CHAPTER 17

STERILE PRODUCT COMPOUNDING
Sterile Product Compounding

Reference:
1) United States Pharmacopeia chapter 797 (USP<797>)
2) CMS: §482.25(b)(1) - All compounding, packaging, and dispensing of drugs and biologicals must be under the supervision of a pharmacist and performed consistent with State and Federal laws.

Interpretive Guidelines §482.25(b)(1)
All compounding, packaging, and dispensing of drugs and biologicals must be conducted by a registered pharmacist or under the supervision of a registered pharmacist and performed consistent with State and Federal laws.

Medications must be prepared safely. Safe preparation procedures could include:

- Only the pharmacy compounds or admixes all sterile medications, intravenous admixtures, or other drugs except in emergencies or when not feasible (for example, when the product’s stability is short).
- Whenever medications are prepared, staff uses safety materials and equipment while preparing hazardous medications.
- Wherever medications are prepared, staff uses techniques to assure accuracy in medication preparation.
- Whenever medications are prepared, staff uses appropriate techniques to avoid contamination during medication preparation, which include but are not limited to the following:
  - Using clean or sterile technique as appropriate;
  - Maintaining clean, uncluttered, and functionally separate areas for product preparation to minimize the possibility of contamination;
  - Using a laminar airflow hood or other appropriate environment while preparing any intravenous (IV) admixture in the pharmacy, any sterile product made from non-sterile ingredients, or any sterile product that will not be used with 24 hours; and
  - Visually inspecting the integrity of the medications.

3) Joint commission standards – prepared in pharmacy using aseptic technique unless emergency or short stability
4) Florida Regulations (64B16-27.797) Standards of Practice for Compounding Sterile Preparations (CSPs).

Health care institutions
Pharmacies
Physician offices
Facilities where compounded sterile preparations are prepared, stored & dispensed

Applies to Facilities that:
- Prepare sterile products according to manufacturer recommendations where manipulations are performed during the compounding
- Compounding using devices or non-sterile ingredients
- Includes baths & soaks for live organs and tissues, implants, inhalations, injections, irrigations, metered sprays, ophthalmic and otic preparations.
Enforceable by FDA
Joint Commission
FL Board of Pharmacy
ISO Classification of Particulate Matter in Room Air

<table>
<thead>
<tr>
<th>ISO 5</th>
<th>Class 100</th>
<th>Air quality inside a laminar air flow hood</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISO 7</td>
<td>Class 10,000</td>
<td>Buffer area – preparation area where hoods are located</td>
</tr>
<tr>
<td>ISO 8</td>
<td>Class 100,000</td>
<td>Ante area – where hand hygiene, garbing, staging for compounding and labeling occurs</td>
</tr>
</tbody>
</table>

Flow Hood with HEPA (high efficiency particle air) filter.

- Air Flow either horizontal or vertical
- Biological safety cabinet for hazardous drug preparations (vertical)
- Barrier Isolator or Glove box

REQUIRES KNOWLEDGE of RISK LEVEL for COMPOUNDING STERILE PRODUCTS

**Low Risk:** ISO Class 5 or better air quality using only sterile ingredients, transferring drugs from the manufacturer’s original packaging (e.g., vials or ampules), and no more than 3 products and entries into one container to compound sterile products.

Examples: 20 mEq KCl to liter 0.9% sodium chloride; cefazolin 1 gm to 50 ml D5W

Beyond Use Dating for Low Risk compounds prior to administration cannot exceed the following unless sterility testing is performed:
- 48 hours room temperature
- 14 days cold temperature
- 45 days solid frozen at –25 to -10 C
Low Risk with 12 hour or less Beyond Use Dating:
ISO Class 5 or better air quality NOT located in ISO 7 buffer area
Follow requirements for garbing, cleaning, personnel training, microbiological monitoring, etc.
Only used for compounding low risk and non-hazardous sterile products.

Use within 12 hours of preparation or as recommended by manufacturer (whichever is less).

Medium Risk: Multiple individual or small doses of sterile products are compounded or pooled to prepare a sterile product that will be administered either to multiple patients or to one patient on multiple occasions (i.e. prepare a batch), or there are complex aseptic manipulations, or the dissolution or mixing takes a long duration and the compounded sterile products do not contain a broad spectrum bacteriostatic substance and are administered over several days.

Beyond Use Dating for Medium Risk compounds prior to administration can not exceed the following unless sterility testing is performed:
- 30 hours room temperature
- 9 days cold temperature
- 45 days solid frozen at –25 to -10°C

Examples:
TPN using manual or automated devices
Filling reservoirs of infusion devices with multiple sterile drug products where the air is removed from the device or the solution is administered over several days at ambient temperatures between 25-40 degrees C.
Transferring multiple vials or ampules into the final product.

High Risk: Using non-sterile ingredients that will be terminally sterilized.

Beyond Use Dating for High Risk compounds prior to administration can not exceed the following unless sterility testing is performed:
- 24 hours room temperature
- 3 days cold temperature
- 45 days solid frozen at –25 to -10°C

Examples:
Dissolving non-sterile powder to make solution that will be terminally sterilized
Ingredients, devices or components stored or exposed to air quality with less than ISO Class 5
Using non-sterile devices before sterilization is performed

Sterilization methods are defined in the standards (filtration, steam, dry heat)
Immediate Use Compounding:
Low risk compounding used within 1 hour of preparation is exempt from requirements.

Beyond Use Dating:
1. Single Dose containers (vials, bags) opened in < ISO 5 must be used within 1 hour and remaining contents are discarded.
2. Single Dose containers opened in ISO 5 or better quality air may be used up to 6 hours.
3. Ampuls are not stored for any period of time
4. Multi-dose vials (contains a preservative) may be used up to 28 days unless otherwise specified by the manufacturer.
5. Based on the compound’s risk level (described above).

Personnel Training
Training prior to beginning to prepare products
Perform didactic review, written testing and the following suggested training, competency and process validation methods:

1. Cleansing and garbing competency
2. Aseptic work practice assessment with glove fingertip sampling
3. Aseptic manipulation competency with media fill test procedures
4. Surface cleaning and disinfection sampling assessment
5. Cleaning and disinfecting competency evaluation
6. Suggested standard operating procedures (SOPs) defined in the standards

Clean rooms
Hoods are located in rooms with smooth walls & floors without cracks, non-shedding, and resistant to sanitizing chemicals.

Positive pressure exists between buffer and ante area and ante area and the general environment that is measured and documented each work shift (at least daily). At least 30 air changes per hour.

No cardboard boxes to minimize air particles.

Gowning and Personal Protective Equipment (PPE)
1. Artificial nails are prohibited
2. Staff with sunburn, rashes, conjunctivitis, and upper respiratory infections cannot prepare sterile compounds
3. Remove lab coat, make-up, hand and wrist jewelry and visible piercings that may interfere with PPE
4. Apply shoe covers
5. Apply head and facial hair covers
6. Apply face mask
7. Wash hands and forearms for 30 seconds and dry with hand dryer or non-shedding towels
8. Put on non-shedding gown closed at neck and snug at wrists
9. Enter buffer area and use waterless alcohol-based surgical hand scrub. Allow to dry
10. Put on sterile powder-free gloves
11. Disinfect sterile gloves with Sterile 70% Isopropyl Alcohol after touching non-sterile surfaces during compounding

Cleaning and sanitizing the work space

<table>
<thead>
<tr>
<th>Hood</th>
<th>Beginning of each shift, before each batch, every 30 minutes during compounding, after spill or contamination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Counters and Floors</td>
<td>Daily</td>
</tr>
<tr>
<td>Walls, ceiling, shelves</td>
<td>Monthly</td>
</tr>
</tbody>
</table>

Cleaning and disinfection agents
Sanitation with Sterile 70% Isopropyl Alcohol

Environmental Monitoring
Includes monitoring for airborne microorganisms and determining air particulate counts.
Hoods are certified every 6 months.

Validation of automated compounding devices for nutrition compounding
Validate accuracy & precision

Hazardous Drugs/Chemotherapy
Storage is in negative pressure room (≥ 0.01 inch water column negative pressure to adjacent positive pressure), at least 12 air changes per hour, and 100% vented and HEPA filtered to the outside air or barrier isolator.

Hazardous drug preparation training is required.

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

- OSHA guidelines
- NIOSH recommendations
- Material Safety Data Sheets (MSDS)

Radiopharmaceutical and Allergen Extracts
The Joint Commission expects that in house compounding is under the supervision of an appropriately trained pharmacist or physician (MM.05.01.07).
Examples of Preparations

Large volume parenterals
- 250ml, 500ml, 1000ml.
- Usually continuous infusions
- IV infusion pump guidelines

IV piggy back (IVPB)
- Usually intermittent infusions over 30-60 minutes
- 50ml – 100ml volume (adults)

Pediatric patients
- Special dilutions
- Syringe pumps

Quality Assurance
- Based on Risk level
- Problems identified
- Microbiologic/ pyrogen testing
- Refractive index

Training: The Joint Commission (HR 01.02.01 EP 19) If blood transfusions and IV medications are administered by staff other than physicians, staff have special training and documentation of competency is maintained.

Resources:
1. United States Pharmacopeia, Chapter 797 – Pharmaceutical Compounding – Sterile Preparations, the Second Supplement to USP31-NF26 (official on June 1, 2008)
3. “ASHP Technical Assistance Bulletin on Handling Cytotoxic and Hazardous Drugs”


6. ASHP Links: Manufacturers, Products, and Services
   Compounding Courses
   - Pharmaceutics Laboratory, UNCH
   Compounding-Related Journals
   - A2C2
   - Cleanroom.com
   - International Journal of Pharmaceutical Compounding
   - Pharmacy Purchasing & Products Magazine

   Online Engineering Control Manufacturers (Laminar Airflow Workbenches and Barrier Isolators)
   - The Baker Company
   - Containment Technologies Group
   - Germfree Laboratories

   Closed System Transfer Devices
   - Baxa Corporation

   Quality Control Kits
   - Valiteq
   - Q. I. Medical

   Culture Media
   - Hardy Diagnostics

7. ASHP Products (www.ashp.org)
   - ASHP's 797 Compliance Advisor
   - Basics of Aseptic Compounding Technique Video Training Program
   - Safe Handling of Hazardous Drugs Video Training Program
   - Compounding Sterile Preparations, 2nd ed. (formerly titled Principles of Sterile Product Preparation, revised 1st ed.)
   - Compounding Sterile Preparations Video Training Program (formerly titled Quality Assurance for Pharmacy-Prepared Sterile Products Videotape & Workbook)
Standards of Practice for Compounding Sterile Preparations (CSPs).

The purpose of this section is to assure positive patient outcomes through the provision of standards for 1) pharmaceutical care; 2) the preparation, labeling, and distribution of sterile pharmaceuticals by pharmacies, pursuant to or in anticipation of a prescription drug order, and 3) product quality and characteristics. These standards are intended to apply to all sterile pharmaceuticals, notwithstanding the location of the patient (e.g., home, hospital, nursing home, hospice, doctor’s office).

(1) Definitions:

(a) “Anteroom” means an area where personnel perform hand hygiene and garbing procedures, staging of components, order entry, CSP labeling, and other high-particulate generating activities. It is also a transition area that provides assurance that pressure relationships are constantly maintained so that air flows from clean to dirty areas. The Anteroom area is to be maintained within ISO Class 8 level of particulate contamination.

(b) “Antineoplastic” means a pharmaceutical agent that has the intent of causing cell death targeted to cancer cells, metastatic cells, or other cells involved in a severe inflammatory or autoimmune response.

(c) “Beyond-use-date” means the date after which a compounded preparation should not be used and is determined from the date the preparation was compounded.

(d) “Biological safety cabinet” means a containment unit suitable for the preparation of low, moderate, and high risk agents where there is a need for protection of the product, personnel, and environment.

(e) “Bulk Compounding” means the compounding of CSPs in increments of twenty-five (25) or more doses from a single source.

(f) “Buffer area” (Clean room) is an area where the activities of CSP take place; it shall not contain sinks or drains. In High-Risk compounding this must be a separate room. The Buffer area is to be maintained within ISO Class 7 level of particulate contamination.

(g) “Class 100 environment” means an atmospheric environment which contains no more than one hundred particles of 0.5 microns in diameter or larger per cubic foot of air. A class 100 environment is equivalent to ISO Class 5 level of particulate contamination.

(h) “Compounding Aseptic Isolator” (CAI) – is a form of barrier isolator specifically designed for compounding pharmaceutical ingredients or preparations. It is designed to maintain an aseptic compounding environment within the isolator throughout the compounding and material transfer process. Air exchange into the isolator from the surrounding environment should not occur unless it is first passed through a microbially retentive filter (HEPA minimum 0.2 microns).

(i) “High-Risk Level CSPs” – are products compounded under any of the following conditions are either non-sterile or at high risk to become non-sterile with infectious microorganisms.

1. Non-sterile ingredients, including manufactured products for routes of administration other than sterile parenteral administration are incorporated or a non-sterile device is employed before terminal sterilization.

2. Sterile contents of commercially manufactured products, CSP that lack effective antimicrobial preservatives, sterile surfaces of devices and containers for the preparation, transfer, sterilization, and packaging of CSPs are exposed to air quality worse than ISO Class 5 for more than one (1) hour.

3. Before sterilization, non-sterile procedures such as weighing and mixing are conducted in air quality worse than ISO Class 7, compounding personnel are improperly garbed and gloved, or water-containing preparations are stored for more than 6 hours.

4. For properly stored sterilized high-risk preparation, in the absence of passing a sterility test, the storage periods cannot exceed the following time periods: before administration, the CSPs are properly stored and exposed for not more than 24 hours at controlled room temperature, and for not more than 3 days at a cold temperature (2-8
degrees Celsius) and for not more than 45 days in solid frozen state at -20 degrees Celsius or colder.

5. Examples of high-risk compounding include: (1) dissolving non-sterile bulk drug and nutrient powders to make solutions, which will be terminally sterilized; (2) exposing the sterile ingredients and components used to prepare and package CSPs to room air quality worse than ISO Class 5 for more than one (1) hour; (3) measuring and mixing sterile ingredients in non-sterile devices before sterilization is performed; (4) assuming, without appropriate evidence or direct determination, that packages of bulk ingredients contain at least 95% by weight of their active chemical moiety and have not been contaminated or adulterated between uses.

6. All high risk category products must be rendered sterile by heat sterilization, gas sterilization, or filtration sterilization in order to become a CSP.

7. Quality assurance practices for high-risk level CSPs include all those for low-risk level CSPs. In addition, each person authorized to compound high-risk level CSPs demonstrates competency by completing a media-filled test that represents high-level compounding semiannually.

(j) Immediate Use CSPs:

1. Requires only simple aseptic measuring and transfer manipulations are performed with not more than three (3) sterile non-hazardous drug or diagnostic radiopharmaceutical drug preparations, including an infusion or dilution solution.
2. The preparation procedure occurs continuously without delays or interruptions and does not exceed 1 hour.
3. At no point during preparation and prior to administration are critical surfaces and ingredients of the CSP directly exposed to contact contamination such as human touch, cosmetic flakes or particulates, blood, human body substances (excretions and secretions, e.g., nasal or oral) and non-sterile inanimate sources.
4. Administration begins not later than one (1) hour following the start of preparing the CSP.
5. When the CSP is not administered by the person who prepared it, or its administration is not witnessed by the person who prepared it, the CSP container shall bear a label listing patient identification information (name, identification numbers), and the names and amounts of all active ingredients, and the name or identifiable initials of the person who prepared the CSP, and one (1) hour beyond-use time and date.
6. If administration has not begun within one (1) hour following the start of preparing the CSP, the CSP is promptly and safely discarded. Immediate use CSPs shall not be stored for later use.

(k) ISO Class 5 guidelines are met when particulate contamination is measured at “not more than 3,520 particles 0.5 micron size or larger per cubic meter of air for any laminar airflow workbench (LAWF), BSC, or CAI. (Also referred to as a “Class 100 environment.”)

(l) ISO Class 7 guidelines are met when particulate contamination is measured at “not more than 352,000 particles 0.5 micron size or larger per cubic meter of air for any buffer area (room).”

(m) ISO Class 8 guidelines are met when particulate contamination is measured at “not more than 3,520,000 particles 0.5 micron size or larger per cubic meter of air for any anteroom (area).”

(n) Low-Risk Level CSPs compounded under all of the following are at a low risk of contamination:

1. The CSPs are compounded with aseptic manipulations entirely within ISO Class 5 (class 100) or better air quality using only sterile ingredients, products, components, and devices.
2. The compounding involves only transfer, measuring, and mixing manipulations using no more than three commercially manufactured sterile products and entries into one container (e.g., bag, vial) of sterile product to make the CSP.
3. Manipulations are limited to aseptically opening ampoules, penetrating sterile stoppers on vials with sterile needles and syringes, and transferring sterile liquids in sterile syringes to sterile administration devices, package containers for storage and dispensing. The contents of ampoules shall be passed through a sterile filter to remove any particles.
4. For low-risk preparation, in the absence of passing a sterility test or a documented validated process, the storage periods cannot exceed the following time periods; before administration, the CSPs are properly stored and exposed for not more than 48 hours at controlled room temperature, and for not more than 14 days at a cold temperature (2-8 degrees Celsius) and for 45 days in solid frozen state at -20 degrees Celsius or colder.

5. Quality Assurance practices include, but are not limited to, the following: (1) routine disinfection and air
quality testing of the direct compounding environment to minimize microbial surface contamination and maintain ISO Class 5 air quality; (2) Visual confirmation that compounding personnel are properly donning and wearing appropriate items and types of protective garments; (3) Review of all orders and packages of ingredients to ensure that the correct identity and amounts of ingredients were compounded; (4) Visual inspection of CSPs to ensure the absence of particulate matter in solutions, the absence of leakage from vials and bags, and accuracy and thoroughness of labeling.

6. All compounding personnel are required to demonstrate competency by completing a media-filled test that represents low-level compounding annually. A media-filled test is a commercially available sterile fluid culture media that shall be able to promote exponential colonization of bacteria that are both likely to be transmitted to CSP from the compounding personnel and environment. Media filled vials are incubated at 25-35 degrees celsius for 14 days. Failure is indicated by visible turbidity in the medium on or before 14 days.

(o) Medium-Risk Level CSPs – When CSPs are compounded aseptically under Low-Risk Conditions, and one or more of the following conditions exist, such CSPs are at a medium risk of contamination:

1. CSPs containing more than three (3) commercial sterile drug products and those requiring complex manipulations and/or preparation methods.
2. Multiple individual or small doses of sterile products are combined or pooled to prepare a CSP that will be administered either to multiple patients or to one patient on multiple occasions.
3. The compounding process requires unusually long duration, such as that required to complete dissolution or homogeneous mixing.
4. For Medium-risk preparation, in the absence of passing a sterility test or a documented validated process, the storage periods cannot exceed the following time periods; before administration, the CSPs are properly stored and exposed for not more than 30 hours at controlled room temperature, and for not more than 9 days at a cold temperature and for 45 days in solid frozen state at -20 degrees celsius or colder.
5. These include compounding of total parenteral nutrition (TPN) using either manual or automated devices during which there are multiple injections, detachments, and attachments of nutrient source products to the device or machine to deliver all nutritional components to a final sterile container.
6. Filling of reservoirs of injection and infusion devices with more than three (3) sterile drug products and evacuation of air from those reservoirs before the filled devices are dispensed.
7. Transfer of volumes from multiple ampules or vials into one or more final sterile containers.
8. Quality assurance practices for medium-risk level CSPs include all those for low-risk level CSPs.
9. Demonstrates competency by completing a media-filled test that represents medium-level compounding annually.

(p) Parenteral means a sterile preparation of drugs for injection through one or more layers of the skin.
(q) Risk level of the sterile preparation means the level assigned to a sterile product by a pharmacist that represents the probability that the sterile product will be contaminated with microbial organisms, spores, endotoxins, foreign chemicals or other physical matter.
(r) Sterile preparation means any dosage form devoid of viable microorganisms, including but not limited to, parenterals, injectables, ophthalmics, and aqueous inhalant solutions for respiratory treatments.

2) Compounded sterile preparations include, but are not limited, to the following:
(a) Total Parenteral Nutrition (TPN) solutions;
(b) Parenteral analgesic drugs;
(c) Parenteral antibiotics;
(d) Parenteral antineoplastic agents;
(e) Parenteral electrolytes;
(f) Parenteral vitamins;
(g) Irrigating fluids;
(h) Ophthalmic preparations; and
(i) Aqueous inhalant solutions for respiratory treatments.

(3) Sterile preparations shall not include commercially manufactured products that do not require compounding.
prior to dispensing.

(4) Policy & Procedure Manual. A policy and procedure manual shall be prepared and maintained for the compounding, dispensing, and delivery of sterile preparation prescriptions. The policy and procedure manual shall be available for inspection by the Department and include at a minimum:

(a) Use of single dose and multiple dose containers not to exceed United States Pharmacopeia 797 guidelines.
(b) Verification of compounding accuracy and sterility.
(c) Personnel training and evaluation in aseptic manipulation skills.
(d) Environmental quality and control:
   1. Air particle monitoring for hoods (or Barrier Isolator), clean room and buffer area (or anteroom) when applicable;
   2. Unidirectional airflow (pressure differential monitoring);
   3. Cleaning and disinfecting the sterile compounding areas;
   4. Personnel cleansing and garbing;
   5. Environmental monitoring (air and surfaces).
(e) Personnel monitoring and validation.
(f) Finished product checks and tests.
(g) Method to identify and verify ingredients used in compounding.
(h) Labeling requirements for bulk compounded products:
   1. Contents;
   2. Beyond-Use-Date; and
   3. Storage requirements.
(i) Packing, storage, and transportation conditions.

(5) Physical Requirements.

(a) The pharmacy shall have a designated area with entry restricted to designated personnel for preparing parenteral products. This area shall have a specified ante area and buffer area; in high risk compounding, this shall be separate rooms. This area shall be structurally isolated from other areas with restricted entry or access, and must be designed to avoid unnecessary traffic and interference with unidirectional airflow. It shall be used only for the preparation of these sterile preparations. It shall be of sufficient size to accommodate a laminar airflow hood and to provide for the proper storage of drugs and supplies under appropriate conditions of temperature, light, moisture, sanitation, ventilation, and security.

(b) The pharmacy compounding parenteral and sterile preparation shall have the following:
   1. Appropriate environmental control devices capable of maintaining at least class 100 conditions in the work place where critical objects are exposed and critical activities are performed; furthermore, these devices must be capable of maintaining class 100 conditions during normal activity. Examples of appropriate devices include laminar airflow hoods and zonal laminar flow of high efficiency particulate air (HEPA) filtered air;
   2. Appropriate disposal containers for used needles, syringes, and if applicable, for antineoplastic waste from the preparation of chemotherapy agents;
   3. Appropriate environmental control including approved biohazard cabinetry when antineoplastic drug products are prepared;
   4. Appropriate temperature and transport containers;
   5. Infusion devices and equipment, if appropriate.
(c) The pharmacy shall maintain and use supplies adequate to preserve an environment suitable for the aseptic preparation of sterile preparations, such as:
   1. Gloves, masks, shoe covers, head and facial hair covers, and non-shedding gowns;
   2. Needles and syringes of various standard sizes;
   3. Disinfectant cleaning agents;
   4. Clean towels;
   5. Hand washing materials with bactericidal properties;
   6. Vacuum containers and various transfer sets;
7. “Spill kits” for antineoplastic agent spills.
   (d) The pharmacy should have current reference material in hard copy or readily available online:
      1. USP Pharmacist Pharmacopeia (optional) or Handbook of Injectable Drugs by American Society of Hospital Pharmacists; or other nationally recognized standard reference; and
      2. “Practice Guidelines for Personnel Dealing with Cytotoxic Drugs,” or other nationally recognized standard cytotoxic reference if applicable.
   (e) Barrier isolator is exempt from all physical requirements subject to manufacturer guidelines for proper placement.

6. Antineoplastic Drugs. The following requirements are necessary for those pharmacies that prepare antineoplastic drugs to ensure the protection of the personnel involved:
   (a) All antineoplastic drugs shall be compounded in a vertical flow, Class II, biological safety cabinet placed in a negative pressure room unless using barrier isolators. Other preparations shall not be compounded in this cabinet.
   (b) Protective apparel shall be worn by personnel compounding antineoplastic drugs. This shall include at least gloves and gowns with tight cuffs.
   (c) Appropriate safety and containment techniques for compounding antineoplastic drugs shall be used in conjunction with the aseptic techniques required for preparing sterile products.
   (d) Disposal of antineoplastic waste shall comply with all applicable local, state, and federal requirements.
   (e) Written procedures for handling both major and minor spills of antineoplastic agents shall be developed and shall be included in the policy and procedure manual.
   (f) Prepared doses of antineoplastic drugs shall 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.

7. Quality Assurance:
   (a) There shall be a documented, ongoing quality assurance control program that monitors personnel performance, equipment, and preparations. Appropriate samples of finished preparations shall be examined to assure that the pharmacy is capable of consistently preparing sterile preparations meeting specifications:
      1. All clean rooms and laminar flow hoods shall be certified by an independent contractor or National Sanitation Foundation Standard 49, for operational efficiency at least semiannually for high risk CSPs and annually for low and medium risk CSPs or any time the hood is relocated or the structure is altered and records shall be maintained for two years.
      2. There shall be written procedures developed requiring sampling if microbial contamination is suspected for batches greater than 25 units.
      3. High risk greater than 25 units have antimicrobial testing prior to dispensing.
      4. There shall be referenced written justification of the chosen beyond-use-dates for compounded products.
      5. There shall be documentation of quality assurance audits at regular planned intervals, including infection control and sterile technique audits.
   (b) Compounding personnel shall be adequately skilled, educated, instructed, and trained to correctly perform and document the following activities in their sterile compounding duties:
      1. Demonstrate by observation or test a functional understanding of USP Chapter 797 and definitions, to include Risk Category assessment;
      2. Understand the characteristics of touch contamination and airborne microbial contaminants;
      3. Perform antiseptic hand cleaning and disinfections of non-sterile compounding surfaces;
      4. Select and appropriately don protective garb;
      5. Demonstrate aseptic techniques and requirements while handling medications;
      6. Maintain and achieve sterility of CSPs in ISO Class 5 (Class 100) primary engineering devices and protect personnel and compounding environments from contamination by antineoplastic and chemotoxic or other hazardous drugs or substances;
      7. Manipulate sterile products aseptically, sterilize high-risk level CSPs (where applicable) and quality inspect CSPs;
      8. Identify, weigh and measure ingredients;
9. Prepare product labeling requirements and “beyond use” requirements of product expiration;
10. Prepare equipment and barrier requirement work requirements to maintain sterility;
11. Prepare end point testing and demonstrated competencies for relevant risk levels;
12. Prepare media fills to test aseptic technique.

(8) Radiopharmaceuticals as Compounded Sterile Products

(a) Upon release of a Positron Emission Tomography (PET) radiopharmaceutical as a finished drug product from a PET production facility, the further manipulation, handling, or use of the product will be considered compounding and will be subject to the rules of this section.

(b) Radiopharmaceuticals compounded from sterile components in closed, sterile containers and with a volume of 100 ml or less for single dose injection or not more than 30 ml taken from a multiple dose container, shall be designated as, and conform to, the standards for low risk compounding.

(c) Radiopharmaceuticals shall be compounded using appropriately shielded vials and syringes in a properly functioning ISO Class 5 PEC (Primary Engineering Control), located in an ISO Class 8 or better buffer area environment in compliance with special handling, shielding, air flow requirements, and radiation safety programs to maintain radiation exposure as low as reasonably achievable.

(d) Radiopharmaceuticals designed for multi use, compounded with Tc-99m, exposed to an ISO Class 5 environment by components with no direct contact contamination, may be used up until the time indicated by manufacturers recommendations.

(e) Technetium 99/Molybdenum 99 generator systems shall be stored and eluted in an ISO Class 8 or cleaner environment to permit special handling, shielding, and airflow requirements.

(f) Manipulation of blood or blood derived products (e.g. radiolabeling white blood cells) shall be conducted in an area that is clearly separated from routine material handling areas and equipment, and shall be controlled by specific standard operating procedures to avoid cross contamination of products. The buffer area for manipulation of blood or blood derived products shall be maintained as an ISO 7 environment and direct manipulations shall occur in an ISO 5 PEC suitable for these products (e.g. biological safety cabinet).

1. Current demand for IV therapy in the Nursing Home

   Less than before the Prospective Payment System started but most nursing homes do some IV therapy.

2. Policy regarding the use of IV’s - often a completely separate P&P manual

   a. Who may administer IVs in Florida?
      RN’s, LPN’s, and the Director Of Nursing. Nurses require certification training before being allowed to administer IV drugs

   b. Training required
      The vendor Pharmacy may be asked to provide IV certification programming for the nursing staff. This is typically a 32 hour training program provided by a nurse specializing in IV therapy. There are several companies throughout the state that provided IV training and IV start services for a fee

   c. Who should mix IVs?
      Whenever possible IV’s should be prepared by the Pharmacist in a laminar flow hood. There may be times when Baxter Plus or Abbott’s Add-Vantage system can be mixed on the nursing unit

   d. Flexible bag IV solutions have a shortened expiration date after removing the manufacturer’s “overwrap” packaging

      50 ml of less size - expires in 15 to 21 days
      100 ml or greater – expires in 30 days
Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings

Warning!

Working with or near hazardous drugs in health care settings may cause skin rashes, infertility, miscarriage, birth defects, and possibly leukemia or other cancers.

Health care workers who work with or near hazardous drugs may be exposed to these agents in the air or on work surfaces, clothing, medical equipment, or patient urine or feces. Hazardous drugs include those used for cancer chemotherapy, antiviral drugs, hormones, some bioengineered drugs, and other miscellaneous drugs (see Appendix A of NIOSH Alert: Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings for a List of Hazardous Drugs). The health risk depends on how much exposure a worker has to these drugs and how toxic they are.

Health care workers should take the following steps to protect themselves from hazardous drugs:

- Read all information and material safety data sheets (MSDSs) your employer provides to you for the hazardous drugs you handle.

- Participate in any training your employer provides on the hazards of the drugs you handle and the equipment and procedures you should use to prevent exposure.

- Be familiar with and able to recognize sources of exposure to hazardous drugs. Sources of exposure include
  — all procedures involving hazardous drugs (including preparation, administration, and cleaning), and
  — all materials that come into contact with hazardous drugs (including work surfaces, equipment, personal protective equipment [PPE], intravenous [IV] bags and tubing, patient waste, and soiled linens).

- Prepare hazardous drugs in an area that is devoted to that purpose alone and is restricted to authorized personnel.

- Prepare hazardous drugs inside a ventilated cabinet designed to protect workers and others from exposure and to protect all drugs that require sterile handling.

- Use two pairs of powder-free, disposable chemotherapy gloves, with the outer one covering the gown cuff whenever there is risk of exposure to hazardous drugs.
• Avoid skin contact by using a disposable gown made of polyethylene-coated polypropylene material (which is nonlinting and nonabsorbent). Make sure the gown has a closed front, long sleeves, and elastic or knit closed cuffs. Do not reuse gowns.

• Wear a face shield when splashes to the eyes, nose, or mouth may occur and when adequate engineering controls (such as the sash or window on a ventilated cabinet) are not available.

• Wash hands with soap and water immediately before using personal protective clothing (such as disposable gloves and gowns) and after removing it.

• Use syringes and IV sets with Luer-LokTM fittings for preparing and administering hazardous drugs.

• Place drug-contaminated syringes and needles in chemotherapy sharps containers for disposal.

• When supplemental protection is needed, use closed-system drug-transfer devices, glove bags, and needleless systems inside the ventilated cabinet.

• Handle hazardous wastes and contaminated materials separately from other trash.

• Clean and decontaminate work areas before and after each activity involving hazardous drugs and at the end of each shift.

• Clean up small spills of hazardous drugs immediately, using proper safety precautions and PPE.

• Clean up large spills of hazardous drugs with the help of an environmental services specialist.

Employers of health care workers should take the following steps to protect their workers from exposure to hazardous drugs:

• Make sure you have written policies about the medical surveillance of health care workers and all phases of hazardous drug handling—including receipt and storage, preparation, administration, housekeeping, decontamination and cleanup, and disposal of unused drugs, contaminated spills, and patient wastes.

• Seek input from workers who handle hazardous drugs when developing these policies and other programs to prevent exposures.

• Prepare a written inventory of all hazardous drugs used in the workplace, and establish a procedure for regular review and updating of this inventory.
- Train workers to recognize and evaluate hazardous drugs and to control exposure to them.

- Provide workers who handle or work near hazardous drugs with appropriate information and MSDSs.

- Provide a work area that is devoted solely to preparing hazardous drugs and is limited to authorized personnel.

- Do not permit workers to prepare hazardous drugs using laminar-flow work stations that move air from the drug toward the worker.

- Provide and maintain ventilated cabinets designed to protect workers and others from exposure to hazardous drugs and to protect all drugs that require sterile handling. Examples of ventilated cabinets include biological safety cabinets (BSCs) and containment isolators designed to prevent hazardous drugs from escaping into the work environment.

- Filter the exhaust from ventilated cabinets with high-efficiency particulate air filters (HEPA filters). Make sure these cabinets are exhausted to the outdoors wherever feasible—well away from windows, doors, and other air-intake locations. Consider providing supplemental equipment to protect workers further—for example, glove bags, needleless systems, and closed-system drug-transfer devices.

- Establish and oversee appropriate work practices for handling hazardous drugs, patient wastes, and contaminated materials.

- Provide workers with proper PPE on the basis of a risk assessment and train workers how to use it—as required by the Occupational Safety and Health Administration (OSHA) PPE standard [29 CFR 1910.132]. PPE may include chemotherapy gloves, nonlinting and nonabsorbent disposable gowns and sleeve covers, and eye and face protection.

- Ensure the proper use of PPE by workers.

- Use NIOSH-certified respirators [42 CFR 84].

  *Note: Surgical masks do not provide adequate respiratory protection.*

- Provide syringes and IV sets with Luer-LokTM fittings for preparing and administering hazardous drugs. Also provide containers for their disposal.

- Consider using closed-system drug-transfer devices and needleless systems to protect nursing personnel during drug administration.
Periodically evaluate hazardous drugs, equipment, training effectiveness, policies, and procedures in your workplace to reduce exposures as much as possible.

Comply with all relevant U.S. Environmental Protection Agency/Resource Conservation and Recovery Act (EPA/RCRA) regulations related to the handling, storage, and transportation of hazardous waste.

*Code of Federal Regulations.

For additional information, see NIOSH Alert: Preventing Occupational Exposures to Antineoplastic and other Hazardous Drugs in Health Care Settings [DHHS (NIOSH) Publication No. 2004–165]. Single copies of the Alert are available from the following:

NIOSH—Publications Dissemination
4676 Columbia Pkwy
Cincinnati, OH 45226–1998

E-mail: pubstaff@cdc.gov

or visit the NIOSH Web site at www.cdc.gov/NIOSH

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

Printer friendly version: Summary of Worker/Employer Recommendations (PDF, 3 pages, 129kb)
December 6, 1986.

Your Baxter representative, Craig Pfeifer, has requested that I respond to your inquiry regarding the protective overwrap pouch used on Vialite® plastic containers manufactured by Baxter Healthcare Corporation.

The purpose of the overwrap pouch is to retard moisture evaporation. Water vapor transmission through plastic is a well-recognized phenomenon. Water can condense through the vinyl container and condensate resulting in water droplets between the overwrap and container. This is the moisture which is frequently seen between the container and overwrap.

The process of water migration is dependent upon:

- The temperature and humidity of the storage environment.
- The thickness of the overwrap pouch.

Products with an injection volume less than 500 ml. have a thicker overwrap to provide the appropriate barrier to moisture loss.

The effect of storage environment depends on relative humidity. Water vapor moves from a greater to a lesser relative humidity. Since Vialite® plastic containers are filled with aqueous solutions, a 100% relative humidity is always present in the solution container. Condensation may be more pronounced during the winter months when outside temperature and humidity are both low. Under typical storage conditions, the water which transpires from the solutions will remain in a corresponding increase in the concentration of any drug in solution. However, the concentration of the drug will remain within acceptable concentration limits throughout the shelf life of the product.

Once removed from the overwrap, Baxter Healthcare Corporation recommends Vialite® plastic containers be stored at room temperature for no more than the following time periods:

- 50 ml. or less: 18 days
- 100 ml. or greater: 8 days
Hospital Products Division
Abbott Laboratories
One Abbott Park Road
Abbott Park, Illinois 60064-8000

Dear Clinician,

I am pleased to provide information regarding the length of time Abbott large volume parenteral solutions in LifeCare® flexible containers can be stored once the overwrap has been removed.

Product stability once the overwrap has been removed is dependent on the solution and the type of solution container. Abbott flexible containers are made primarily of two types of materials: polyvinylchloride (PVC) or acrylonitrile thermoplastic co-polyester (CR3).

**PVC Containers**

LifeCare® flexible containers are made of PVC, a material which is permeable to moisture vapor. Once the overwrap is removed, moisture escapes from the bag at a faster rate than when the overwrap is in place. Continuous water evaporation causes the contents of the bag to become progressively more concentrated. At a certain point enough water loss will occur so that 5% dextrose becomes 5.5% dextrose, at which time the contents of the bag are technologically out of the labeled specification range (±10%).

Our recommendation for PVC LifeCare containers greater than 25 mL in size, out of their overwrap, is that they should be used within 30 days. LifeCare containers 25 mL in size should be used within 21 days after removal from the overwrap. The containers should be kept at room temperature, and no additives should be made. Under these conditions the solution remains sterile, nonpyrogenic and within labeled specifications.

This recommendation applies to the following Abbott products:

1) General I.V. Solutions
2) ADD-Vantage® Partial-Fill and LifeCare Partial-Fill Solutions
3) LifeCare Premix I.V. Solutions
   - Dextrose 5% Injection
   - Lactated Ringer’s Injection
   - Heparin Sodium 5000 USP ( Baxter # 7630 )
   - Heparin Sodium 10,000 USP ( Baxter # 7630 )
   - 0.9% Sodium Chloride (Baxter # 7640 & 7651)
   - 0.45% Sodium Chloride (Baxter # 7650 & 7652)
   - 1.8% Sodium Chloride (Baxter # 7620)
4) Multiple Electrolytes I.V. Solutions, Normosol® or Normosol® M in D5-W, etc.
5) Premixed Potassium Chloride I.V. Solutions