**Modified As a result of May 2011 Board meeting and discussion at Convention 61-02-01-03. Pharmaceutical compounding standards; again on September 13th, 2011 by Katie Miller and reviewed at the September 17th, 2011 Board Meeting and revised as a result of the rule hearing comments November 17, 2011.** 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 preparation label that is intended to indicate to the patient or caregiver a time beyond which the contents of the preparation are not recommended to be used. The beyond-use date is determined from the date and 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 does not include: **tablet splitting**; reconstitution of oral or topical products as intended by the manufacturer; repackaging of non-sterile dosage forms for redistribution, dispensing or administration. Compounding includes:
      (1) Preparation of drugs or devices in anticipation of prescription drug orders based on routine, regularly observed prescribing patterns.
      (2) The addition of one (1) or more ingredients to a commercial product as a result of a licensed practitioner's prescription drug order.
      (3) Preparation of drugs or devices for the purposes of, or as an incident to, research, teaching, or chemical analysis.
      (4) Categories of compounding.
         (i) Category 1 – Non-sterile Simple.
            a. Simple – Mixing of two (2) or more commercial products.
            b. Complex – Compounding with the bulk drug substances or when calculations are required.
         (ii) Category 2 – Sterile Compounds. 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. Immediate-Use Compounded Sterile Preparations
               (1) 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:

I. 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.

II. Unless required for the preparation, such as a long dissolution time, the compounding procedure is a continuous process not to exceed one (1) hour.

III. 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 supervision 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.

IV. Administration begins no later than one (1) hour following the start of the preparation and must be completed within 12 hours.

V. Must be immediately and completely administered by the person who prepared it, or immediate and complete administration is witnessed by the preparer**, the CSP 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 CSP, 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 must be promptly, properly, and safely discarded and not stored for later use.

b. Low- Risk – Level Compounded Sterile Preparations

(1) 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 -25C and -10C, 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 infusion and 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.

c. Medium- Risk Level Compounded Sterile Preparations

(1) Medium Risk Preparations are compounded sterile preparations prepared aseptically under Low-Risk Level conditions and one (1) or more of 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 and for forty-five (45) days in solid frozen state, between -25C and -10C, unless supported by manufacturer or medical literature.

V. Examples of Medium Risk compounded sterile preparations include:
   a. Total parenteral nutrient fluids using manual or automated devices.
   b. Filling reservoirs of injection and infusion devises with more than three (3) sterile drug products.
   c. 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.

d. High- Risk – Level Compounded Sterile Preparations

(1) High Risk Preparations are compounded sterile preparations that 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:

a. If non-sterile ingredients, including manufactured products not intended for sterile routes of administration (e.g., oral) are incorporated or a non-sterile device is employed before terminal sterilization.

b. 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.

c. If personnel are improperly garbed and gloved.

d. If non-sterile water-containing preparations are stored for more than six (6) hours before being sterilized.

I. Storage periods cannot exceed twenty-four (24) hours at controlled room temperature; three (3) days at refrigerated temperature or forty-five (45) days in solid frozen state, between -25C and -10C, 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 an 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 semi-annual Media Fill Tests by each of the compounding personnel specific for High Risk preparations.

( iii.) Category 3 – Radiopharmaceuticals. See NDAC Article 61-05.

(iv.) Category 4 – Veterinary pharmaceuticals.

a. Standards for veterinary pharmaceuticals are consistent with all parts NDAC 61-02-01-03.

f) "Compounded Sterile Preparation" (CSP) will include all of the following:

(1) Preparations prepared according to the manufacturer's labeled instructions and other manipulations when manufacturing sterile products that expose the original contents to potential contamination.

(2) Preparations containing non-sterile ingredients or employing non-sterile components or devices that must be sterilized before administration.

(3) 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 or registered 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. This may be the pharmacist on duty or the pharmacist-in-charge.

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) **"Hazardous Drug" are those which studies in animals or humans indicate that exposures to them have a potential for causing cancer, development or reproductive toxicity, or harm to organs.**

m) "ISO Class" is the description of an atmospheric environment characterized by the number of particles 0.5 microns of larger, within a cubic foot of air.
   (1) "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 ingredient 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%) Sterile Isopropyl " or IPA is a antimicrobial 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.

(1) 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

(2) Compounding personnel must be familiar with USP Standards and North Dakota regulations including but not limited to:

i. Certifying all prescription orders.

ii. 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.

iii. 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.

iv. 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.

v. 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.

(3) 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:

(1) Be familiar with Pharmaceutical Compounding – Non-Sterile Compounding (USP 795), Pharmaceutical Compounding – Sterile Compounding (USP 797), and Pharmaceutical Calculations in Prescription Compounding (USP 1160).

(2) Be familiar with all procedures relating to compounding specific to your facility, equipment, personnel, compounding process, evaluation, packaging, storage, and dispensing.

(3) Compounding supervisors must be responsible to follow the instructions below to show that personnel are appropriately trained:

i. Demonstrate compounding procedures to compounding personnel.
ii. Guide personnel through the compound process with assistance.
iii. Observe personnel performing a compound without assistance but under supervision.
iv. Review the compound, correct mistakes and answer questions concerning compounding and associated processes.
v. Confirm verbal and functional knowledge of the personnel concerning compounding.
vi. Have personnel perform a compounding procedure without supervision, yet checking off the final preparation.
vii. If properly compounded and when satisfied, sign the documentation records confirming appropriate training.
viii. Continually monitor the work of the personnel including calculations.

(4) The pharmacist on duty and the pharmacist-in-charge 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) Non-Sterile Drug Compounding Facilities must include all of the following:

(1) Compounding facilities and equipment that are clean, accurate, of appropriate size and construction and properly inspected and the compounding environment is properly maintained, isolated and inspected.

i. Personnel must have a written plan and schedule while maintaining records of cleaning and disinfecting.

(2) Aseptic processes must be conducted in an area separate from the area used for non-sterile preparations.

(3) 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.

(4) Heating, ventilation, and air conditioning systems are controlled to avoid decomposition of chemicals.

(5) 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.

i. Plumbing system should be free of defects that could contribute to contamination of the compounded product.

(6) All areas maintained in a clean and sanitary condition; trash, sewage and other refuse should be disposed of in a safe and timely manner.

(7) 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) Non-Sterile Drug Compounding Equipment.

(1) 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.

(2) 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.

(3) 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 for Non-Sterile Preparations.

(1) Containers and container closures.

i. Must meet USP requirements found under Containers – Glass (USP 660), Containers – Plastic (USP 661), and Containers – Performance Testing (USP 671).

ii. 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).

iii. Must be stored off the floor, handled and stored to prevent contamination.

iv. Must be stored in a way to facilitate inspection and cleaning

v. Must be constructed in such a way that surfaces are not reactive, additive, or absorptive.

vi. The containers and closures shall be of suitable material so as not to alter the quality, strength, or purity of the compounded drug.

(2) Storage area.

ii. Compounded preparations must be stored strictly in accordance with the conditions stated on the label of ingredient products and finished preparations.

iii. 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.

b. Controlled cold temperature, 2° C to 8°C.

c. Controlled freezing temperature, -25° C to -10° C.

(3) Beyond-Use dates for Non-Sterile Preparations

i. 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.

ii. Compounders establish a beyond-use date considering the nature of the drug, degradation mechanism, purposed container, expected storage conditions, and intended duration of therapy.

iii. Beyond-use dating is assigned conservatively to all compounded preparations. Immediate-use preparations do not require a beyond-use date.

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 is 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.

g) Compounding Controls for Non-Sterile Preparations.

(1) 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.

(2) Procedures must be established that give a description of the following:

i. Components and their amounts.

ii. Order of component additives.

iii. Compounding process.

iv. Drug product.

v. Required equipment and utensils including container and closure system.

(3) The compounder will accurately weigh, measure, and subdivide all components as appropriate.

i. Compounder will check and re-check each procedure at each point of the process to ensure that each weight or measure is correct.

ii. 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.

(4) The compounder must write procedures that describe the tests or examinations that prove uniformity and integrity of the compounded preparations.

(5) Control procedures must be established to monitor the output and validate the performance of compounding personnel that affect variability of final preparations such as:

i. Capsule weight variation.

ii. Adequacy of mixing to assure uniformity and homogeneity.

iii. Clarity, completeness, or pH of solutions.

(6) The compounder must establish an appropriate beyond-use date for each compounded preparation.

(7) Facilities engaging in compounding must have a specifically designated and adequate space for orderly compounding, including the placement and storage of equipment and materials.

h) Labeling of Non-Sterile Preparations.

(1) 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, plus the beyond-use date and assigned lot number.

(2) The compounder will label any excess compounded products so as to refer to the formula used.

(3) 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:

i. Complete list of ingredients or preparation time and reference or established chemical name or generic name.
ii. Dosage form.
iii. Strength.
iv. Preparation date and time.
v. Inactive ingredients.
vi. Batch or lot number.
vii. Assigned beyond-use date.
viii. Storage conditions

(4) The compounder must examine the preparation for correct labeling after completion.

i) Records and Reports for Non-Sterile Preparations.

(1) Records must be maintained including, but not limited to, a hard copy of the prescription with formulation and compounding records.

(2) Adequate records of controlled substances used in compounds.

(3) All records must be kept for 5 years according to North Dakota state law and be available for inspection.

(4) Formulation Record provides a consistent source document for preparing the preparation to allow another compounder to reproduce the identical prescription at a future date and must list:

i. Name, strength, and dosage form of the preparation compounded.
ii. All ingredients and their quantities.
iii. Equipment needed to prepare the preparation, when appropriate.
iv. Mixing instructions including order of mixing, mixing temperatures, and other valid instructions such as duration of mixing.
v. Assigned beyond-use date.
vi. Container used in dispensing.
vii. Storage requirements.
viii. Any quality control procedures.

(5) Compounding Record documents the actual ingredients in the preparation and the person responsible for the compounding activity and includes:

i. Name and strength of the compounded preparation.
ii. The formulation record reference.
iii. Sources and lot numbers of the ingredients.

iv. Total number of dosage units compounded.
v. Name of compounding personnel who prepared the preparation.
vi. The date of preparation.
vii. The assigned internal identification number, lot number and prescription number(s).
viii. Assigned beyond-use date.
ix. Results of all quality control procedures.

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

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 or compounding record 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 for the 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:
      (1) Remove all jewelry from hands and arms, no artificial nails allowed,
      (2) Don proper garb including shoe covers, head and facial hair covers, face mask, and non-shedding gown, **if the manufacture of the primary engineering control has research and documentation demonstrating that specific things are not necessary, they are not required.**

(3) Wash hands and arms prior to donning powder-free gloves.
(4) Abstain from gum chewing, candy or food items in or near the compounding area.

f) Clean and sanitize the compounding area and needed equipment.
(1) At the beginning each work shift and after spills, the surface of the compounding area should be cleaned with sterile water to remove water soluble residues, then immediately with seventy percent (70%) sterile isopropyl alcohol, or another antimicrobial agent, using non-linting wipe.
(2) All rubber stops of vials and bottles and the neck of ampules must be sanitized with seventy percent (70%) sterile isopropyl alcohol prior to introduction of a needle or spike for the removal of a product.
(3) After procedures are completed, used syringes, bottle, vials, and other supplies must be removed.
(4) Only one (1) preparation can be compounded at a time in the specified compounding area.
(5) Assess weight variation, adequacy of mixing, clarity, odor, color consistency, and pH as appropriate of the completed compounded sterile preparation.
(6) If preparing in anticipation of future orders, annotate the compounding and formulation records with date of preparation, ingredients and their lot numbers, total number of dosage units prepared, initials of preparer and pharmacist who checked the batch, assigned beyond-use date and assigned internal batch or lot number.
(7) Label the preparation containers with name and strength of preparation, internal batch or lot number, appropriate beyond use date.,
(8) Sign and date the compounding record affirming that all procedures were carried out to ensure uniformity, identity, strength, quantity, purity, and sterility.

5. Facilities for Sterile Compounding

a) The facilities that engage in Low and Medium Risk preparations must meet the standards including but not limited to:
(1) Limits access and activities to qualified personnel, materials, and processes that are directly related to productions of sterile compounded products.
(2) Structurally isolated from other areas including other non-sterile compounding areas.
(3) Designed to avoid unnecessary traffic and airflow disturbances.
(4) Of sufficient size to accommodate all primary engineering control devices, as required by the compounding risk level.
(5) Able to provide storage and preparation of drugs, supplies, and finished products under appropriate temperature, light, moisture, sanitation, ventilation, and security conditions.
i. Ventilation must maintain appropriate ISO Class designations of each separate working area and avoid disruption and cross-room currents.
ii. 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.
iii. Policies and procedures 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.

iv. Policies and procedures must be established for cleaning and sanitizing.
   a. All cleaning and sanitizing must not occur simultaneously with aseptic operations.
   b. Counters and easily cleanable work surfaces cleaned and sanitized daily.
   c. Storage shelving cleaned and sanitized monthly.
   d. Floors must be mopped daily. Trash must be collected and removed daily.

b) The facilities that engage in High-Risk preparations must meet the standards including but not limited to:

(1) All of the facilities listed for Low and Medium-Risk preparations.

(2) Buffer areas must have the following standards; but not limited to:

i. Maintain ISO Class 7 or superior air quality during compounding activity.

ii. 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.

iii. 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.

iv. 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.

v. 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.

vi. 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.

(3) Anteroom must have the following standards, but not limited to:

i. Located adjacent to the buffer area and maintained at ISO Class 8 or superior air quality during compounding activity.

ii. 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.

iii. Hands free sinks and closed system soap dispenser must be used for hand and arm washing.

iv. Procedures must be established for cleaning and sanitizing.
   a. Compounding 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 and walls must be emptied and cleaned and sanitized monthly.

(4) 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 (40C) for more than four (4) hours, they must be discarded.

6. Equipment Specific for Sterile Compounding

~~a)~~ Primary Engineering Controls~~: such as: 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.~~

(1) Are not required for immediate use compounding.

(2) One primary engineering control is required for compounding low and medium risk preparations.

(3) For compounding high risk preparations the primary engineering control must be placed in a buffer area, if required, where HEPA filters are employed and the air quality is maintained at ISO Class 7 or superior. If the manufacturer has research and documentation demonstrating that the primary engineering control does not need to be in a buffer area, this is not required. If used, the primary engineering control must be maintained as continuously powered on, if turned off however, the blowers must be allowed to run continuously for at least 30 minutes before using.

b) Environmental Monitoring

(1) 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.

(2) 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

(3) Where High Risk sterile preparations are being compounded air sampling via sterile nutrient agar plates or suitable electric air samplers must be performed semi-annually at locations judged by compounding personnel to be the most prone to contamination during compounding activities.

(4) Instructions and verification of air sampling devices must be located with the equipment.

(5) Passive exposure processes of sterile nutrient agar settling plates can be found in USP Standards

~~**6. A policy and procedure manual is required. Policies and procedures must be in place pertinent to the level of volume and complexity of the compounding operation of the practice.**~~

7. Poison record book and suitable prescription files.

8. Suitable current reference sources either in book or electronic data form (available in the pharmacy or on-line) which might include the United States Pharmacopeia and National Formulary, the United States Pharmacopeia Dispensing Information, Facts & Comparisons, Micro Medex, the ASHP Formulary, or other suitable references determined by the board which are pertinent to the practice carried on in the licensed pharmacy.

9. 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.

10. The board of pharmacy recognizes that the equipment needed will depend on the type of pharmaceutical services offered, and therefore, variations for required equipment may be granted by the board of pharmacy.

11. Hazardous drugs as compounded sterile products (CSPs)
    a) Hazardous drugs, when prepared for administration only, shall be prepared under conditions that protect the health care worker and other personnel in the preparation and storage areas.
    b) Hazardous drugs shall be stored **and prepared** separately from other ~~inventory~~ **non-hazardous drugs** in a manner to prevent contamination and personnel exposure.
    c) Hazardous drugs shall be handled with caution at all times using appropriate chemotherapy gloves during receiving, distribution, stocking, inventorying, preparation for administration and disposal.
    d) 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 specified in this chapter.
    e) All hazardous drugs shall be prepared in a Biological Safety Cabinet (BSC) or a Compounding Aseptic Containment Isolator (CACI). The BSC or CACI shall be placed in an ISO Class 7 area that is physically separated (i.e., a different area from other preparation areas) and with negative pressure to adjacent positive pressure ISO Class 7 or better ante-areas. If the CACI is used outside of a buffer area, the compounding area shall maintain a minimum negative pressure of 0.01 inch water column and have a minimum of 12 air changes per hour.
        (1) When closed-system vial-transfer devices (CSTDs) are used, they shall be used within the ISO Class 5 environment of a BSC or CACI. This may be done in a non-negative pressure room when this two tier containment method is used.
        (2) Appropriate personnel protective equipment shall be worn when compounding hazardous drugs.
    f) All personnel who compound hazardous drugs shall be fully trained in the storage, handling and disposal of these drugs. This training shall occur prior to preparing or handling hazardous drugs and this training shall be by testing specific hazardous drug handling techniques. Such training shall be documented for each person at least annually.

**All compounders of sterile and non-sterile products must be in compliance with this rule by January 1, 2015.**