed and updated as necessary, at least annually. The Pharmacist-in-Charge (PIC) is responsible for the completeness, accuracy, and enforcement of compliance with the procedures by all pharmacy personnel. This P&P manual will be available at all times to staff and at the request of a Board of Pharmacy Inspector. All staff will review the P&P manual before engaging in sterile compounding and annually thereafter. If the PIC changes, the new PIC must review, date, and initial the P&P manual within thirty (30) days.

(b) The Policies and Procedures manual will contain procedures detailing at least the following:

- (i) Responsibilities of compounding personnel;
- (ii) Personnel training and testing;

- (iii) Competency practices and assessment of compounding personnel;
- (iv) Quality Assessment and Quality Improvement activities;
- (v) Proper use and deployment of environmental controls;
- (vi) Gowning and garbing practices;
- (vii) Inspection of finished products, labeling, storage, and transfer to final use areas for storage or use;
- (viii) Introduction of supplies and products into the compounding area;
- (ix) The formulation, process for compounding, BUD, and storage requirements of each routinely compounded CSP.

Section 10. Elements of Quality Control.

(a) Compounding facility.

(i) All pharmacies engaging in sterile compounding shall have a Quality Assurance Program that is in written format with documentation that illustrates that the Program is being followed. Documentation of compliance with the Quality Assurance Program will be available for evaluation by Inspectors of the Wyoming Board of Pharmacy and other pertinent regulatory agencies. The Quality Assurance Program shall include, though not be limited to:

- (A) Adequacy of training and evaluation of personnel;
- (B) Verification, monitoring, and review of the adequacy of the compounding process;
- (C) Maintenance of an appropriate environment for compounding sterile preparations;
- (D) Review of the final product for accuracy of preparation, quality, and purity and, where appropriate, sterility and bacterial endotoxin content;
- (E) Monitoring for adverse or negative patient outcomes due to utilization of a compounded sterile preparation or other quality related issue, and that identified issues are included in the facility's overall Quality Assurance Program.
- (F) Addressing problems or issues identified by the Quality Assurance Program, including follow-up and assurance of correction.

(b) Personnel.

(i) All personnel engaged in preparation of sterile products will be adequately trained before they begin compounding.

(ii) Training shall include didactic learning and experiential components with results validated by testing of aseptic skills and knowledge including, but not limited to:

- (A) Gowning and garbing assessment;

(B) Media-Fill Testing that is representative of compounding performed;

(C) Gloved fingertip testing done three (3) times prior to initial compounding and annually thereafter;

(D) Knowledge of sterile compounding processes; facility policies, procedures and quality programs; and legal requirements of state, federal, and pertinent regulating agencies.

(iii) All documentation of results will be available for review by pertinent individuals or agencies.

(c) Compounding Risk Levels.

(i) The Quality Assurance Program will correspond to the level of compounding risk that is undertaken at the individual facility. The facility's Quality Assurance Program shall include the following for each level:

(A) Low-Risk Level Compounding.

(I) Routine disinfection and air quality testing conducted to minimize microbial surface contamination and maintenance of ISO Class 5 conditions;

(II) Visual confirmation of personnel practices and garbing;

(III) Review of all orders and materials to ensure that the correct identity and quantity of ingredients were compounded;

(IV) Visual inspection of the sterile product to ensure the absence of particulate matter in the solution; appropriateness of color, clarity, and volume; the adequacy and competence of the container; and appropriateness of labeling. Visual inspection of Low-Risk Level radiopharmaceutical CSPs will be limited, in accordance with radiation safety practices.

(V) Annual basic Media-Fill Testing that is conducted in conditions of equal stress to the actual compounding process.

(B) Medium-Risk Level Compounding.

(I) All elements of the Low-Risk Level compounding quality requirements plus a more challenging Media-Fill Test performed at least annually.

(C) High-Risk Level Compounding.

(I) All elements of the Low-Risk Level compounding quality requirements plus a Media-Fill Test that represents High-Risk Level compounding completed semiannually by all compounding personnel.

(d) Verification of accuracy and sterility in High-Risk Level compounding.

(i) The compounding facility will have policies and procedures detailing standard practices that assure compounded sterile products are accurately produced and that the quality procedures in place achieve and maintain sterility.

(ii) High-Risk Level compounding shall have additional procedures and quality assurance to ensure accurate and sterile products.

(iii) Sterility and depyrogenation shall be achieved when necessary by the appropriate application of dry-heat, steam-heat, or filtration. Appropriate resources shall be used to determine the appropriate method for sterilization while maintaining strength, purity, quality, and package integrity.

(iv) Sterility and Bacterial Endotoxin testing shall be done when there are batches of more than twenty-five (25) identical individual single-dose packages; when in multiple-dose vials for administration to multiple patients; or when exposed longer than twelve (12) hours at two-to-eight degrees Centigrade (2°C to 8°C), or longer than six (6) hours at above eight degrees Centigrade (8°C).

(v) If dispensed before results are obtained, daily monitoring of the testing will occur and, if positive results come back, the product will be immediately recalled and notification of results will be forwarded to the end patient and physician.

(e) Environmental quality and control.

(i) The facility producing compounded sterile preparations will have policies and procedures sufficient to ensure preparation of products that are sterile and of accurate strength, purity, quality, and package integrity. A Quality Assurance Program will be present that illustrates the adequacy of the processes used. The Quality Assurance Program will include, but not be limited to:

(A) Viable and nonviable environmental air sampling performed:

(I) As part of commissioning and certification of facilities or equipment;

(II) Following servicing of facilities or equipment;

(III) As part of re-certification (every six (6) months);

(IV) In response to identified problems with end products, staff technique or work practices, or patient-related infections that could be due to the compounded sterile preparation.

(B) Primary Engineering Controls and equipment will be monitored as part of the comprehensive Quality Assurance Program that assures maintenance of appropriate air quality and the ability to produce sterile and stable compounded products.

(f) Patient monitoring.

(i) The compounding facility will have policies and procedures detailing its Quality Assurance Program that monitor for adverse effects, negative outcomes, and medication errors.

(ii) The compounding facility will have a process that allows patients and other recipients to address their questions and to report any concerns they may have with the compounded sterile preparation or administrative device.

(iii) Reports of adverse events will be reviewed promptly and thoroughly by compounding supervisors to correct and prevent future occurrences.

(iv) Compounding personnel are encouraged to participate in the adverse event reporting and product defects programs of the FDA and USP.

Section 11. Verification of Automated Compounding Devices for Parenteral Nutrition Compounding.

(a) Wherever possible, Parenteral nutritional solutions should be compounded using an automated compounder or repeater pump to ensure accuracy and sterility of these compounded products.

(b) Written procedures outlining use of equipment, calibration, appropriate maintenance, monitoring for proper function, and specified time frames for these activities shall be established and followed. Results and logs of calibration and maintenance reports shall be kept on file at the pharmacy for at least two (2) years and shall be available for inspection.

(c) Manufacturer recommendations regarding calibration and maintenance shall be made part of each facility's policies and procedures.

(d) The automated compounder shall be cleaned prior to each set-up and as necessary according to the manufacturer's guidelines.

(e) Accuracy assessments of automated compounding devices shall be conducted and daily or on each day used. At routine intervals, the pharmacist in charge or his/her designee will review these assessments to avoid potentially clinically significant cumulative errors over time.