

Rules for Compounded Sterile Preparations (CSPs)

Introduction:

Despite the attention in this document to describe the provision, maintenance, and evaluation of air quality, the avoidance of direct or physical contact contamination is paramount. Since it is acknowledged that direct or physical contact of critical sites of compounded sterile preparations (CSPs) with containments, especially microbial sources, poses the greatest possibility of risk to patients.

This document provides *minimum practice and quality standards* for CSPs of drugs and nutrients based upon current scientific information and best sterile compounded practices. The use of technologies, techniques, materials, and procedures other than those specifically described herein is not prohibited, so long as they have been proven to be equivalent or superior to the included standards.

Section I. Purpose and Scope

The purpose of this section is to describe conditions and practices to prevent harm, including death, to patients that could result from any of the following:

1. Microbial contamination (non-sterility)
2. Excessive bacterial endotoxins
3. Variability in the intended strength of correct ingredients that exceeds Compendial limits.
4. Unintended chemical and physical contaminants
5. Ingredients of inappropriate quality in compounded sterile preparations (CSPs)

These rules are intended to apply to all persons who compound CSPs, notwithstanding the location of the patient. They shall apply to places where CSPs are prepared (e.g., home, hospital, nursing home, hospice, doctor's office).

All Compounding Pharmacies, Pharmacists, and Supervising Personnel shall practice in accordance with these Rules, the New York State Board of Pharmacy's statutes, rules, and regulations, and the current United States Pharmacopeia-National Formulary (USP-NF) chapters on Compounding and sterile pharmaceutical preparations.

For clarity, Compounded Sterile Preparations (CSPs) include any of the following:

1. Compounded biologics, diagnostic, drugs, nutrients, and radiopharmaceuticals, including but not limited to the following dosage forms that must be sterile when they are administered to patients; aqueous bronchial and nasal inhalations, baths and soaks for live organs and tissues, injections (e.g. colloidal dispersions, emulsions, solutions,

Rules for Compounded Sterile Preparations (CSPs)

suspensions), irrigations for wounds and body cavities, ophthalmic drops and ointments, and tissue implants.

Commercially available sterile products that are either prepared strictly according to the instructions appearing in the manufacturers' approved labeling (product package inserts) or prepared differently than published in such labeling.

Section II. The Responsibility of Compounding Personnel

Compounding Personnel are responsible for ensuring that CSPs are accurately identified, measured, diluted, and mixed and are correctly purified, sterilized, packaged, sealed, labeled, stored, dispensed, and distributed. These performance responsibilities include maintaining appropriate cleanliness conditions, and providing labeling and supplementary instructions for proper clinical administration of CSPs.

Qualified licensed healthcare professionals who supervise compounding and dispensing of CSPs (Supervising Personnel) shall be defined as a licensed New York State professional holding one of the following credentials;

A Registered Pharmacist

A Registered Professional Nurse/Nurse Practitioner/Midwife

A Physician or Physician Assistant

Supervising Personnel shall ensure that through either direct measurement or appropriate informational sources that the CSPs prepared and dispensed maintain their labeled strength within monograph limits until their labeled Beyond-Use Date (BUD).

Supervising Personnel shall, when appropriate, obtain and evaluate the results of testing for identity, strength, purity, and sterility before a CSP is dispensed.

Supervising Personnel shall ensure the following core objectives are achieved:

1. All personnel who compound CSPs are adequately skilled, educated, instructed, and trained to correctly perform and document the following:
 - a. Perform aseptic hand hygiene and disinfect non-sterile compounding surfaces;
 - b. Select and appropriately don protective garb;
 - c. Maintain or achieve sterility of CSPs in ISO Class 5 PEC devices and protect personnel and compounding environments from contamination;
 - d. Identify, weigh, and measure ingredients; and
 - e. Manipulate sterile products aseptically, sterilize high-risk level CSPs, and label and quality inspect CSPs.

Rules for Compounded Sterile Preparations (CSPs)

2. Ingredients have their correct identify, quality, and purity.
3. Opened or partially used packages of ingredients are properly stored under restricted access conditions consistent with their package insert.
4. Water-containing CSPs that are non-sterile during any phase of the compounding procedure are sterilized within 6 hours after completing the preparation in order to minimize the generation of bacterial endotoxins.
5. Sterilization methods achieve sterility of CSPs while maintaining the labeled strength of active ingredients and physical integrity of packaging.
6. Measuring, mixing, sterilizing, and purifying devices are clean, appropriately accurate, and effective for their intended use.
7. Potential harm from added substances and differences in the rate and extent of bioavailability of active ingredients from other than oral route of administration are carefully evaluated before such CSPs are dispensed and administered.
8. Packaging selected for CSPs is appropriate to preserve the sterility and strength until the labeled BUD.
9. While being used, the compounding environment maintains the sterility, or the pre-sterilization purity, whichever is appropriate, of the CSP.
10. Labels on CSPs list the names and amounts or concentrations of active ingredients, and the labels or labeling of injections consistent with prevailing regulation.
 - a. Before being dispensed or administered the clarity of the solutions must be visually confirmed.
 - b. Specific release criteria are reviewed to ensure the accuracy and safety of the CSPs.
11. Beyond-Use Dates for all CSPs are assigned on the basis of direct testing or extrapolation from reliable literature and other documentation.
12. Procedures for measuring, mixing, dilution, purification, sterilization, packaging, and labeling conform to the correct sequence and quality established for the specified CSP.
13. Deficiencies in compounding, labeling, packaging, and quality testing, and inspection can be rapidly identified and corrected.
14. When time and personnel availability permit, compounding manipulations and procedures are separated from post-compounding quality inspection and review before CSPs are dispensed.

Section III. CSP Microbial Contamination Risk Levels

The characteristics described below are intended as a guide to the breadth and depth of care necessary in compounding, but are not intended to be complete. Compounding personnel who engage in these activities or supervise the compounding of CSPs are responsible for determining the procedural and environmental quality practices and attributes that are necessary for the risk-level they assign to specific CSPs.

Rules for Compounded Sterile Preparations (CSPs)

These risk-levels apply to the quality of CSPs immediately after the final aseptic mixing or filling, or immediately after the final sterilization, unless precluded by the specific characteristics of the preparation.

The three contamination categories for CSPs described herein are assigned primarily according to the potential for microbial contamination during the compounding of low-risk level CSPs and medium-risk level CSPs or the potential for not sterilizing high-risk level CSPs, and of which would subject patients to risk of harm, including death.

The appropriate risk-level (LOW, MEDIUM, or HIGH) is assigned according to the corresponding probability of contaminating a CSP with:

1. Microbial contamination (microbes, spores, endotoxins)
2. Chemical or physical contaminations (foreign chemicals, physical matter)

A. LOW RISK CONDITIONS

1. The CSPs are compounded with proper aseptic manipulations entirely within an ISO Class 5 or better air quality using only sterile ingredients, commercially available products, components, and devices.
2. This risk-level compounding involves only simple transfer, measuring, and mixing manipulations using no more than three commercially manufactured packages of sterile products and not more than two entries into any one sterile container, or package (e.g. bag or vial) of sterile product or administration container or device to prepare the CSP.
3. Manipulations are limited to aseptically opening ampoules, penetrating disinfected stoppers on vial or other attachment devices with sterile needles and syringes, and transferring sterile liquids in sterile syringes to sterile administration devices, package containers of other sterile products, and containers for storage and dispensing.
4. For LOW-risk CSPs in the absence of passing a sterility test (as described in USP General Chapter <71>) storage periods cannot exceed the following time periods: **48 hours at room temperature and 14 days under refrigeration.**

A1. LOW RISK LEVEL CSPs with a 12-HOUR or LESS Beyond Use Date

If the Primary Engineering Control (PEC) is a Compounding Aseptic Isolator (CAI) or Compounding Aseptic Containment Isolator (CACI) that does not meet the requirements described in **Section V. Physical Requirements** or is a laminar air-flow workbench (LAFW) or a biological safety cabinet (BSC) that

Rules for Compounded Sterile Preparations (CSPs)

cannot be located within and ISO Class 7 buffer area, then ONLY low-risk-level non-hazardous and radio-pharmaceutical CSPs pursuant to a physician's order for a specific patient may be prepared, and administration of such CSPs shall commence within 12-hours of preparation or as recommended in the manufacturers' package insert, whichever is LESS.

Compounding personnel must recognize that the absence of the surrounding ISO Class 7 buffer environment in a general uncontrolled environment increases the potential of microbial contamination.

Low risk-level CSPs with a 12-hour or less BUD shall meet ALL of the following criteria:

1. Primary Engineering Controls (LAFWs, BSCs, CAIs, and CACIs) shall be certified and maintain ISO Class 5 and shall be located in a segregated compounding area restricted to sterile compounding activities that minimize the risk of CSP contamination.
2. The segregated compounding area shall be located in an area which has no unsealed windows or doors that connect to the outdoors, areas of high traffic flow, or that is adjacent to construction sites, warehouses, or food preparation.
3. Personnel shall follow the organization's standard operating procedures described in their policy manual for proper aseptic technique, gowning, garbing, and gloving.
4. Sinks shall not be located adjacent to the ISO Class 5 PEC.
5. These PECs shall also follow the organization's standard operating procedures for:
 - a. Cleaning and disinfecting
 - b. Personnel training and competency evaluation
 - c. Environmental sampling & testing

B. MEDIUM RISK CONDITIONS

When CSPs are compounded aseptically under low-risk conditions and one or more of the following conditions exists, such CSPs are at a medium risk of contamination:

1. Multiple individual or small doses of sterile products are combined or pooled to prepare a CSP that will be administered whether to multiple patients or to one patient on multiple occasions.

Rules for Compounded Sterile Preparations (CSPs)

2. Compounding processes include complex aseptic manipulations other than a single volume transfer.
3. Compounding processes that require unusually long durations to completely dissolve or homogeneously mix the CSP.
4. For medium-risk CSPs in the absence of passing sterility test (as described in USP General Chapter <71>) storage periods cannot exceed the following time periods: **30 hours at room temperature and 9 days under refrigeration.**

C. HIGH RISK CONDITIONS

CSPs compounded under any of the following conditions are considered to be either contaminated or at a high risk of being contaminated:

1. Any use of 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.
2. Any of the following are exposed to air quality worse than ISO Class 5 for more than one hour:
 - a. Sterile contents of commercially manufactured products.
 - b. CSPs that lack effective antimicrobial preservatives, AND
 - c. Sterile surfaces of devices and containers for the preparation, transfer, sterilization, and packaging of CSPs.
3. Compounding personnel are improperly garbed and gloved.
4. Non-sterile water-containing preparations are stored for more than six (6) hours before being sterilized.
5. For a **sterilized** HIGH-risk CSPs in the absence of passing sterility test (as described in USP General Chapter <71>) storage periods cannot exceed the following time periods: **24 hours at room temperature and 3 days under refrigeration.**
6. All non-sterile measuring, mixing, and purifying devices are rinsed thoroughly with sterile, pyrogen-free water, and then thoroughly drained or dried immediately before use for high-risk compounding.
7. ALL high-risk level CSPs solutions subjected to terminal sterilization are pre-filtered by passing through a filter with a nominal porosity not larger than 1.2 microns preceding or during filling into their final containers to remove particulate matter.

Rules for Compounded Sterile Preparations (CSPs)

8. Sterilization of high-risk level CSPs by filtration shall be performed with a sterile 0.2 micron or 0.22 micron porosity filter entirely within an ISO Class 5 or superior air quality environment.

Section IV. Policy and Procedure Manual

A policy and procedure manual shall be prepared and maintained for the Compounding, Dispensing, Delivery, Administration, storage, and use of Compounded Sterile Preparations.

The Policy and Procedure manual shall be reviewed at least annually by Supervising Personnel, and shall reflect the actual compounding best practices for CSP production in use by the operation.

The policy and procedure manual shall at a minimum:

1. Contain a quality assurance program for the purpose of monitoring patient care, adverse drug reactions, personnel qualifications, training and performance, compounded preparation integrity, equipment, facilities, disinfection processes, personnel hygiene and gowning, and guidelines regarding patient or caregiver education
2. Be current and available for inspection by the Board of Pharmacy or its - designated agent
3. Include a plan designed to prevent microbiological contamination of compounded sterile preparations and procedures concerning the validation of any sterilization process
4. Include training and other requirements for Pharmacy Compounding personnel involved in aseptic manipulations to ensure adherence to the basic principles of aseptic technique
5. Address the management and proper disposal of Hazardous drug and/or infectious waste, if applicable; and
6. Address how Supervising Personnel will monitor the ongoing adherence to procedures and sound aseptic compounding practices

Section V. Physical Requirements

1. The Pharmacy or office shall have a designated sterile compounding area with entry restricted to compounding personnel for preparing compounded sterile preparations (CSPs). This area shall be physically designed and environmentally controlled to minimize air-borne contamination from contacting critical sites. This area shall also provide a comfortable and well-lighted working environment, so that compounding personnel can perform flawlessly when attired in required aseptic compounding garb. It shall be used only for the preparation of these CSPs.

Rules for Compounded Sterile Preparations (CSPs)

2. Air-borne contamination control is achieved by providing HEPA filtered air.
3. It shall be of sufficient size to accommodate a device capable of maintaining ISO Class 5 laminar flow air. Maintaining the sterility and cleanliness of critical components is a primary safeguard for CSPs. The most common sources of ISO Class 5 air quality for exposure of critical sites are horizontal and vertical LAFWs, CAIs, and CACIs. These primary engineering controls (PECs) shall be operated within their manufacturer's recommendations and in good repair.
4. The Pharmacy or office preparing compounded sterile preparations (CSPs) shall have:
 - a. Appropriate environmental controls Capable of maintaining at least ISO Class 5 conditions in the workplace where Critical Areas and Critical Surfaces are exposed and critical activities are performed and providing for appropriate environment control in accordance with current USP Chapter 797 and current CETA (Controlled Environmental Testing Association Document 02-2006) recommendations. Furthermore, these Devices shall be capable of maintaining ISO Class 5 conditions during all Compounding activities and include laminar airflow hoods and unidirectional zonal laminar flow of High Efficiency Particulate Air (HEPA) filtered air. The principles of HEPA filtered unidirectional airflow in the work environment shall be understood and practiced in the compounding process in order to achieve the desired environmental conditions.
 - b. The buffer areas containing these primary engineering controls (PECs) (i.e. LAFWs, CAIs, CACIs) shall be supplied with HEPA filtered air and maintain ISO 7 conditions. Optimally HEPA filtered air will be introduced at the ceiling and returns should be mounted low on the walls, creating a general top-down dilution of air with HEPA filtered make up air. Ceiling mounted air returns are NOT recommended. Activities carried out within the buffer area shall be limited to only those necessary when working within a controlled environment. Only the furniture, equipment, supplies, and essential materials shall be brought into this area. All items shall be non-shedding, non-permeable, easily cleanable, and resistant to disinfectants. Whatever items are brought into this area, they shall be first cleaned and disinfected prior to introduction into this critical space.
 - c. Floors, walls, and ceilings shall be smooth, free from cracks and crevices, and non-shedding, promoting easy cleaning and will withstand repeated sanitations; Junctures of ceilings to walls shall be coved or chalked to avoid cracks and crevices where dirt can

Rules for Compounded Sterile Preparations (CSPs)

accumulate. If the ceiling consists of inlaid panels, these panels shall be impregnated with a polymer to render them imperious and hydrophobic; they shall be secured around each panel to seal them to the support frame. Walls may be constructed of flexible material (e.g. heavy gauge polymer) or epoxy-coated gypsum board. Floors are overlaid with wide sheet vinyl flooring with heat welded seams and coving to the side walls. Dust-collecting overhangs, such as ledges, pipes, and windowsills should be avoided. Exterior lenses of lighting fixtures should be smooth, flush mounted, and sealed. Any other penetrations through the ceilings or walls must be sealed. Buffer areas shall NOT contain any sources of water (sinks) or floor drains.

- d. Appropriate disposal containers for used trash or debris generated during the compounding processes shall be provided and these materials removed at least daily. Appropriate disposal of needles, syringes, and other regulated wastes and “sharps” shall conform to prevailing statutes, rules and regulations.
- e. When hazardous drugs are prepared as CSPs, they shall only be prepared under conditions that protect the healthcare worker and other personnel in the preparation and storage areas. Storage of these agents shall be segregated from other non-hazardous drug stocks and preferably within a negative pressure room. This storage area at a minimum should have good general ventilation (at least 12 ACEH) to dilute and remove any airborne contaminants. Hazardous drugs shall be handled with caution at all times using appropriate chemotherapy gloves. This includes Receiving, shipping, stocking, distribution, inventorying, and disposal activities.
- f. When compounding these hazardous drugs appropriate environmental controls shall be maintained consistent with standards that comply with current CDC, OSHA and NIOSH guidelines for healthcare workers. These environmental controls should be physically separated from other compounding areas and optimally demonstrate not less than 0.01 inch water column negative pressure to adjacent positive pressure ISO class 7 or better ante areas, thus providing a general inward flow to contain any air-borne drug. A pressure indicator shall be installed that can be readily monitored for correct room pressurization.
- g. Any biohazard cabinetry used in these areas to protect the healthcare worker compounding the drug from occupational exposure per current OSHA & NIOSH guidelines and standards shall be maintained in good repair and vented to the outside.

Rules for Compounded Sterile Preparations (CSPs)

- h. It is preferred that Hazardous drug preparation be conducted under the conditions described above. However, in facilities that prepare a very low volume of hazardous drug, use of two tiers of containment is acceptable (e.g. Use of a closed system transfer device (CSTD) within a BSC or CACI that is located in a non-negative pressure room).
 - i. All personnel who compound hazardous drug shall be fully trained in the storage, handling and disposal of these agents. Training must occur prior to the preparing, handling or compounding of these drugs and its effectiveness shall be verified by testing specific hazardous drug handling techniques. Documentation for each person shall be done at least annually.
 - j. Compounding personnel of reproductive capability shall conform in writing that they understand the risks of handling these drugs. (4e) Appropriate PPE shall be worn at all times when compounding these drugs regardless of the configuration of the compounding area.
5. The pharmacy or office compounding CSPs shall ensure that all equipment and devices used in the preparation of CSPs is in proper working order and maintained according to the manufacturer's recommendations for this equipment Certification of all controlled environments (PECs and SECs) by an independent certification company consistent with current CETA recommendations for these areas and devices is done at least semi-annually. This shall include viable and non-viable environmental particle testing for bacteria and fungi in all compounding areas.
6. The pharmacy or office compounding CSPs shall maintain supplies adequate to ensure an environment suitable for the aseptic preparation of Sterile Pharmaceuticals. This should include:
 - Dedicated cleaning supplies
 - Gowning, gloving, and other garb needed for operations
7. The Pharmacy shall have sufficient current reference materials related to sterile compounding and compatibility, where appropriate, to meet the needs of the operation.

Section VI. Records, Documents and Reports

In addition to standard record and reporting requirements for all prescription medications, the following records, documents, and reports must be maintained for at least five (5) years for all compounded sterile pharmaceuticals:

Rules for Compounded Sterile Preparations (CSPs)

1. Regular maintenance & cleaning logs, for all controlled environments (PECs and SECs) including documentation of cleaning and disinfecting the room and equipment where these CSPs are made;
2. Documentation of the regular certification of all controlled environments (PECs and SECs) by an independent certification company consistent with current CETA recommendations for these areas and devices. This shall include viable and non-viable environmental particle testing for bacteria and fungi in all compounding areas. Documentation of all repairs, maintenance and calibration of all equipment and devices used in the preparation of CSPs shall be maintained for the life of the devices and equipment.
3. Records demonstrating that adequate disinfection (or Sterilization) was performed for the laminar flow hood and supplies used in the aseptic Compounding operation.
4. Dispensing or distribution records to document who received the compounded prescriptions.
5. Lot numbers and expiration dates of all components used in compounding to expedite a recall process if necessary.
6. Orientation and training records of all personnel who supervise or compound CSPs shall be maintained. This will include but not be limited to:
 - a. Aseptic technique
 - b. Hand hygiene and garbing
 - c. Aseptic Media qualifications
 - d. Fingertip and thumb testing
 - e. Good compounding practices
 - f. Hazardous Drug compounding (if applicable)
 - g. Cleaning & Disinfecting of Controlled environments
 - h. Competency in the use of any automated compounding devices (if applicable)

Section VII. Delivery Service

Supervising Personnel shall ensure the environmental control and stability of all CSPs shipped. Therefore, any Compounded Sterile Preparations must be shipped or Delivered to a facility, patient or patient's agent in appropriate temperature-controlled (as defined by USP Standards) delivery containers and stored appropriately upon their arrival. Information on appropriate storage shall be provided to the facility, patient or patient's agent.

Rules for Compounded Sterile Preparations (CSPs)

Section VIII. Disposal of Hazardous and/or Infectious Wastes

Supervising Personnel are responsible for ensuring that there is a system for the disposal of Hazardous and/or infectious waste in a manner so as not to endanger the public health and consistent with prevailing Federal, state, and local, statutes, rules and regulations.

Section IX. Hazardous Drugs as CSPs

In addition to the minimum requirements for a pharmacy established by rules of the Board, the following requirements are necessary for those pharmacies or offices that prepare hazardous drugs to ensure the protection of the personnel involved.

1. All Hazardous Drugs shall be Compounded in a the appropriate primary engineering controls consistent with current OSHA & NIOSH guidelines for healthcare workers vertical flow, Class II, Biological Safety Cabinet. Other CSPs should not be compounded in this cabinet.
2. Personal Protective equipment (PPE) apparel shall be worn by personnel Compounding Hazardous Drugs. This shall include disposable masks, gloves, and gowns with tight cuffs consistent with current OSHA guidance.
3. Appropriate safety and containment techniques for Compounding Hazardous Drugs shall be used in conjunction with the aseptic techniques required for preparing CSPs.
4. Disposal of hazardous waste shall comply with all applicable local, state, and federal statutes, rules and regulations.
5. Written procedures for handling both major and minor spills of Hazardous agents must be developed and must be included in the policy and procedure manual.
6. Prepared doses of Hazardous Drugs must be dispensed, labeled with proper precautions inside and outside, and shipped in a manner to minimize the risk of accidental rupture of the primary container.

Section X. Quality Assurance/Compounding and Preparation of CSPs.

There shall be a documented, ongoing quality assurance control program that monitors personnel performance, component verification and usage, disinfection, sterilization, equipment, and facilities that are appropriate to the Risk Level of the Sterile Pharmaceutical(s) being prepared.

Appropriate samples of finished CSPs shall be examined to ensure that the Pharmacy is capable of consistently preparing Sterile Pharmaceuticals meeting specifications.

Rules for Compounded Sterile Preparations (CSPs)

1. All controlled environments (clean rooms and laminar flow hoods, BSCs, CAIs, and CACIs) shall be certified by an independent contractor according to the International Organization of Standardization Classification of Particulate Matter in Room Air (ISO14644-1) for operational efficiency at least every six months. Appropriate records shall be maintained for the lifetime of each device. Recommendations for the sampling of the controlled environments shall be consistent with current CETA guidelines.
2. There shall be written procedures requiring environmental sampling on a frequent basis and special measures taken when microbial contamination is demonstrated or suspected.
3. If bulk compounding of sterile solutions is performed using chemicals that initially are non-sterile, extensive end-product microbial testing must be documented prior to the release of the product from quarantine. This process must include appropriate tests for sterility, endotoxins, particulate matter, pH, potency, pyrogens, and microbes.
4. There shall be a formal process with written justification of the chosen Beyond-Use Dates for Compounded preparations. This file must be maintained by compounding supervisors and available for reference and review by all compounding personnel and regulatory bodies. Appropriate documentation shall be attached to this written justification reinforcing the determinations and maintained on file consistent with the organization's records retention policy and applicable statutes, rules and regulations.
5. There shall be documentation of quality assurance audits at regular, planned intervals, including infection control and sterile technique audits. Intervals shall be based on the type of operations performed and shall increase as the Risk Level increases. Audits shall be announced and unannounced and any corrective action documented.
6. There shall be policies and procedures on the orientation, retraining or recertification of trained Pharmacy Compounding Personnel in various aspects of aseptic compounding behavior. The training program shall include a demonstration of ongoing competency. Training to ensure skills such as proper hand hygiene and garbing, proper aseptic technique, good cleanroom behavior, and knowledge of the hazards posed by contaminated drugs shall be conducted and documented. Training programs shall be multi-media, return demonstrated, and documented in an employee training record ready for inspection by qualified personnel and regulatory bodies.
7. Pharmacy Compounding Personnel shall wear sterile garb when conducting aseptic manipulations of CSPs..
8. An effective Cleaning & Disinfection program shall be implemented and maintained, including adequate provisions for identifying and preventing emergence of unsafe levels of micro organisms (both fungi & bacteria).

Rules for Compounded Sterile Preparations (CSPs)

9. A system shall be in place for monitoring the compounding competency of Pharmacy Compounding Personnel and all controlled environmental conditions.
10. A system shall be in place for maintaining any equipment or Devices used to control aseptic conditions or employed in any compounding processes. This program will take into consideration the device's manufacturer's recommendations for cleaning, calibration, maintenance, and upkeep of the device. All records shall be maintained and retained for the life of the device and ready for inspection. No changes in these devices shall be permitted without the knowledge and approval of Supervising Personnel.

Rules for Compounded Sterile Preparations (CSPs)

APPENDIX 1. DEFINITIONS

Beyond-Use Date (BUD)- a date or time placed on a prescription label at the time of Dispensing that is intended to clearly indicate to the patient or caregiver a time beyond which the contents of the compounded prescription cannot be used.

Bio-burden - the total number of microorganism associated with a specific item prior to sterilization.

Biological Safety Cabinet (BSC)- a containment unit suitable for the preparation of low to moderate risk agents where there is a need for protection of the product, personnel, and environment, according to National Sanitation Foundation (NSF) Standard 49.

Critical Areas - areas of ISO Class 5 or better designed to maintain sterility of sterile materials. Sterilized product, container/closures, and equipment may be exposed in critical areas.

Critical Site- a location that includes any component or fluid pathway surfaces (e.g. vial septa, injection ports, beakers) or openings (e.g. opened ampoules, needle hubs) exposed and at risk of direct contact with air (ambient or HEPA filtered), moisture. Or touch contamination. Risk of microbial particulate contamination of the critical site increase with the size of the openings and the exposure time.

Critical Surfaces – surfaces which may come into contact with or directly impact sterilized product or containers/closures.

Demarcation Line – A clear and noticeable line of demarcation between the ante area(s) and the buffer area(s).

Disinfection - the process by which surface bioburden is reduced to a safe level or eliminated.

Enteral -within or by way of the gastrointestinal tract or intestine.

First Air – the air exiting the HEPA filter in a unidirectional air stream that is essentially particle free.

ISO Class - the description of an atmospheric environment characterized by the number of particles within a diameter per cubic foot of air. (ISO 14644-1: 1999)

Rules for Compounded Sterile Preparations (CSPs)

Compounding Aseptic Isolator (CAI) -a decontaminated unit, specifically designed for compounding pharmaceutical ingredients or preparations supplied with ISO Class 5 or higher air quality that provides uncompromised, continuous isolation of its interior from the external environment (e.g., surrounding cleanroom air and Compounding Pharmacy personnel).

Compounding Aseptic Containment Isolator (CACI)- is designed to provide the healthcare worker protection from exposure to undesirable effects of airborne drug throughout the compounding and material transfer processes and to provide an aseptic environment for the compounding of CSPs. Air exchange with the surrounding environment should NOT occur unless the air is first passed through a microbial retentive filter (HEPA minimum) system capable of containing airborne concentrations of the physical size and state of the drug being compounded. Where volatile hazardous drugs are prepared, the exhaust air from this device should be appropriately removed by properly designed building ventilation.

Parenteral – defined as; by some other route than through the gastrointestinal tract such as, but not limited to, intravenous, subcutaneous or intramuscular routes.

Product Quality and Characteristics - include sterility, potency, identity, strength, quality, and purity associated with environmental quality, preparation activities, and checks and tests.

Risk Level of the Sterile Pharmaceutical - the level assigned to a Sterile Pharmaceutical by a Pharmacist or Supervising Personnel that represents the probability that the Sterile Pharmaceutical will be contaminated with microbial organisms, spores, endotoxins, foreign chemicals, or other physical matter.

Negative Pressure Room- a room that is at a lower pressure than the adjacent spaces and therefore the net flow of air is INTO the room.

Positive Pressure Room- a room that is at a higher pressure than the adjacent spaces and therefore the net flow of air is OUT of the room.

Unidirectional Airflow - air flow moving in a single direction in a robust and uniform manner at sufficient speed to reproducibly sweep particles away from critical compounding, processing or testing areas.

Rules for Compounded Sterile Preparations (CSPs)

APPENDIX II. SAMPLE TABLE of CONTENTS

- I. ADMINISTRATIVE
 - a. Annual review of policy & procedure manual
 - b. Good documentation practices
 - c. Signature Log of compounding persons
- II. FACILITY MANAGEMENT
 - a. Facility preventive maintenance practices
 - b. Cleaning & disinfecting of the compounding area(s)
- III. QUALITY ASSURANCE
 - a. Conduct of Personnel in Compounding Area(s)
 - b. The activity of Pharmacy Supportive Personnel
 - c. Environmental Monitoring of the compounding area(s)
 - i. Viable & non-viable air sampling
 - ii. Surface sampling procedures
 - iii. Personnel aseptic media qualification
 - iv. Gloved fingertip & thumb sampling
 - d. Equipment and Process Verification
 - e. Determination of Beyond-use dating of CSPs
- IV. RISK MANAGEMENT
 - a. Variance reporting policy & procedure
 - b. Federal Med-Watch procedures
- V. PERSONNEL TRAINING
 - a. Orientation and Training of new compounding personnel
 - i. Hand Hygiene and Garbing assessment
 - ii. Aseptic Technique assessment
 - iii. Cleaning and disinfecting of controlled environment(s)