

**61-02-01-03. Pharmaceutical compounding standards.** The minimum standards and technical equipment to be considered as adequate shall include:

1. **Definitions.**

- a. “Active Chemical or Ingredient” refers to chemicals, substances, or other components of articles intended for use in the diagnostics, cure, mitigation, treatment, or prevention of diseases.
- b. “Aseptic Processing” is the method of preparing pharmaceutical and medical products that involves the separate sterilization of the product and of the package, the transfer of the product into the container and closure of the container under ISO Class 5 or superior conditions and using procedures designed to preclude contamination of drugs, packaging, equipment, or supplies by microorganisms during the process.
- c. “Beyond Use Date” refers to the date placed on a prescription label that is intended to indicate to the patient or caregiver a time beyond which the contents of the prescription are not recommended to be used. The beyond-use date is determined from the date or time compounding of the preparation is completed.
- d. “Component” is any ingredient used in the compounding of a drug product, including any that are used in its preparation, but may not appear on the labeling of such a product .
- e. “Compounding” is the preparation, mixing, assembling, packaging, and labeling of a drug or device in accordance to a licensed practitioner’s prescription or medication order. Compounding includes:
  - i. Preparation of drugs or devices in anticipation of prescription drug orders based on routine, regularly observed prescribing patterns.
  - ii. Reconstitution or manipulation of commercial products that may require the addition of one (1) or more ingredients as a result of a licensed practitioner’s prescription drug order.
  - iii. Preparation of drugs or devices for the purposes of, or as an incident to, research, teaching, or chemical analysis.
  - iv. Categories of compounding.
    - 1. Category 1 – Non-sterile Simple.
      - a. Simplex – Mixing of two (2) or more commercial products.
      - b. Complex – Compounding with the bulk drug substances or when calculations are required.

2. Category 2 – Sterile Compounds.

- a. Immediate Use (containing no more than three (3) sterile, commercially supplied non-hazardous drugs with administration starting within one (1) hour of the beginning of preparation and completed within twelve (12) hours.
  - b. Low Risk – Risk Level I
  - c. Medium Risk – Risk Level II
  - d. High Risk – Risk Level III
- 3. Category 3 – Radiopharmaceuticals.
- 4. Category 4 – Veterinary pharmaceuticals.
- f. “Compounded Sterile Preparation” (CSP) will include all of the following:
  - i. Preparations prepared according to the manufacturer’s labeled instructions and other manipulations when manufacturing sterile products that expose the original contents to potential contamination.
  - ii. Preparations containing non-sterile ingredients or employing non-sterile components or devices that must be sterilized before administration.
  - iii. Biologics, diagnostics, drugs, nutrients, and radiopharmaceuticals that possess either of the above two characteristics, and which include, but are not limited to, baths and soaks for live organs and tissues, implants, inhalations, injections, powders for injection, irrigations, metered sprays, and ophthalmic preparations.
- g. “Compounder or Compounding Personnel” is the pharmacist or other licensed health care professional responsible for preparing the compounded preparations.
- h. “Compounding supervisor” is a person who supervises and is responsible for the compounding and dispensing of a non-sterile or sterile preparation.
- i. “Critical Site” is 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.
- j. “Direct and Contiguous Compounding Area” refers to the specific area where a compound is prepared.
- k. “Disinfection” is the process by which the total number of microorganisms is reduced to a safe level or eliminated by applying an agent to inanimate objects that destroys disease-causing pathogens or other harmful microorganisms but may not kill bacterial and fungal spores.
- l. “Immediate-Use” is defined as a compound prepared with no more than three (3) sterile, commercially supplied non-hazardous drugs; using commercial, sterile devices; the compounding process is a continuous process not to exceed one (1) hour and administration begins not later than one (1) hour following the start of the preparation of the compound and to be completed within twelve (12) hours, not including any chemotherapy or other hazardous drug preparations.
- m. “ISO Class” is the description of an atmospheric environment characterized by the number of particles within a diameter per cubic foot of air.

- i. “ISO Class 5” atmospheric environment contains less than 100 particles, 0.5 microns or larger in diameter per cubic foot of air.
- n. “Media Fill Test” refers to tests used to validate aseptic techniques of compounding personnel and of processes that ensure the personnel and processes used are able to produce sterile products without microbial contamination; testing uses a microbiological growth medium to substitute for the actual drug product to simulate admixture compounding in determining the quality of a person’s technique.
- o. “NDC Number “is the National Drug Code given to each drug separately and specifically approved by the Food and Drug Administration for identification and reporting.
- p. “Preparation” is a drug dosage form, dietary supplement, or a finished device; it contains one (1) or more substances formulated for use on or for the patient or consumer.
- q. “Primary Engineering Control” or PEC refers to a device or room that provides an ISO Class 5 or superior environment during the compounding process; including, but not be limited to, laminar airflow workbenches (LAFWs), biological safety cabinets (BSCs), compounding aseptic isolators (CAIs), and compounding aseptic containment isolators (CACIs).
- r. “Product “is a commercially manufactured drug or nutrient that has been evaluated for safety and efficacy by the FDA; accompanied by full prescribing information.
- s. “Repackaging” is the transfer of an excipient from one container to another.
- t. “Risk levels” of CSPs determine the level assigned that represent the probability that it will be contaminated with microbial organisms, spores, endotoxins, foreign chemicals, or other physical matter.
- u. “Stability” is defined as the extent to which a preparation retains, with specified limits, and throughout its period of storage and use, the same properties and characteristics it possessed at the time of compounding.
- v. “Seventy Percent (70%) Isopropyl Alcohol” or IPA is a sterile microbial used to clean surfaces used in sterile preparations.
- w. “US Pharmacopeia” or USP is the book of official compendia of standards for the United States.

## 2. **General Compounding.**

### **a. Responsibility of the Compounder.**

- i. Personnel engaging in compounding must be proficient, capable, and qualified to perform assigned duties in the compounding area while expanding his or her knowledge of compounding through seminars or appropriate literature

- ii. Compounding personnel must be familiar with USP Standards and North Dakota regulations including but not limited to:
    - 1. Certifying all prescription orders.
    - 2. Approving or rejecting all components, drug product containers, closures, in-process materials, and labeling ensuring preparations and ingredients are of acceptable strength, quality, and purity, with appropriate packaging.
    - 3. Preparing and reviewing all compounding records to assure that errors have not occurred in the compounding process and the finished product has expected qualities as well as implement procedures to prevent cross-contamination.
    - 4. Assuring the proper maintenance, cleanliness, sanitization and use of all equipment used in prescription compounding practice including the direct and contiguous compounding area allowing for the compounding environment to be suitable for its intended purpose.
      - a. Established procedures must be performed at the beginning of each shift, using approved residue-free sanitizers and non-shedding equipment.
    - 5. Assuring that the drug product and components of drug products are not on the list of federally recognized drug products that have been withdrawn or removed from the market for public health reasons.
  - iii. Policies and procedures must be established concerning washing and donning the appropriate clothing specific to the type of process performed to protect the personnel from chemical exposures and prevent drug contamination.
- b. **Training.** All compounding supervisors and all personnel involved in compounding must be well trained and must participate in current, relevant training programs. All training activities will be covered by standard operating procedures and must be properly documented. Steps in the training procedure include:
- i. Be familiar with *Pharmaceutical Compounding – Non-Sterile Compounding* (USP 795), *Pharmaceutical Compounding – Sterile Compounding* (USP 797), and *Pharmaceutical Calculations in Prescription Compounding* (USP 1160).
  - ii. Be familiar with all procedures relating to compounding specific to your facility, equipment, personnel, compounding process, evaluation, packaging, storage, and dispensing.

- iii. Compounding supervisors must be responsible to follow the instructions below to show that personnel are appropriately trained:
    - 1. Demonstrate compounding procedures to compounding personnel.
    - 2. Guide personnel through the compound process with assistance.
    - 3. Observe personnel performing a compound without assistance but under supervision.
    - 4. Review the compound, correct mistakes and answer questions concerning compounding and associated processes.
    - 5. Confirm verbal and functional knowledge of the personnel concerning compounding.
    - 6. Have personnel perform a compounding procedure without supervision, yet checking off the final preparation.
    - 7. If properly compounded and when satisfied, sign the documentation records confirming appropriate training.
    - 8. Continually monitor the work of the personnel including calculations.
  - iv. Compounding supervisors are ultimately responsible for the finished product.
- c. Procedures and Documentation.** Procedures must be developed for the facility, equipment, personnel, preparation, packaging and storage of the compounded preparation to ensure accountability, accuracy, quality, safety, and uniformity in compounding. This allows for a compounder, whenever necessary, to systematically trace, evaluate, and replicate the steps included throughout the preparation process of a compounded preparation.
- d. Drug Compounding Facilities** must include all of the following:
- i. Compounding facilities and equipment are clean, accurate, of appropriate size and construction and properly inspected and the compounding environment is properly maintained, isolated and inspected.
    - 1. Personnel must have a written plan and schedule while maintaining records of cleaning and disinfecting.
  - ii. Aseptic processes must be conducted in an area separate from the area used for non-sterile preparations.
  - iii. Areas designated for compounding including space for storage must have adequate space, designed and well-lighted to prevent mix-ups, errors or adventitious cross-contamination.
  - iv. Heating, ventilation, and air conditioning systems are controlled to avoid decomposition of chemicals.

- v. A supply of potable water is available for washing with adequate washing facilities that are easily accessible including, but not limited to, hot and cold water, soap or detergent, and an air dryer or single use towels.
  - 1. Plumbing system should be free of defects that could contribute to contamination of the compounded product.
- vi. All areas maintained in a clean and sanitary condition; trash, sewage and other refuse should be disposed of in a safe and timely manner.
- vii. Bulk drugs, chemicals, or materials must be properly labeled and stored in an area that is clean, dry, at appropriate temperature (i.e., controlled room, refrigerator, or freezer), and protected from contamination .

**e. Drug Compounding Equipment.**

- i. Equipment and utensils must be of appropriate design and capacity and properly stored to avoid contamination while located in a place appropriate for facility operations for its use, maintenance, and cleaning.
- ii. All equipment must be constructed so that surfaces that contact components, in-process materials, or finished preparations are not reactive, additive, or adsorptive to avoid altering the preparation.
- iii. Equipment, apparatus, and devices used to compound a preparation must be calibrated, maintained, and monitored for proper function; records must be kept for the lifetime of the equipment.

**f. Packaging, Drug Preparation Containers, Storage, and Beyond-Use Dating.**

**i. Containers and container closures.**

- 1. Must meet USP requirements found under *Containers – Glass* (USP 660), *Containers – Plastic* (USP 661), and *Containers – Performance Testing* (USP 671).
- 2. Those intended for compounding of sterile and non-sterile preparations must be handled, sterilized (if appropriate), and stored according to *Pharmaceutical Compounding – Sterile Preparations* (USP 797) and *Pharmaceutical Compounding – Non-Sterile Preparations* (USP 795).
- 3. Must be stored off the floor, handled and stored to prevent contamination, and rotated to use the oldest stock first.
- 4. Must be stored in a way to facilitate inspection and cleaning
- 5. Must be constructed in such a way that surfaces are not reactive, additive, or absorptive.
- 6. The containers and closures shall be of suitable material so as not to alter the quality, strength, or purity of the compounded drug.

**ii. Storage area.**

1. Compounded preparations must be stored strictly in accordance with the conditions stated on the label of ingredient products and finished preparations.
2. Monitoring of appropriate temperatures must occur daily for controlled storage areas and temperatures recorded in the Temperature Log.
  - a. Controlled room temperature areas, 20°C to 25°C with mean kinetic temperature 25°C.
  - b. Controlled cold temperature, 2° C to 8°C with mean kinetic temperature 8°.
  - c. Controlled freezing temperature, -25° C to -10° C.

iii. Beyond-Use dates.

1. The compounder must establish an appropriate beyond-use date determined by drug-specific chemical and physical stability parameters of the components in conjunction with the manufacturer's product label, appropriate literature and USP Standards.
2. Compounders establish a beyond-use date considering the nature of the drug, degradation mechanism, purposed container, expected storage conditions, and intended duration of therapy.
3. Beyond-use dating is assigned conservatively to all compounded preparations excluding immediate-use preparations.
  - a. For non-aqueous liquids and solid formulations where the manufactured drug product is the source of active ingredient, the beyond-use date is no later than twenty-five percent (25%) of the time remaining until the product's expiration date or six (6) months, whichever earlier.
  - b. For water-containing, liquid formulations prepared from ingredients in solid form, the beyond-use date is no later than fourteen (14) days when stored at cold temperatures between two and eight degrees Celsius (2°C to 8°C).
  - c. For all other formulations the beyond-use date is no later than the intended duration of therapy or thirty (30) days, whichever is earlier unless supporting valid scientific stability information can be applied.
4. Solid or liquid forms of drugs without manipulation that are transferred from one container to another is defined as repackaging and not compounding; the beyond use date is not to exceed the manufacturer's date or one (1) year use date, whichever is less.

g. Compounding Controls.

- i. Compounder must ensure that the written procedures for compounding are available electronically or in hard copy and assure the finished products have the correct identity, strength, quality, and purity.
- ii. Procedures must be established that give a description of the following:
  1. Components and their amounts.
  2. Order of component additives.
  3. Compounding process.
  4. Drug product.
  5. Required equipment and utensils including container and closure system.
- iii. The compounder will accurately weigh, measure, and subdivide all components as appropriate.
  1. Compounder will check and re-check each procedure at each point of the process to ensure that each weight or measure is correct.
  2. If a component is transferred from the original container to another, the new container must be identified with the component name, weight or measure, the lot or control number, the expiration or beyond-use date, and the transfer date.
- iv. The compounder must write procedures that describe the tests or examinations that prove uniformity and integrity of the compounded preparations
- v. Control procedures must be established to monitor the output and validate the performance of compounding personnel that affect variability of final preparations such as:
  1. Capsule weight variation.
  2. Adequacy of mixing to assure uniformity and homogeneity.
  3. Clarity, completeness, or pH of solutions.
- vi. The compounder must establish an appropriate beyond-use date for each compounded preparation.
- vii. Facilities engaging in compounding must have a specifically designated and adequate space for orderly compounding of non-sterile and sterile preparations, including the placement and storage of equipment and materials.



**h. Labeling.**

- i. The compounder's preparation label will contain all information required by North Dakota state law and accepted standards of practice found under Chapter 61-04-06 Prescription Label Requirements.
- ii. The compounder will label any excess compounded products so as to refer to the formula used.
- iii. Preparations compounded in anticipation of a prescription prior to receiving a valid prescription should be made in a regularly used amount based on the history of prescriptions filled, they should be labeled with:
  - 1. Complete list of ingredients or preparation time and reference or established chemical name or generic name.
  - 2. Dosage form.
  - 3. Strength.
  - 4. Preparation date and time.
  - 5. Inactive ingredients.
  - 6. Batch or lot number.
  - 7. Assigned beyond-use date.
  - 8. Storage conditions
- iv. The compounder must examine the preparation for correct labeling after completion.

**i. Records and Reports.**

- i. Records must be maintained including, but not limited to, a hard copy of the prescription with formulation and compounding records.
- ii. Adequate records of controlled substances used in compounds.
- iii. All records must be kept for 5 years according to North Dakota state law and be available for inspection.
  - 1. **Formulation Record** provides a consistent source document for preparing the preparation and must list:
    - a. Name, strength, and dosage form of the preparation compounded.
    - b. All ingredients and their quantities.
    - c. Equipment needed to prepare the preparation, when appropriate.

- d. Mixing instructions including order of mixing, mixing temperatures, and other valid instructions such as duration of mixing.
- e. Assigned beyond-use date.
- f. Container used in dispensing.
- g. Storage requirements.
- h. Any quality control procedures.

2. **Compounding Record** documents the actual ingredients in the preparation and the person responsible for the compounding activity and includes:

- a. Name and strength of the compounded preparation.
- b. The formulation record reference.
- c. Sources and lot numbers of the ingredients.
- d. Total number of dosage units compounded.
- e. Name of compounding personnel who prepared the preparation.
- f. The date of preparation.
- g. The assigned internal identification number or prescription number.
- h. Assigned beyond-use date.
- i. Results of all quality control procedures.

3. **Temperature Log** records the daily monitoring of temperatures in the storage area specifically for the controlled room temperature, refrigerator, freezer or incubator

- j. **It is acceptable** to compound drug products to be used by practitioners in their office for administration to patients. These products cannot be dispensed or sold to others. Sales to other pharmacies, clinics, or hospitals are manufacturing and are not allowed.
3. **Non-Sterile Compounding.** Compounders are to use the following steps to minimize error and maximize the prescriber's intent, specifics can be found in *Pharmaceutical Compounding – Non-Sterile Compounding* (USP 795):
- a. Judge the suitability of the prescription of the preparation in terms of safety and intended use.
  - b. Perform necessary calculations to establish the amounts of ingredients needed

- c. Identify equipment and utensils needed.
  - d. Don the proper attire and properly wash hands and arms.
  - e. Clean the compounding area and needed equipment .
  - f. Only one (1) prescription can be compounded at a time in the specified compounding area.
  - g. Assess weight variation, adequacy of mixing, clarity, odor, color consistency, and pH as appropriate of the completed preparation.
  - h. Annotate the compounding and formulation records.
  - i. Label the prescription containers appropriately.
  - j. Sign and date the prescription affirming that all procedures were carried out to ensure uniformity, identity, strength, quantity, and purity.
  - k. Thoroughly clean the facility and all equipment immediately when finished.
4. **Compounding Process for Compounded Sterile Preparations.** Compounders are to use the following steps to minimize error and maximize the prescriber's intent, specifics can be found in *Pharmaceutical Compounding-Sterile Compounds* (USP 797):
- a. Judge the suitability of the prescription of compounded sterile preparation in terms of safety and intended use.
  - b. Perform necessary calculations to establish the amounts of ingredients needed.
  - c. Identify equipment and utensils needed for the preparation of the compounded sterile preparation.
  - d. Sterile compounding areas and critical areas must be structurally isolated from other areas designated to avoid unnecessary traffic and airflow disturbances, separate from non-sterile compounding areas, and restricted to qualified compounding personnel.
  - e. Policies and procedures must be established for personnel cleaning and garbing for protection and avoidance of contamination including, but not limited to:
    - i. Remove all jewelry from hands and arms.
    - ii. Wash hands and arms.
    - iii. Abstain from gum chewing, candy or food items in or near the compounding area.
  - f. Clean and sanitize the compounding area and needed equipment.
    - i. At the beginning of each day and after spills, the surface of the compounding area should be cleaned with purified water to remove water

soluble residues, then immediately with seventy percent (70%) isopropyl alcohol, or another antimicrobial agent, using non-linting wipe.

- ii. All rubber stops of vials and bottles and the neck of ampules must be sanitized with seventy percent (70%) isopropyl alcohol prior to introduction of a needle or spike for the removal of a product.
- iii. After procedures are completed, used syringes, bottle, vials, and other supplies must be removed.
- g. Only one (1) prescription can be compounded at a time in the specified compounding area.
- h. Assess weight variation, adequacy of mixing, clarity, odor, color consistency, and pH as appropriate of the completed compounded sterile preparation.
- i. If preparing in anticipation of future orders, annotate the compounding and formulation records.
- j. Label the prescription containers appropriately.
- k. Sign and date the prescription affirming that all procedures were carried out to ensure uniformity, identity, strength, quantity, purity, and sterility

## 5. RISK LEVELS OF COMPOUNDED STERILE PREPARATIONS

Risk levels are assigned according to the corresponding probability of contaminating a preparation with microbial organisms, spores, and endotoxins, or chemical and physical contamination such as foreign chemicals and physical matter.

- a. Low risk preparations are compounded sterile preparations under the following conditions:
  - i. Compounded with aseptic manipulations entirely with ISO Class 5 or superior air quality using only sterile ingredients, products, components, and devices.
  - ii. 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.
  - iii. Manipulations must be 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.
  - iv. 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, or forty-five (45) days in solid frozen state, between -25°C and -10°C, unless supported by manufacturer or medical literature.
  - v. Examples of Low Risk compounded sterile preparations include:

1. Single volume transfers of sterile dosage forms from ampules, bottles, bags, and vials with sterile needles.
  2. Simple aseptic measuring and transferring with not more than three (3) packages of manufactured sterile products including and infusion or diluents solutions. The solution content of ampules must be passed through a sterile filter to remove any particles.
- vi. Low Risk Quality Assurance programs must include 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 in addition to annual Media Fill Tests by each of the compounding personnel specific for Low-Risk Preparation.
- b. Medium Risk Preparations are compounded sterile preparations prepared aseptically under Low-Risk Level conditions and one (1) or more the following conditions exist:
- i. Multiple small doses of sterile products are combined or pooled to prepare the sterile preparation that will be administered either to multiple patients or to one (1) patient on multiple occasions.
  - ii. The compounding process includes complex aseptic manipulations other than the single volume transfer.
  - iii. The compounding process requires unusually long duration such as that required to complete dissolution.
  - iv. 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 unless and for forty-five (45) days in solid frozen state, between -25<sup>0</sup>C and -10<sup>0</sup>C, unless supported by manufacturer or medical literature.
  - v. Examples of Medium Risk compounded sterile preparations include:
    1. Total parenteral nutrient fluids using manual or automated devices.
    2. Filling reservoirs of injection and infusion devises with more than three (3) sterile drug products.
    3. Transfer volumes from multiple ampules or vials into one (1) or more final sterile containers.
  - vi. Medium Risk Quality Assurance includes all elements of Low Risk compounded sterile preparations in addition to annual Media Fill Tests by each of the compounding personnel specific for Medium Risk preparations.

- c. High Risk Preparations are compounded sterile preparations are either contaminated or at a high risk to become contaminated.
  - i. When the following criteria take place, the preparations will be considered High Risk:
    - 1. If non-sterile ingredients are incorporated or a non-sterile is employed before terminal sterilization.
    - 2. If there has been exposure to air quality inferior to ISO Class 5 for more than one (1) hour by the sterile contents, sterile surfaces of devices and containers, or a lack of effective antimicrobial preservatives.
    - 3. If personnel are improperly garbed and gloved.
    - 4. If non-sterile water-containing preparations are stored for more than six (6) hours before being sterilized.
    - 5. If the storage periods have exceeded twenty-four (24) hours at controlled room temperature; three (3) days at refrigerated temperature or forty-five (45) days in solid frozen state, between -25°C and -10°C, unless supported by manufacturer or medical literature.
  - ii. All non-sterile measuring, mixing, and purifying devices must be rinsed thoroughly with sterile pyrogen free water, then thoroughly drained or dried immediately before use for High Risk compounding.
  - iii. All High Risk solutions subjected to terminal sterilization are pre-filtered by passing through a filter not larger than 1.2 microns. Sterilization of High Risk Level solutions by filtration should be performed with a sterile 0.2 micron normal pore size filter entirely within and ISO Class 5 or superior air quality environment.
  - iv. An example of High Risk compounded sterile preparations is dissolving non-sterile bulk drug and nutrient powders to make solutions that will be terminally sterilized.
  - v. High Risk Quality Assurance includes all elements of Low-Risk compounded sterile preparations in addition to bi-annual Media Fill Tests by each of the compounding personnel specific for High Risk preparations.

## 6. Facilities for Sterile Compounding

- a. The facilities that engage in Low and Medium Risk preparations must meet the standards including but not limited to:
  - i. Limits access and activities to qualified personnel, materials, and processes that are directly related to productions of sterile compounded products.

- ii. Structurally isolated from other areas including other non-sterile compounding areas.
- iii. Designed to avoid unnecessary traffic and airflow disturbances.
- iv. Of sufficient size to accommodate at least one primary engineering control device.
- v. Able to provide storage and preparation of drugs, supplies, and finished products under appropriate temperature, light, moisture, sanitation, ventilation, and security conditions.
  - 1. Ventilation must maintain appropriate ISO Class designations of each separate working area and avoid disruption and cross-room currents.
  - 2. Walls, floors, and ceilings, along with fixtures, counters, shelves, and cabinets must be resistant to damage that could occur from routine disinfection with cleaning agents.
  - 3. Procedures and policies must be established for personnel in the sterile compounding area regarding proper hand washing, proper donning of appropriate attire, and restrictions on items and practices within the compounding area.
- b. The facilities that engage in High-Risk preparations must meet the standards including but not limited to:
  - i. All of the facilities listed for Low and Medium-Risk preparations.
  - ii. Buffer areas must have the following standards; but not limited to:
    - 1. Maintain ISO Class 7 or superior air quality during compounding activity.
    - 2. Be physically divided or have designated boundaries that separate it from the anteroom with appropriate ventilation that assures contamination from the anteroom does not enter the buffer area through utilization of filtered Unidirectional Flow and principles of air displacement.
    - 3. Must not have unsealed windows or doors that connect to the outdoors, or be located adjacent to a construction site, warehouse, or food preparation area.
    - 4. Must 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.
    - 5. The construction, arrangement, and ventilation must not allow conditions that could adversely affect compounding, such as

aberrant heating, cooling, door-drafts, and personnel traffic air currents.

6. Policies and procedures must be established for cleaning and sanitizing.

- a. Cleaning and sanitizing must occur in the buffer area first, then move to the anteroom and other areas.
- b. All cleaning and sanitizing must not occur simultaneously with aseptic operations.
- c. Storage shelving cleaned and sanitized weekly.
- d. Floors must be mopped daily. Trash must be collected and removed daily.

iii. Anteroom must have the following standards, but not limited to:

- 1. Located adjacent to the buffer area and maintained at ISO Class 8 or superior air quality during compounding activity.
- 2. Must be established with the purpose of unpacking and disinfecting supplies for storage and areas to support hand and arm washing and donning of appropriate attire.
  - a. Hands free sinks and closed system soap dispenser must be used for hand and arm washing.
- 3. Procedures must be established for cleaning and sanitizing.
  - a. Must occur secondary to cleaning and sanitizing.
  - b. All cleaning and sanitizing must not occur simultaneously with aseptic operations.
  - c. Counters and easily cleanable work areas must be cleaned daily.
  - d. Supplies and equipment must be removed and wiped with a sanitizing agent weekly.
  - e. Floors must be mopped daily.
  - f. Storage shelving must be emptied and cleaned and sanitized monthly.

c. Storage areas for Sterile Preparations

- i. When ingredients and finished preparations are exposed to temperatures warmer than the warmest labeled limit, but not exceeding forty degrees Celsius (40°C) for more than four (4) hours, they must be discarded.

7. Equipment Specific for Sterile Compounding



- a. Primary Engineering Controls (i.e. Laminar Airflow Workbenches, Biological Safety Cabinets, Compounding Aseptic Isolators, and Compounding Aseptic Containment Isolators) must be used to prepare all sterile preparations except those compounded for immediate-use and must be capable of maintaining ISO Class 5 or superior air quality during normal compounding activity.
    - i. Must be placed in the buffer area, if required, where HEPA filters are employed and the air quality is maintained at ISO Class 7 or superior.
    - ii. Must be maintained as continuously powered on, if turned off; however, allow the blowers to run continuously for at least 30 minutes before using.
  - b. Environmental Monitoring
    - i. Barrier certification for proper functioning and ISO Class 5 air flow requirements must be tested every 6 months and after relocation of the primary engineering control.
    - ii. Maintain the air quality of the buffer area and anteroom, if required, at ISO Class 7 and ISO Class 8, respectively must be tested every 6 months and after any renovation of the compounding area
    - ii. Where High Risk sterile preparations are being compounded air sampling via sterile nutrient agar plates or suitable electric air samplers must be performed monthly at locations judged by compounding personnel to be the most prone to contamination during compounding activities.
      - 1. Instructions and verification of air sampling devices must be located with the equipment.
      - 2. Passive exposure processes of sterile nutrient agar settling plates can be found in USP Standards
- 8. Immediate-Use Preparations.** Immediate-use preparations must not be medium-risk level or high-risk level compounded sterile preparations. Immediate-use Preparations must be designed for immediate administration and are exempt from the requirements described for Low-Risk Level compounded sterile preparations only when all the following criteria are met:
- a. The compounding process involves simple transfer of no more than three (3) commercially manufactured packages of sterile non-hazardous products from the manufacturer's original containers and no more than two (2) entries into any one (1) container.
  - b. Unless required for the preparation, the compounding procedure is a continuous process to exceed one (1) hour.
  - c. During preparation and prior to administration, aseptic technique must be followed. At no point are critical sites and ingredients of the compounded sterile preparation directly exposed to contact contamination. If not immediately administered, the finished compounded sterile preparation is under continuous supervisions to minimize the potential for contact with non-sterile surfaces.

introduction of particulate matter, or biological fluids, mix-ups with other products, and direct contact of outside surfaces.

- i. Administration begins no later than one (1) hour following the start of the preparation.
  - 1. Must be immediately and completely administered by the person who prepared it, or immediate and complete administration is witnessed by the preparer.
  - 2. If administration has not begun within one (1) hour following the start of preparing the compounded sterile preparation, must be promptly, properly, and safely discarded; not be stored for later use.