Table of Contents

An Overview of BOC Compounding Pharmacy Accreditation

6/23/2017

Back to Top

An Overview of BOC Compounding Pharmacy Accreditation

The Board of Certification/Accreditation (BOC) Compounding Pharmacy Accreditation Standards, inclusive of the U.S. Pharmacopeial Convention (USP); U.S. Department of Health and Human Services (HHS); the Food and Drug Administration (FDA); Drug Enforcement Agency (DEA); and insurance provider manuals, are developed to assure the public of the availability of comprehensive pharmaceutical compounding services which are consistent with federal, state and local laws and regulations.

Compounding Pharmacy Accreditation is provided by BOC upon reasonable proof that applicants meet the compliance requirements in this standard guide and by their local Pharmacy Board. Pharmacy accreditation is a prerequisite for Compounding Pharmacy Accreditation. BOC requires all accredited pharmacies to submit any documentation necessary to show continued compliance with these standards at the time of annual renewal, or as requested. Accredited pharmacies are required to reapply every three years. Compounding Pharmacy Accreditation is available in conjunction with Pharmacy and/or Durable Medical Equipment, Prosthetics, Orthotics and Supplies (DMEPOS) accreditation.

The Pharmacy must follow standards of the USP, HHS, CMS, DEA, FDA, any respective state Board of Pharmacy and specifically the following:

- *USP <795> Pharmaceutical Compounding - Nonsterile Preparations*
- *USP <1075> Good Compounding Practices*
- *USP <1160> Pharmaceutical Calculations in Prescription Compounding*
- *USP <1163> Quality Assurance in Pharmaceutical Compounding*
- *USP <800> Hazardous Drugs – Handling in Healthcare Settings will be added once these standards have been finalized*

Chapter 1 - Regulatory Compliance

Section 1.1 - Facility Licensure

Section 1.1.1: The Pharmacy must assure continuity of all relevant licensure and display all federal, state, local licenses, registrations or certifications of the Pharmacy and all personnel who maintain a license, including but not limited to:

- Pharmacy Licenses (all state licenses)
- DEA License
- Pharmacist Licenses (all state licenses)
- Pharmacist Intern Licenses
- Pharmacy Technician certifications and/or licenses
- Registered Nurses

Section 1.1.2: Proof of license verification is required.

Back to Top

Section 1.2 - External Standards

Section 1.2.1: The Pharmacy shall comply with USP-NF General Chapters on compounding. These are generally referred to as USP <795>, USP <797>, USP <1075>, USP <1160>, USP <1163>, and USP <800> (upon effective date).

Section 1.2.2.: The Pharmacy shall comply with all federal standards, including but not limited to:

- HHS
- FDA
- DEA

Section 1.2.3: The Pharmacy shall comply with all state Board of Pharmacy regulations, when applicable. This includes all states in which compounded products are sent to patients.

Section 1.3 - Good Compounding Practices, USP <1075>

Section 1.3.1: The Pharmacy is required to comply with USP <1075>, Good Compounding Practices. The Pharmacy must have the following policies and procedures in place to comply with USP guidelines:

- Applicable Definitions
- Responsibilities of the Compounder
- Drug Compounding Equipment
- Labeling
- Training
- Component Selection Requirements
- Drug Compounding Facilities
- Procedures and Documentation
- Records and Reports
- Compounding for a Prescriber's Office Use (***Note: not permitted in all states, check with your board of pharmacy***)
- Compounding Veterinarian Products
- Packaging and Drug Preparation Containers
- Compounding Controls

Section 1.4 - Applicable Definitions

Section 1.4.1: Compounding personnel must understand, demonstrate understanding of and have access to definitions identified in USP <795> and USP <1075>.

Section 1.4.2: Compounding personnel must understand the difference between USP <795> Nonsterile Compounding and USP <797> Sterile Compounding, and what is permitted to be compounded and dispensed from the pharmacy.

Back to Top

Section 1.5 - Procedures and Documentation

Section 1.5.1: Policies and procedures will be established for all significant operations within the compounding area, which include facility, equipment, personnel, preparation (recipe), packaging and storage of compounded preparations to ensure accountability, accuracy, quality, safety and uniformity of compounding.

Section 1.5.2: Documentation controls will be established to trace, evaluate, and replicate each step of the process of completing each compound.

Section 1.6 - Compounding Controls, USP <1075>

Section 1.61: The Compounder will ensure USP <1075> controls for compounding are established and implemented.

a. The Compounder will ensure there are written procedures for the compounding of drug products to assure the finished products have the identity, strength, quality, and purity they purport to have. These procedures should be available in written form or electronically stored with printable documentation.
b. The Compounder shall establish procedures that include a description of:
    (1) components, their amounts, the order of component additives, and the compounding process;
    (2) the required equipment and utensils; and
    (3) the drug product container and closure system.
c. The written procedures described above shall be followed in execution of the compounding process.
d. The Compounder shall accurately weigh, measure, and subdivide as appropriate for each individual compounded product.
e. The Compounder shall check and recheck each procedure at each stage of the process to ensure each weight or measure is correct as stated in the written compounding procedures.
f. If a component is transferred from the original container to another container (e.g., a powder is taken from the original container, weighed, placed in a different container, and stored in that other container), the new container shall be identified with the component name, weight, or measure; the lot or control number; the expiration or beyond-use date; and the transfer date.
g. The Compounder should have established written procedures that will describe the tests or examinations to be conducted on the preparation compounded (e.g., the degree of weight variation among capsules) to assure uniformity and integrity of compounded drug preparations.
h. Appropriate control procedures should be established to monitor the output and validate the performance of those

Back to Top

compounding processes that may be responsible for causing variability in the final compounded preparations. Factors that may cause variability include (1) capsule weight variation; (2) adequacy of mixing to assure uniformity and homogeneity; and (3) clarity, completeness or pH of solutions.

i. Appropriate written procedures should be designed to prevent microbiological contamination of compounded drug preparations purporting to be sterile, and these procedures shall be followed. Such procedures shall include validation of sterilization processes (see USP <797> Pharmaceutical Compounding—Sterile Preparations).
j. The Compounder should establish appropriate beyond-use dates determined either from available USP–NF monographs, appropriate testing, or from peer-reviewed literature.
k. The Compounder should adopt appropriate storage requirements as provided in Preservation, Packaging, Storage and Labeling under USP General Notices and Requirements.

Section 1.7 - Standard Operating Procedures

Section 1.7.1: Standard Operating Procedures (SOPs) will be established for the operation of each piece of equipment and its use within the pharmacy.

Section 1.7.2: SOPs shall be established for each formulary. The SOP from a compounding software or a compounding manufacturer may be used.

Chapter 2 - Personnel

Section 2.1 - Personnel Compliance

Section 2.1.1: The Pharmacist-In-Charge (PIC) is responsible for personnel licensing in compliance with state and federal regulatory and licensing departments.

Section 2.1.2: The PIC will ensure no member of the staff is listed on the OIG/GSA/SAM Exclusion Verification lists. Proof of verification must be kept for 10 years. Verification reports may be in printed or electronic format.

Section 2.2 - Responsibilities of the Compounder, USP <795> & <1075>

Section 2.2.1: The Compounder is the primary leader for the compounding operation. The Compounder must be a licensed pharmacist and may also be the PIC.

Section 2.2.2: Personnel are capable and qualified to perform their assigned duties.

Section 2.2.3: Ingredients used in compounding have their expected identity, quality, and purity.

Back to Top

Section 2.2.4: Compounded preparations are of acceptable strength, quality, and purity, with appropriate packaging and labeling, and prepared in accordance with good compounding practices, official standards and relevant scientific data and information.

Section 2.2.5: Critical processes are validated to ensure that procedures, when used, will consistently result in the expected qualities in the finished preparation.

Section 2.2.6: The compounding environment is suitable for its intended purpose.

Section 2.2.7: Appropriate stability evaluation is performed or determined from the literature for establishing reliable beyond-use dating to ensure the finished preparations have their expected potency, purity, quality, and characteristics, at least until the labeled beyond-use date.

Section 2.2.8: There is assurance that processes are always carried out as intended or specified and are under control.

Section 2.2.9: Compounding conditions and procedures are adequate for preventing errors.

Section 2.2.10: Adequate procedures and records exist for investigating and correcting failures or problems in compounding, testing, or in the preparation itself.

Section 2.2.11: Compounders who are engaged in drug compounding or nutraceutical compounding shall be proficient in compounding and should continually expand their compounding knowledge by participating in seminars and/or studying appropriate literature.

Section 2.2.12: A Compounder must be familiar with all the details of USP <795> Pharmaceutical Compounding – Nonsterile Preparations, USP <797> Pharmaceutical Compounding – Sterile Preparations, USP <1160> Pharmaceutical Calculations in Prescription Compounding and other applicable state or federal compounding guidelines or laws. In addition, the Compounder must be responsible for the following:

- Certifying all prescription orders for compounding
- Approving or rejecting all components, drug product containers, closures, in-process materials, and labeling
- Preparing and reviewing all compounding records to assure that errors have not occurred in the compounding process
- Assuring the proper maintenance, cleanliness, and use of all equipment used in a prescription compounding practice

Back to Top

- Assuring that only authorized personnel shall be in the immediate vicinity of the drug compounding operations
- Assuring that the drug products 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

Section 2.2.13: The Compounder must ensure that personnel engaged in compounding wear clean clothing appropriate to the type of compounding performed, e.g., coats, gowns, gloves, masks, shoes, aprons, or other items needed to protect personnel from chemical exposures and prevent drug contamination.

Section 2.2.14: The Compounder must implement procedures to prevent cross-contamination when compounding with drugs that require special precaution to prevent cross-contamination (e.g., penicillin).

Section 2.3 - Responsibilities of the Pharmacist-In-Charge

Section 2.3.1: The PIC is the licensed pharmacy professional who is responsible for the entirety of pharmacy operations.

Section 2.3.2: The PIC must demonstrate awareness and knowledge of the respective state(s) Board of Pharmacy, DEA, and FDA regulations.

Section 2.4 - Responsibilities of Staff Pharmacists

Section 2.4.1: Staff Pharmacists must have adequate understanding of compounding operations and a knowledge of current USP standards related to nonsterile, and if applicable, sterile compounding.

Section 2.4.2: Staff Pharmacists must demonstrate proficiency with compounded preparations prepared, packaged, labeled, stored, and dispensed according to SOPs of the pharmacy.

Section 2.4.3: Staff Pharmacists are responsible for patient counseling and/or patient care services required by applicable state law or practice standards.

Section 2.4.4: Staff Pharmacists will verify that all SOPs related to compounding are followed.

Section 2.5 - Responsibilities of Pharmacy Technicians

Section 2.5.1: Pharmacy Technicians who are compounding under the direction of a Pharmacist must be trained and demonstrate proper use of SOPs and good compounding procedures.

Back to Top

Section 2.5.2: Pharmacy Technicians must have annual competency reviews, at minimum.

Section 2.6 - Compounding Training, USP <1075>

Section 2.6.1: All personnel involved in the compounding, evaluation, packaging, and dispensing of compounded preparations shall be properly trained for the type of compounding conducted. All training activities will be covered by appropriate SOPs and documentation.

Section 2.6.2: All Compounders and all personnel involved in compounding must be well-trained and must participate in current, relevant training programs. It is the responsibility of the Compounder to ensure that an ongoing training program has been implemented. Standards of practice require all employees to be adequately trained in their job functions and all training to be properly documented. Steps in the training procedure will include the following:

Section 2.6.2.a: All employees involved in pharmaceutical compounding shall read and become familiar with USP <795> Pharmaceutical Compounding — Nonsterile Preparations, USP <797> Pharmaceutical Compounding — Sterile Preparations, and USP <1060> Pharmaceutical Calculations in Prescription Compounding.

Section 2.6.2.b: All employees shall read and become familiar with each of the procedures related to compounding, including those involving the facility, equipment, personnel, actual compounding, evaluation, packaging, storage, and dispensing. Familiarity with procedures will be demonstrated and documented.

Section 2.6.2.c: The Compounder shall meet with employees to review their work and answer any questions employees may have concerning SOPs.

Section 2.6.2.d: The Compounder shall demonstrate procedures for the employee, and observe and guide the employee throughout the training process. The employee will then repeat the procedure without any assistance from, but under the direct supervision of, the Compounder.

Section 2.6.2.e: When the employee has demonstrated to the Compounder a verbal and functional knowledge of the procedure, then and only then will the employee be permitted to perform the procedure without direct supervision. However, the Compounder should be physically present and should check off the final preparation.

Back to Top

Section 2.6.2.f: When the Compounder is satisfied with the employee's knowledge and proficiency, the compounder will sign off in the employee file to show that the employee was appropriately trained.

Section 2.6.2.g: The Compounder shall continually monitor the work of the employee and assure that the employee's calculations and work are accurate and adequately performed. The Compounder is solely responsible for the finished preparation.

Chapter 3 – Facilities and Equipment

Section 3.1 - Drug Compounding Facilities, USP <1075>

Section 3.1.1: Compounding facilities shall have an adequate space specifically designated for compounding of prescriptions. This area may include a space for the storage of equipment and materials.

Section 3.1.2: Sterile compounded preparations shall be compounded in accordance with the provisions in USP <797> Pharmaceutical Compounding — Sterile Preparations. Aseptic processes shall be conducted in an area separate and distinct from the area used for the compounding of nonsterile products.

Section 3.1.3: The areas used for compounding shall be maintained in clean, orderly, and sanitary conditions.

Section 3.1.4: Drug compounding areas shall be maintained in a good state of repair. The plumbing system shall be free of defects that could contribute to contamination of any compounded product. Adequate hand- and equipment-washing facilities shall be easily accessible to the compounding areas. Such facilities shall include at minimum, hot and cold water, soap or detergent, and an air drier or single-use towels.

Section 3.1.5: Potable water shall be supplied under continuous positive pressure.

Section 3.1.6: Drug compounding areas shall have adequate lighting and ventilation for activities.

Section 3.1.7: Drug compounding areas shall be free of infestation by insects, rodents, and other vermin. Trash shall be held and disposed of in a sanitary and timely manner.

Section 3.1.8: Sewage and other refuse in drug compounding areas shall be disposed of in a safe and sanitary manner.

Back to Top

Section 3.1.9: Bulk drugs and other chemicals or materials used in the compounding of drugs must be stored as directed by the manufacturer or according to USP monograph requirements, in a clean, dry area under appropriate temperature conditions (controlled room temperature, refrigerator, or freezer). The bulk chemicals shall be stored in a manner such that they are protected from contamination. All containers shall be properly labeled.

Section 3.1.10: If parenteral products are compounded, the Compounder shall refer to USP <795> Pharmaceutical Compounding as appropriate.

Section 3.2 - Compounding Environment – Facilities, USP <795>

Section 3.2.1: Areas designated for compounding should have adequate space for the orderly placement of equipment and materials to prevent mix-ups between ingredients, containers, labels, in-process materials, and finished preparations. The compounding area is also to be designed, arranged, used, and maintained to prevent adventitious cross-contamination. Areas used for sterile preparations are to be separated and distinct from the nonsterile compounding area (see Environmental Quality and Control under USP <797> Pharmaceutical Compounding — Sterile Preparations). The entire compounding area is to be well-lighted. Heating, ventilation, and air conditioning systems must be controlled to avoid decomposition of chemicals (see Storage Temperature under Preservation, Packaging, Storage, and Labeling in the USP General Notices and Requirements and the manufacturers labeled storage conditions). Storage areas should provide an environment suitably controlled to ensure quality and stability of bulk chemicals and finished preparations.

Section 3.2.2: Potable water is to be supplied for hand and equipment washing. This water should meet the standards prescribed in the EPA's National Primary Drinking Water Regulations (40 CFR Part 141). Purified Water must be used for compounding nonsterile drug preparations when formulations indicate the inclusion of water. Purified Water must also be used for rinsing equipment and utensils. In those cases when water is used to prepare a sterile preparation, Water for Injection, Sterile Water for Injection, or Bacteriostatic Water for Injection must be used (see USP <1231> Water for Pharmaceutical Purposes and USP <797> Pharmaceutical Compounding — Sterile Preparations).

Section 3.2.3: Compounding areas are to be maintained in a clean and sanitary condition. Adequate washing facilities are to be provided, including hot and cold water, soap or detergent, and air driers or single-service towels. Sewage, trash, and other refuse in the compounding areas must be disposed in a safe, sanitary, and timely manner. Equipment should be thoroughly cleaned promptly

Back to Top

after use to avoid cross-contamination of ingredients and preparations. Special precautions should be taken to clean equipment and compounding areas meticulously after compounding preparations that contain allergenic ingredients (e.g., sulfonamides or penicillin's).

Section 3.3 - Compounding Environment – Equipment, USP <795>

Section 3.3.1: Equipment must be of appropriate design and size for compounding and suitable for the intended uses. The types and sizes of equipment will depend on the dosage forms and the quantities compounded (see USP <41> Weights and Balances, USP <1176> Prescription Balances and Volumetric Apparatus, and equipment manufacturers' instruction manuals). All equipment must be constructed so surfaces that contact pharmaceutical components, in-process materials, or finished preparations are not reactive, additive, or sorptive to avoid altering the safety, identity, strength, quality, or purity of the preparation. The use of micropipettes, electronic or analytical balances, or trituration's or dilutions shall be considered when needed quantities are too small to accurately measure with standard equipment required by a state Board of Pharmacy.

Section 3.3.2: Equipment and accessories used in compounding are to be inspected, maintained, cleaned, and validated at appropriate intervals to ensure the accuracy and reliability of their performance.

Section 3.4 - Component Selection Requirements, USP <1075>

Section 3.4.1: The Compounder must first attempt to use USP–NF drug substances manufactured in an FDA-registered facility.

Section 3.4.2: The Compounder also shall first attempt to use inactive components manufactured in an FDA-registered facility.

Section 3.4.3: If components are not obtainable from an FDA-registered facility, or if the FDA and/or the providing company cannot document FDA registration, Compounders shall use their professional judgment in first receiving, storing, or using the components that meet official USP requirements or are provided by another high-quality source.

Section 3.4.4: If components of USP quality are not obtainable, components of high quality such as those that are chemically pure, analytical reagent grade (RA), American Chemical Society (ACS)-certified, or Food Chemicals Codex (FCC) grade may be used.

Section 3.4.5: When a component is not obtained from an official USP source or is not obtainable from the sources mentioned above, the component may be obtained from a source deemed

Back to Top

acceptable and reliable in the professional judgment of the Compounder.

Section 3.4.6: When a component is derived from ruminant animals (e.g., bovine, caprine, ovine) the supplier shall provide written assurance that these animals were born, raised, and slaughtered in countries where bovine spongiform encephalopathy (BSE) and scrapie are known not to exist.

Section 3.4.7: The Compounder shall not use components listed by FDA to be withdrawn from the market for public health reasons.

Section 3.4.8: Components shall be stored off the floor, handled and stored to prevent contamination, and rotated so the oldest stock is used first.

Section 3.5 - Drug Compounding Equipment, USP <1075>

Section 3.5.1: The equipment or utensils used for compounding of a drug preparation shall be of appropriate design and capacity. The equipment should be stored in such a manner as to protect it from contamination, and shall be located in such a place as to facilitate operations for its use, maintenance, and cleaning.

Section 3.5.2: The equipment should be of suitable composition such that the surfaces that contact components are neither reactive, additive, nor absorptive and therefore will not affect or alter the purity of the compounded preparations.

Section 3.5.3: Automated, mechanical, electronic, and other types of equipment used in compounding or testing of compounded preparations should be routinely inspected, calibrated as necessary, and checked to ensure proper performance.

Section 3.5.4: Immediately prior to initiation of compounding operations, the equipment shall be inspected by the Compounder to determine its suitability for use.

Section 3.5.5: After use, the equipment should be appropriately cleaned. Extra care should be used when cleaning equipment used in compounding preparations requiring special precaution, e.g., antibiotics, cytotoxins, cancer drugs, and other hazardous materials. If possible, special equipment may be dedicated for such use, or if the same equipment is being used for all drug products appropriate procedures must be in place to ensure meticulous cleaning of equipment prior to use with other drugs.

Back to Top

Section 3.6 - Machine and Equipment Maintenance

Section 3.6.1: Each piece of equipment used within the compounding operation must be maintained in accordance with the specific manufacturer's requirements. The operation manual must be readily available to compounding personnel.

Section 3.6.2: Routine and preventive maintenance schedules are defined by the manufacturer.

Section 3.6.3: The Pharmacy must use the manufacturer's operation manual or create a SOP for maintenance, cleaning, calibration, and inspections. Documentation evidence must be available upon request to validate these actions have been completed.

Section 3.7 - Nonsterile Compounding, USP <795>

Section 3.7.1: BOC's accreditation standards follows USP <795> guidelines for nonsterile compounding. Compounding Pharmacy services encompass:

- UPS <795> Pharmaceutical Compounding—Nonsterile Preparations
- USP <1075> Good Compounding Practices
- USP <1160> Pharmaceutical Calculations in Prescription Compounding
- USP <1163> Quality Assurance in Pharmaceutical Compounding
- USP <800> Hazardous Drugs – Handling in Healthcare Settings

Section 3.8 - Sterile Compounding, USP <797>

Section 3.8.1: Sterile compounding follows USP <797> guidelines, which are not part of the current BOC Compounding Pharmacy Accreditation Standards. BOC does not currently provide sterile compounding accreditation.

Section 3.8.2: The Pharmacy may adopt certain requirements from USP <797> to aid in the operation of the compounding processes. Examples are:

- Positive air pressure working areas
- Self-contained ventilation systems
- Personnel wearing protective gear, such as:
    - Face shields
    - Foot coverings
    - Full-body suits
    - Mouth and nose masks
    - Self-contained breathing apparatus
    - Sterile gloves

Back to Top

Chapter 4 – Compound Storage and Handling

Section 4.1 - Bulk Chemicals and Compounds

Section 4.1.1: Storage of bulk chemicals and compounds must follow the manufacturer's guidelines found on the individual product's Safety Data Sheets (SDS). [Note: SDS were formerly known as Material Safety Data Sheets (MSDS).]

Section 4.1.2: The Pharmacy will only use recognized suppliers of bulk chemical ingredients, inactive ingredients, or excipients and other components.

Section 4.1.3: The Pharmacy will use only reputable suppliers for purchasing devices, containers, and closures used in compounding. The supplier must comply with any applicable USP standards.

Section 4.1.4: The Pharmacy will use high-quality active pharmaceutical ingredients. Active pharmaceutical ingredients will meet current USP/NF standards, other USP standards or be components of products approved by the FDA or grandfathered under the Food, Drug & Cosmetic Act of 1938.

Section 4.1.5: The Pharmacy will designate an area to be used for receiving and inspecting chemicals, devices, containers, closures, and other components or supplies used in compounding. Any product that appears to be damaged, tampered with, stored under improper conditions, or in any other way unfit for compounding use will be rejected and quarantined from the pharmacy's general stock. Pharmacists will use professional judgment and/or manufacturer guidelines in the acceptance or rejection of compounding supplies.

Section 4.1.6: No drug substance or chemical will be released for use in compounding until its corresponding Certificate of Analysis is reviewed. Certificates of Analysis will be retained for a period of not less than two years in hard copy or electronic form.

Section 4.2 - Potency

Section 4.2.1: The Pharmacy will document compliance regarding strength, quality, purity, potency, and stability throughout the period of intended use of compounded preparations on the Formulation Record and/or Compounding/Prepack Log.

Section 4.3 - Sterility, USP <795>

Section 4.3.1: Assurance of sterility in a compounded sterile preparation is mandatory. Compounding and packaging of sterile drugs, such as ophthalmic solutions, will require strict adherence to guidelines presented in USP <797> Pharmaceutical

Back to Top

Compounding — Sterile Preparations and in the manufacturers' labeling instructions.

Section 4.4 - Proper Hand Hygiene

Section 4.4.1: Proper hand hygiene is essential for safe compounding practices for both the compounding personnel and the patient.

Section 4.4.2: Ample hand-cleaning supplies must be available within the compounding area and restrooms. Alcohol-based hand gel (60 – 90%), hand moisturizer, and single-use paper towels in ample supplies are to be used throughout the entire compounding operation.

Section 4.4.3: Compounding personnel are responsible for their individual fingernails. Nails should be kept clean and short. Nail polish should not be chipped. Nail enhancement (artificial and gel nails) is strongly discouraged.

Section 4.5 - Safe Glove Procedure

Section 4.5.1: Protective gloves, latex or latex-free, must be used for all compound preparation, packaging, and handling.

Section 4.5.2: Double gloving is required for all hormone pharmaceuticals.

Section 4.5.3: Protective gloves are single use per compound preparation. Used gloves must be placed in a bio-hazard container.

Section 4.6 - Handling, Storage, and Disposal

Section 4.6.1: Temperature control of storage areas must be maintained within the guidelines for the compounded product. The storage unit must have a temperature control log which is checked twice daily or an electronic temperature monitoring system.

Section 4.6.2: A quarantine area must be established for compromised materials. Quarantine materials are comprised of items which are suspected and/or known to be out of manufacturer’s guidelines. The quarantine area must be away from the pharmacy’s general stock.

Section 4.6.3: Items stored in the quarantine area must be labeled “expired,” “damaged,” or “recalled,” and placed in the quarantine area.

Back to Top

Section 4.6.4: Expired, damaged, and quarantined products must be either returned to the vendor or disposed in accordance with state and other environmental laws.

Chapter 5 – Compounding Practices

Section 5.1 - Compounded Preparations - USP <795>

Section 5.1.1: The term “compounded preparations” encompasses compounded dosage forms, compounded drugs, and compounded formulations, and refers to finished forms that are prepared by or under the direct supervision of a licensed Compounder.

Unless otherwise indicated or appropriate, compounded preparations shall be prepared to ensure that each preparation shall contain not less than 90.0% and not more than 110.0% of the theoretically calculated and labeled quantity of active ingredient per unit weight or volume, and not less than 90.0% and not more than 110.0% of the theoretically calculated weight or volume per unit of the preparation. Compounded preparations include, but are not restricted to, the following pharmaceutical dosage forms described under USP <1151> Pharmaceutical Dosage Forms.

Section 5.1.2: When controlled substances are used, always check first with state and federal authorities concerning existing, current legislation and regulations.

Section 5.2: Capsules, Powders, Lozenges, and Tablets

Section 5.2.1 When compounding these dosage forms, the Compounder must prepare an amount of the total formulation sufficient to allow the prescribed amount or quantity to be accurately dispensed. Selected practices and precautions for compounding these dosage forms include the following:

Section 5.2.1(a) - Reducing solid ingredients to an appropriate, clinically applicable particle size

Section 5.2.1(b) - Implementing appropriate checks to ensure all ingredients are blended to achieve a homogeneous mixture

Section 5.2.1(c) - Monitoring humidity if moisture might cause hydrolysis, dosage form adhesion to containers, or softening or partial dissolution of capsule shells

Section 5.2.1(d) - Accurately performing weighing measurements to ensure that each unit shall be not less than 90% and not more than 110% of the theoretically calculated weight for each unit [Note: Preparations classified as dietary supplements are required by FDA

Back to Top

regulations to be not less than 100% of the declared potency]

Section 5.2.1(e) - Packaging dosage units according to container specifications for capsules and tablets of the specific active ingredient unless specified otherwise in individual monographs (see USP <660> Containers—Glass and USP <661> Containers—Plastic)

Section 5.3: Emulsions, Solutions, and Suspensions

Section 5.3.1 When compounding these dosage forms, the Compounder is to prepare a 2% to 3% excess amount of the total formulation to allow the prescribed amount to be accurately dispensed. Selected practices and precautions for compounding these dosage forms include the following:

Section 5.3.1(a) - For single-unit containers, the weight of each filled container, corrected for tare weight, shall be the equivalent of not less than 100% and not more than 110% of the labeled volume.

Section 5.3.1(b) - Aqueous suspensions are prepared by levigating the powder mixture to a smooth paste with an appropriate wetting agent. This paste is converted to a free-flowing fluid by adding adequate vehicle(s). Successive portions of the vehicle(s) are used to wash the mortar, or other vessel, to transfer the suspension quantitatively to a calibrated dispensing bottle or graduate. The preparation may be homogenized to ensure a uniform final dispersion.

Section 5.3.1(c) - Reducing solid ingredients to an appropriate, clinically applicable particle size.

Section 5.3.1(d) - Ensuring solutions contain no visible undissolved matter when dispensed. [Note: An exception may occur with supersaturated solutions such as Potassium Iodide Oral Solution. In such case, appropriate labeling or appropriate additional information shall be provided.]

Section 5.3.1(e) - Labeling emulsions and suspensions “Shake well before using.”

Section 5.4: Suppositories

Section 5.4.1 When compounding suppositories, the Compounder is to prepare an excess amount of total formulation to allow the prescribed quantity to be accurately dispensed. Selected practices and precautions for compounding these dosage forms include the following:

Section 5.4.1(a) - Avoiding ingredients that are caustic or irritating, and thoroughly comminuting solids that are abrasive to the mucous membranes

Back to Top

Section 5.4.1(b) - Selecting a base that allows active ingredients to provide the intended local or systemic therapeutic effect

Section 5.4.1(c) - Reducing solid ingredients to the appropriate, clinically applicable particle size

Section 5.4.1(d) - Weighing a representative number of suppositories to ensure that each is not less than 90% and not more than 110% of the average weight of all suppositories in the batch

Section 5.5: Creams, Topical Gels, Ointments, and Pastes

Section 5.5.1 When compounding semisolid dosage forms, the Compounder is to prepare an excess amount of total formulation to allow the prescribed quantity to be accurately dispensed. Selected practices and precautions for compounding these dosage forms include the following:

Section 5.5.1(a) - Avoiding ingredients that are caustic, irritating, or allergenic to the skin or other application sites unless they are necessary for a defined treatment

Section 5.5.1(b) - Selecting a base or vehicle that allows active ingredients to provide the intended local or systemic therapeutic effect

Section 5.5.1(c) - Reducing solid ingredients to the appropriate, clinically applicable size

Section 5.5.1(d) - Geometrically incorporating the active ingredients with the added substances to achieve a uniform liquid or solid dispersion in the dosage form

Section 5.5.1(e) - Observing the uniformity of the dispersion by spreading a thin film of finished formulation on a flat transparent surface (e.g., clear glass ointment slab).

Section 5.6 - Compounding Process - USP <795>

Section 5.6.1: The Compounders are to consider using the following steps to minimize error and maximize the prescriber's intent.

- Judge the suitability of the prescription to be compounded in terms of its safety and intended use. Determine what legal and clinical limitations, if any, are applicable.
- Perform necessary calculations to establish the amounts of ingredients needed (see Pharmaceutical Calculations in USP <1160> Prescription Compounding).
- Identify equipment needed.
- Don the proper attire and wash hands.
- Clean the compounding area and needed equipment.

Back to Top

- Only one prescription should be compounded at one time in a specified compounding area.
- Assemble all necessary materials to compound the prescription.
- Compound the preparation following the Formulation Record or prescription (see Compounding Records and Documents below) according to the art and science of pharmacy.
- Assess weight variation, adequacy of mixing, clarity, odor, color, consistency, and pH as appropriate.
- Annotate the compounding log and describe the appearance of the formulation.
- Label the prescription containers to include the following items: (1) the name of the preparation; (2) the internal identification number; (3) the beyond-use date (see Beyond-Use Labeling); (4) the initials of the Compounder who prepared the label; (5) any storage requirements; (6) Strength/Concentration; (7) Volume/Quantity; and (8) any other statements required by law.
- Sign and date the prescription affirming that all procedures were carried out to ensure uniformity, identity, strength, quantity, and purity.
- Thoroughly and promptly clean all equipment and store properly.

Section 5.7 - Ingredient Selection – USP <795>

Section 5.7.1: Sources

Official compounded preparations are prepared from ingredients that meet requirements of the USP monograph for those individual ingredients for which monographs are provided.

A USP or an NF grade substance are the preferred sources of ingredients for compounding all other preparations. If that is not available, or when food, cosmetics or other substances must be used, the use of another high-quality source, such as RA, certified ACS, or FCC grade is an option for professional judgment. For any substance used in compounding not purchased from a registered drug manufacturer, the Compounder must establish purity and safety by reasonable means, which may include lot analysis, manufacturer reputation, or reliability of source.

A manufactured drug product may be a source of active ingredient. Only manufactured drugs from containers labeled with a batch control number and a future expiration date are acceptable as a potential source of active ingredients. When compounding with manufactured drug products, the Compounder must consider all ingredients present in the drug product relative to the intended use of the compounded preparation.

Back to Top

Section 5.7.2: Compounding Non-Drug Requirements

If the preparation is intended for use as a dietary or nutritional supplement (to supplement the diet) or cosmetic (e.g. to beautify), then the Compounder must adhere to USP <1075> Good Compounding Practices, this chapter, and must comply with any federal and state requirements.

Section 5.8 - Pharmaceutical Calculations in Pharmacy Practice – USP <1160>

Section 5.8.1: Correct pharmaceutical calculations can be accomplished by using, for example, proper conversions from one measurement system to another and properly placed decimal points; by understanding the arithmetical concepts; and by paying close attention to the details of the calculations. Before proceeding with any calculation, Pharmacists should do the following: (1) read the entire formula or prescription carefully; (2) determine which materials are needed; and then (3) select the appropriate methods of preparation and the appropriate calculation. **Refer to USP <1160> for detailed calculations**.

Section 5.8.2: Basic Mathematical Concepts – Significant Figures Expressed values are considered significant to the last digit shown (see Significant Figures and Tolerances in the USP General Notices). Significant figures are digits with practical meaning. The accuracy of the determination is implied by the number of figures used in its expression. The number of digits used must be appropriate and applicable to devices used by the Compounder.

Section 5.8.3: Basic Pharmaceutical Calculations The Compounder must be able to calculate the amount or concentration of drug substances in each unit or dosage portion of a compounded preparation at the time it is dispensed. Compounders must perform calculations and measurements to obtain, theoretically, 100% of the amount of each ingredient in compounded formulations. Calculations must account for the active ingredient, or active moiety, and water content of drug substances, which includes that in the chemical formulas of hydrates. Official drug substances and added substances must meet the requirements under USP <731> Loss on Drying, which must be included in the calculations of amounts and concentrations of ingredients. The Compounder should consider the effect of ambient humidity on the gain or loss of water from drugs and added substances in containers subjected to intermittent opening over prolonged storage. Each container should be opened for the shortest duration necessary and then closed tightly immediately after use.

Back to Top

Section 5.9 - Stability Criteria and Beyond-Use Dating – USP <795>

Section 5.9.1: The beyond-use date is the date after which a compounded preparation is not to be used and is determined from the date the preparation is compounded. Because compounded preparations are intended for administration immediately or following short-term storage, their beyond-use dates may be assigned based on criteria different from those applied to assigning expiration dates to manufactured drug products.

Section 5.9.2: Compounders are to consult and apply drug-specific and general stability documentation and literature when available, and are to consider the nature of the drug and its degradation mechanism, the container in which it is packaged, the expected storage conditions, and the intended duration of therapy when assigning a beyond-use date (see Expiration Date and Beyond-Use Date under Labeling in the USP General Notices and Requirements). Beyond-use dates are to be assigned conservatively. When using manufactured solid dosage forms to prepare a solution or aqueous suspension, the Compounder is also to consider factors such as hydrolysis and the freeze-thaw property of the final preparation before assigning a beyond-use date. In assigning a beyond-use date for a compounded drug preparation, in addition to using all available stability information, the Compounder is also to use his or her pharmaceutical education and experience.

Section 5.9.3: When a manufactured product is used as the source of active ingredient for a nonsterile compounded preparation, the product expiration date cannot be used to extrapolate directly a beyond-use date for the compounded preparation. However, a Compounder may refer to the literature or to the manufacturer for stability information. The Compounder may also refer to applicable publications to obtain stability, compatibility, and degradation information on ingredients. All stability data must be carefully interpreted in relation to the actual compounded formulation.

Section 5.9.4: At all steps in the compounding, dispensing, and storage process, the Compounder is to observe the compounded drug preparation for signs of instability. For more specific details of some of the common physical signs of deterioration, see Observing Products for Evidence of Instability under USP <1191> Stability Considerations in Dispensing Practice. However, excessive chemical degradation and other drug concentration loss due to reactions may be invisible more often than they are visible.

Section 5.9.5: In the absence of stability information that is applicable to a specific drug and preparation, the following maximum beyond-use dates are recommended for nonsterile compounded drug preparations that are packaged in tight, light-resistant containers and stored at controlled room temperature

Back to Top

unless otherwise indicated (see Preservation, Packaging, Storage, and Labeling in the USP General Notices and Requirements).

Section 5.9.6: For Non-Aqueous Liquids and Solid Formulations –

- Where the Manufactured Drug Product is the Source of Active Ingredient – The beyond-use date is not later than 25% of the time remaining until the product's expiration date or six months, whichever is sooner.
- Where a USP or NF Substance is the Source of Active Ingredient – The beyond-use date is not later than six months.

Section 5.9.7: For Water-Containing Formulations (prepared from ingredients in solid form) – The beyond-use date is not later than 14 days for liquid preparations when stored at cold temperatures between 2^{o} and 8^{o} C (36^{o} and 46^{0} F).

Section 5.9.8: For All Other Formulations – The beyond-use date is not later than the intended duration of therapy or 30 days, whichever is earlier. These beyond-use date limits may be exceeded when there is supporting valid scientific stability information that is directly applicable to the specific preparation (i.e., the same drug concentration range, pH, excipients, vehicle, water content, etc.). See also the beyond-use dating information in the Labeling section under USP <681> Repackaging in to Single-Unit Containers and Unit-Dose Containers for Nonsterile Solid and Liquid Dosage Forms.

Section 5.10 - Beyond-Use Labeling – USP <795>

Section 5.10.1: Federal law requires that manufactured drug products be labeled with an expiration date. Some state laws may require a beyond-use date. The label on the container or package of an official compounded preparation must bear a beyond-use date. Good compounding practices dictate beyond-use labeling for all compounded preparations.

Section 5.11 - Checklist for Acceptable Strength, Quality, and Purity – USP <795>

Section 5.11.1: The following questions are to be considered carefully before compounding, and are usually answered in the Formulary Record.

- Have the physical and chemical properties and medicinal, dietary, and pharmaceutical uses of the drug substances been reviewed?
- Are the quantity and quality of each active ingredient identifiable?

Back to Top

- Will the active ingredients be effectively absorbed, locally or systemically, according to the prescribed purpose, from the preparation and route of administration?
- Are there added substances (see USP Definitions), confirmed or potentially present from manufactured products, that may be expected to cause an allergic reaction, irritation, toxicity, or undesirable organoleptic response from the patient?
- Are there added substances (see USP Definitions), confirmed or potentially present, that may be unfavorable (e.g., unsuitable pH or inadequate solubility)?
- Were all calculations and measurements confirmed to ensure that the preparation will be compounded accurately (see USP <1160> Pharmaceutical Calculations in Prescription Compounding)?

Section 5.12 - Quality Control – USP <795>

Section 5.12.1: The safety, quality, and performance of compounded preparations depend on: correct ingredients and calculations; accurate and precise measurements; appropriate formulation conditions and procedures; and prudent pharmaceutical judgment. As a final check, the Compounder is to review each step in the compounding process. To ensure accuracy and completeness, the Compounder is to observe the finished preparation to ensure it appears to be as expected and is to investigate any discrepancies and take appropriate corrective action before the prescription is dispensed to the patient.

Section 5.13 - Verification – USP <795>

Section 5.13.1: Compounding procedures that are routinely performed, including batch compounding, shall be completed and verified according to written procedures. The act of verification of a compounding procedure involves checking to ensure that calculations, weighing and measuring, order of mixing, and compounding techniques were appropriate and accurately performed.

Section 5.14 - Compounding for a Prescriber's Office Use – USP <1075>

Section 5.14.1: Compounders may prepare compounded drug preparations for a prescriber's office use only where permitted by federal and state requirements. Federal and state requirements may vary.

- An order by the prescriber indicating the formula and quantity ordered may be filled in the Compounder's facility.

Back to Top

- Where compounding for office use is permitted, the Compounder shall compound the preparation for the sole purpose of administration by or for the prescriber.
- A record of the compounding process shall be maintained.
- A label must be generated and a unique identifying number may be assigned.

Section 5.15 - Compounding Veterinarian Products – USP <1075>

Section 5.15.1: Compounders shall compound prescriptions for animals on the basis of prescription orders.

Section 5.15.2: These prescriptions shall be handled and filled according to the guidelines available for compounding of veterinarian products.

Section 5.16 - Enteral Nutritional Products

Section 5.16.1: Enteral nutritional products are generally considered “Sterile Compounds” and are prepared under USP <797> Sterile Compounds. BOC accreditation currently does not extend into sterile compounding.

Section 5.17 - Internal and External Recalls

Section 5.17.1: Product recalls may come from internal reviews or external sources. The Compounder is responsible for identifying specific patients who have received pharmaceuticals that are deemed substandard or suspected to be not prepared by the Physician’s order or the Formulary.

Section 5.17.2: The Compounder must notify all affected prescribers, patients, and caregivers who have received the pharmaceutical that has been recalled. Notification methods include telephone, fax, email, U.S. mail, or commercial transportation carrier.

Section 5.17.3: The Compounder must have documented evidence that the affected individuals received the recall notice and account for the product. Recalled items are kept in a quarantine area until an investigation is completed and the product is either returned to the manufacturer or destroyed in accordance with appropriate state or federal disposal regulations.

Section 5.18 - Product Safety

Section 5.18.1: The Compounder must implement a safety program that ensures compounds are procured, received, stored, accessed, used in compound preparation, packaged, and shipped appropriately.

Back to Top

Section 5.18.2: Compounds which are suspect for contamination, expiration of shelf-life, or mislabeled information must be placed in the quarantine area until the compound is rendered safe for use, returned to the manufacturer, or destroyed.

Section 5.18.3: Safety Data Sheets (SDS) must be maintained and available for all employees. SDS may be maintained electronically or as hard copies.

Section 5.18.4: Personal Protective Equipment (PPE) must be available to employees. Training on the use of PPE must be documented and maintained within the facility.

Section 5.19 - Anticipatory Compounding

Section 5.19.1: The Compounder may prepare compound pharmaceuticals in advance of a prescription when:

- A Physician who practices with a specialty that routinely dispenses a compounded pharmaceutical to be dispensed either by the Physician or the Pharmacy requests
- A Veterinarian requests compounds to dispense to animals. Veterinary medicine can vary depending on the type of animals being treated, i.e.
    - Domestic companion or service pets
    - Large animals or livestock
    - Race horses
    - Reptiles

Section 5.19.2: Compounded products prepared in advance of an order will be labeled in accordance with the Labeling policy and procedure.

Section 5.20 - Stability of Compounded Preparations - Primary Packaging – USP <795>

Section 5.20.1: “Stability” is defined as the extent to which a preparation retains, within specified limits and throughout its period of storage and use, the same properties and characteristics that it possessed at the time of compounding (see the table Criteria for Acceptable Levels of Stability under USP <1191> Stability Considerations in Dispensing Practice).

Section 5.20.2: The Compounder must avoid formulation ingredients and processing conditions that would result in a potentially toxic or ineffective preparation. The Compounder's knowledge of the chemical reactions by which drugs may degrade provides a means for establishing conditions under which the rate of degradation is minimized. The factors that influence the stability of compounded preparations are generally the same as those for manufactured drug products (see Factors Affecting Product

Back to Top

Stability and Responsibility of the Pharmacist under USP <1191> Stability Considerations in Dispensing Practice).

Section 5.21 Packaging and Drug Preparation Containers – USP <795>

Section 5.21.1: Compounded preparations should be packaged in containers meeting USP standards (see Containers under Preservation, Packaging, Storage and Labeling in the General Notices and Requirements, USP <661> Containers — Plastics, and USP <671> Containers — Performance Testing). The container used depends on the physical and chemical properties of the compounded preparation. Container–drug interaction is to be considered with substances such as phenolic compounds and absorptive materials (e.g. polypeptides and proteins).

Section 5.22 - Packaging, Labeling and Delivery for Administration and Dispensing – USP <1075>

Section 5.22.1: The Compounder shall ensure that the containers and container closures used in packaging the compounded preparations meet the requirements under USP <660> Containers — Glass, USP <661> Containers — Plastic, and USP <671> Containers — Performance Testing. The Compounder shall obtain written records from the supplier to show that the containers meet USP requirements.

Section 5.22.2: Containers and container closures intended for compounding of sterile preparations and nonsterile preparations must be handled, sterilized (if appropriate) and stored as described in USP <797> Pharmaceutical Compounding — Sterile Preparations and USP <795> Pharmaceutical Compounding — Nonsterile Preparations. The use of commercially available pre-sterilized containers is encouraged for sterile preparations.

Section 5.22.3: The containers and closures shall be stored off the floor, handled and stored to prevent contamination, and rotated so that the oldest stock is used first.

Section 5.22.4: The containers and container closures shall be stored in such a way as to permit inspection and cleaning of the work area.

Section 5.22.5: The containers and container closures shall be made of clean materials that are neither reactive, additive, nor absorptive.

Section 5.22.6: The containers and closures shall be of suitable material so as not to alter the quality, strength, or purity of the compounded drug.

Back to Top

Section 5.23 - Labeling – USP <795>

Section 5.23.1: The Compounder's preparation label should contain information required by state and federal law and accepted standards of practice. [Notes: (1) The Compounder shall use the established name or distinct common name (cannot use the trademarked name of a manufactured product). (2) The Compounder cannot indicate that the compounded product is therapeutically equivalent to a manufactured product. (3) The label should state that this is a compounded preparation. (4) The Compounder shall not use an NDC number assigned to another product.]

Section 5.23.2: The Compounder shall label any excess compounded products so as to reference them to the formula used, the assigned control number, and beyond-use date based on the Compounder's appropriate testing, published data, or USP–NF standards.

Section 5.23.3: Preparations compounded in anticipation of a prescription (prior to receiving a valid prescription) should not be prepared in an inordinate amount. A regularly used amount should be prepared on the basis of a history of prescriptions filled by the Pharmacy. These preparations should be labeled or documentation referenced with the following:

- A complete list of ingredients or preparation name and reference, established, or distinct common name
- Dosage form
- Strength
- Preparation date
- Name and address of Compounder
- Inactive ingredients
- Batch or lot number
- Assigned beyond-use date based on published data, appropriate testing, or USP–NF standards.
- Storage conditions for these preparations should be dictated by their composition and sterility, e.g. stored in a clean, dry place under appropriate temperature conditions (controlled room temperature, refrigerator or freezer.)

Section 5.23.4: The Compounder should examine the preparation for correct labeling after completion of the compounding process.

Section 5.24 - Shipping

Section 5.24.1: The Compounder will ensure all compounds shipped to prescribers and patients are shipped with a tracking number and the carrier obtains a signed delivery receipt. All shipping must assure adequate maintenance of product stability.

Back to Top

Section 5.24.2: Some compounds require refrigeration when shipped. The use of wet ice or dry ice is required to protect the compound. When shipping with either type of ice, an approved packaging must be used. The compound must be double-bagged to ensure it is not directly exposed to the ice.

Section 5.24.3: If dry ice is used, Express Mail shipment is not permitted. Dry ice is considered a hazardous material for air shipment by the International Air Transport Association (IATA). A Shipper's Declaration must be prepared and given to the carrier at the time of pickup.

Chapter 6 – Compounding Records

Section 6.1 - Documentation

Section 6.1.1: Documentation must exist that references Protected Health Information (PHI) under the federal Health Insurance Portability and Accountability Act (HIPAA), Title 45 CFR 164.316(b) and Title 45 CFR 164.530(j). The Compounding Facility must establish policies and procedures to maintain written and electronic documentation. These procedures must demonstrate how to properly secure PHI until such time as the documents are destroyed under the direction of the HIPAA Privacy and/or Security Officer.

Section 6.1.2 Retention of documentation is established by different agencies of the U.S. Department of Health and Human Services (HHS). Individual state requirements may be more stringent than federal statutes; in this case, the most stringent will apply. A current list of documentation retention requirements is as follows:

- 2 years – (Average) State Pharmacy and Medical Boards
- 6 years – HIPAA Compliance
- 7 years – Medicare Part B
- 10 years – Medicare Part C and Part D

Section 6.1.3: Policies and procedures, written or electronic, must be available to all authorized staff and outside regulatory agencies upon request.

Section 6.1.4: Policies and procedures and documentation must be kept up to date as new or revised standards and guidelines are published.

Section 6.1.5: Documents containing PHI care considered "Confidential." Access to these documents is limited to authorized staff or other entities who are permitted by regulatory statutes or a signed Business Associate agreement.

Back to Top

Section 6.1.6: Designated storage areas for PHI must be established and limited access to these areas must be maintained.

Section 6.1.7: The Pharmacy will take the necessary steps to ensure the proper disposal of documents containing PHI to include:

- Shredding documents containing PHI when being disposed of in the facility (or other locations that are authorized to have PHI)
- Securing documents containing PHI until incineration
- Securing documents containing PHI until pick-up for vendor destruction

- If incineration is the designated method of destruction, obtaining and maintaining written verification that the incineration did in fact occur.

Section 6.2 - Compounding Records and Documents USP <795>

Section 6.2.1: All Compounders who dispense prescriptions must comply with the record-keeping requirements of each individual state for which they hold licensure. If the Compounder compounds a preparation according to the manufacturer's labeling instructions, then further documentation is not required. All other compounded preparations require further documentation. Such compounding documents are to list the ingredients and the quantity of each in the order of the compounding process.

The objective of the documentation is to allow another Compounder to reproduce the identical prescription at a future date. The Formulation Record provides a consistent source document for preparing the preparation, and the Compounding Record documents the actual ingredients in the preparation and the person responsible for the compounding activity. These records are to be retained for the same period of time that is required for any prescription under state law. The record may be a copy of the prescription in written or machine-readable form that includes a Formulation Record, a Compounding Record and a SDS file.

Section 6.2.2: The Formulation Record is a file of individually compounded preparations. This record must list the name, strength, and dosage form of the preparation compounded, all ingredients and their quantities, equipment needed to prepare the preparation, when appropriate, and mixing instructions. Mixing instructions should include the order of mixing; mixing temperatures or other environmental controls, such as the duration of mixing; and other factors pertinent to the replication of the preparation as compounded. The Formulation Record must include an assigned beyond-use date, the container used in

Back to Top

dispensing, the storage requirements, and any quality control procedures.

Section 6.2.3: The Compounding Record contains documentation of the name and strength of the compounded preparation, the Formulation Record reference for the preparation, and the sources and lot numbers of ingredients. The Compounding Record also includes information on the total number of dosage units compounded; the name of the person who prepared the preparation; the name of the Compounder who approved the preparation; the date of preparation; the assigned internal identification number or the prescription number and an assigned beyond-use date; and the prescription number. For all compounded preparations, results of quality control procedures are to be recorded (e.g. weight range of filled capsules). When compounding problems occur with preparations prepared according to USP compounding monographs, the Compounder must complete a USP Monograph Experience Reporting Form and submit the form to USP for evaluation.

Section 6.2.4: SDS are to be readily accessible to all employees working with drug substances or bulk chemicals located on the Compounding Facility premises. Employees are to be instructed on how to retrieve and interpret all needed information.

Section 6.3 - Records and Reports USP <1075>

Section 6.3.1: The Compounder shall maintain records, including but not limited to the hard or electronic copy of the prescription, to indicate that the prescription is compounded and to provide Formulation Records and Compounding Records.

Section 6.3.2: The Compounder shall keep all required records of Controlled Dangerous Substances (CDS or ‘scheduled drugs’) used in compounding.

Section 6.3.3: All records of all compounded preparations shall be kept for a period as set forth in the federal and state laws or regulations. Such records shall be readily available for authorized inspection.

Section 6.3.4: The Compounding Records shall include the manufacturer and lot number of all ingredients.

Section 6.4 - Formulation Record and Compounding Record

Section 6.4.1: The Pharmacy must document Formulation Records to indicate the strength, quality, purity, integrity and, where applicable, sterility of all compounded preparations.

Back to Top

Section 6.4.2: The Formulation Record must contain all information necessary to reproduce the compounding preparation including:

- Name
- Strength
- Dosage form of the compounded preparation
- Calculations needed to determine and verify quantities of components and doses of active pharmaceutical ingredients
- Description of all components and ingredients, and their quantities
- Compatibility and stability information, including references when available
- Equipment used to prepare the compounded preparation
- Mixing instructions that include, at a minimum:
    - Order of mixing
    - Mixing temperatures or other environmental controls
    - Duration of mixing and other factors pertinent to the replication of the compounded preparation
    - Assigned beyond-use date of the compounded preparation
    - Container used in dispensing
    - Packaging and storage requirements
    - Quality control procedures
    - References used in the development of the Formulation Record

Section 6.4.3: A Compounding Record of each instance that a compound preparation is made to verify accurate compounding in accordance with the Formulation Record. The Compounding Record contains:

- Name and strength of the compounded preparation
- Formulation Record reference for the preparation
- Sources
    - Lot numbers
    - Quantities
    - Expiration dates of components and ingredients
- Total quantity compounded and actual net measurements
- Name of the personnel involved in the compounding process and the name of the Pharmacist who approved the compounded preparation
- Date of preparation
- Assigned internal identification number or prescription number
- Equipment used
- Assigned beyond-use date of the compounded preparation
- Results of quality control procedures

Back to Top

Section 6.5 - Prescriber Communication

Section 6.5.1: The Pharmacy will communicate with the prescribing Physician(s) or other authorized prescriber(s) when instructions are unclear or in question. The Pharmacist will document the communication on the prescription or in the pharmacy software comments/notes for the specific prescription.

Section 6.5.2: In the event of an adverse reaction to a compound, the prescribing Physician or other authorized prescriber must be contacted and all communication documented. The documentation must include:

- Patient
- Type of reaction
- Ingredients
- Method of compounding

Section 6.6 - Patient Education

Section 6.6.1: A Pharmacist is responsible for counseling the patient and/or caregiver regarding how the compound is to be used and written instructions are to accompany the compound. All information provided must match that given for any prescription.

Chapter 7: Quality Assurance, USP <1163>

Section 7.1 - Standard Operating Procedures

Section 7.1.1: SOPs for pharmaceutical compounding are documents that describe how to perform routine and expected tasks in the compounding environment including; formulation development, purchasing, compounding, testing, maintenance, training, materials handling and storage, quality assurance, labeling, beyond-use dating, cleaning, safety, and dispensing. SOPs are itemized instructions that describe how a task will be performed, who will do it, why it is done, any limits, and what to do if a deviation occurs.

Section 7.1.2: SOPs must be reviewed regularly and updated as necessary. The SOP should be specific to each device, process, and decision used in compounding. Properly maintained and implemented SOPs should result in quality preparations and fewer compounding errors.

Section 7.2 - Documentation

Section 7.2.1: The purpose of the documentation is to provide a permanent record of all aspects of each compounding operation. Two essential compounding documents, the Formulation Record and the Compounding Record, are described in USP <795>

Back to Top

Pharmaceutical Compounding - Nonsterile Preparations. The Compounding Record is completed and reviewed for accuracy during the compounding process for the preparation being made.

Section 7.2.2: In addition, many SOPs require specific cross-referenced data collection forms (e.g. air temperature and humidity records and balance maintenance and calibration records). Data collection forms required by SOPs are completed during routine tasks directed by the SOPs and may provide fill-in-the blank spaces for data, including logbook entries, data printouts, and reports.

Section 7.3 - Verification

Section 7.3.1: Verification involves assurance and documentation that a process, procedure, or piece of equipment is functioning properly and producing the expected results.

USP <795> Pharmaceutical Compounding - Nonsterile Preparations states: “The act of verification of a compounding procedure involves checking to ensure that calculations, weighing and measuring, order of mixing, and compounding techniques were appropriate and accurately performed.”

Verification may require outside laboratory testing when in-house capabilities are not adequate. Equipment verification methods are sometimes available from manufacturers of the specific equipment or can be developed in-house.

The responsibility for assuring that equipment performance is verified, including work completed by contractors, resides with the Compounder.

Section 7.4 - Testing of Finished Compounded Preparations

Section 7.4.1: A quality assurance program should include testing of finished compounded preparations. It is important for the Compounder to have a basic understanding of pharmaceutical analysis to ensure that valid results are obtained when tests are being conducted, whether they are done in-house or outsourced. While it is not practical to test every compounded preparation, it is incumbent on the Compounder to know:

(1) the importance of testing in the overall quality program in the Compounding Facility,
(2) when to test,
(3) what to test,
(4) what method(s) to use,
(5) how to interpret the results,
(6) the limits of the test, and
(7) what to do if the preparations listed do not meet specifications. Investigative and corrective action should extend to other

Back to Top

preparations that may have been associated with the specific failure or discrepancy.

Section 7.4.2: The goal in testing is to produce results as accurately, efficiently and quickly as possible. Any testing method used should have accuracy, speed, reproducibility, and specificity. No single testing method is suited for all drugs. There are a number of factors that determine the validity and reliability of results.

Section 7.4.3: Compounding Facilities have two options when testing is required. Some testing methods can easily be performed in-house, but some may need to be outsourced to a contract laboratory. Relatively basic testing methods that can be conducted in-house with proper training and a modest investment in instrumentation include weight and volumetric measurements, pH, density/specific gravity, refractive index, and UV and visible spectroscopy (see USP <41> Weights and Balances, USP <31> Volumetric Apparatus, USP <1176> Prescription Balances and Volumetric Apparatus, USP <791> pH, USP <841> Specific Gravity, USP <831> Refractive Index, and USP <851> Spectrophotometry and Light-Scattering). Testing methods often outsourced to a contract laboratory include chromatography (high-pressure liquid chromatography (HPLC) and gas chromatography (GC), (see USP <621> Chromatography), mass spectroscopy (MS) (see USP <736> Mass Spectrometry), hyphenated methods (HPLC-MS and GC-MS), UV and visible spectroscopy (see USP <851> Spectrophotometry and Light-Scattering) and other sophisticated methods.

Section 7.4.4: If testing is done in-house appropriate equipment must be obtained, verified either by the manufacturer or by the Compounder upon purchase, maintained, calibrated, and used properly. If testing is outsourced, the Compounder needs to determine what to outsource and how to select a laboratory, and should develop ongoing relationships with the laboratories chosen. Contract laboratories should follow USP general chapter standards, as appropriate.

Section 7.4.5: Selection of a Testing Method — One general consideration in testing method selection is the type of information that is needed, such as quantitative (potency, concentration), semi-quantitative (where a tolerance level is involved, as in endotoxin levels) or qualitative (presence/absence type of testing, including substance identification, sterility). Another consideration involves the physical and chemical characteristics of the analyte, including solubility, partition coefficient, dissociation constant (pKa), volatility, binding, and the quantity present.

Section 7.4.6: The degree of quantitative measurement and specificity must be considered in the validation process. The typical analytical characteristics used in method validation include accuracy, precision, specificity, detection limit, quantitation limit, linearity, range, and ruggedness (see USP <1225> Validation of Compendial Procedures). Generally, the greater the level of accuracy, precision, or specificity

Back to Top

required, the more sophisticated and expensive the testing methods needed. The methods used are also governed by the types of instrumentation available and the standards available for comparison.

Section 7.4.7: Pharmaceutical analysis decisions include not only method selection but also administrative and economic factors, obtaining a representative sample, storage/shipping of the sample, sample preparation for analysis, the actual analysis, data acquisition, data treatment, and interpretation.

Section 7.4.8: Factors Involved in Method Selection— The testing method selected depends upon a number of factors, including sample requirements, sample handling/preparation/purification requirements, type of data needed, and levels of specificity and accuracy required.

Section 7.4.9: Sampling Requirements-- Prior to collecting samples for testing, the following factors should be considered: the number of samples needed, appropriate methods of obtaining representative samples, the physical state of the samples (solid, liquid, or gas), the type of container required for collection and storage, and possible shipping requirements or restrictions. Storage requirements for samples must be specified, such as type of container, temperature, humidity, and light protection (see USP General Notices and Requirements).

Section 7.4.10: The effect of any substances in the formulation that may interfere or alter the results must be known beforehand. When sending a preparation to a contract laboratory, the Compounder should provide the complete formulation so the laboratory can quickly determine if there may be any interfering substances.

Section 7.4.11: Controlled Dangerous Substances (CDS), dangerous or hazardous chemicals, flammable or caustic substances, and refrigerated or frozen preparations require special handling during shipping.

Section 7.4.12: Data Interpretation Requirement--The collection of raw data from the testing process must be completed accurately. One must ensure that appropriate and valid descriptive statistics are used to analyze the data, and that the operating parameters of the analytical instruments are well established. Reference values, if available, should be provided with the analytical results. A description of the analytical controls used by the laboratory is important documentation, as is the source of reference standards used to establish standard curves.

Section 7.4.13: Personnel Requirements and Considerations – If testing is done in-house, personnel involved in this activity must be appropriately trained and evaluated with documentation of the training and evaluation. If testing is outsourced, the Compounder must be assured of the credentials, proper training, and continuing competency activities of the personnel in the contract laboratory. It is

Back to Top

preferable that the contract laboratory be registered with the FDA. It may also be advantageous if the contract laboratory performs testing for pharmaceutical companies.

Section 7.4.14: Testing Methods— Testing methods can be generally divided into physical testing methods, methods that interact with electromagnetic radiation, conductometric techniques, immunoassay methods, separation techniques, and others.

Section 7.4.14.1: Classification of Analytical Methods (Refer to USP <1163> for Tables)

- Physical Testing Procedures
- Weight
- Volumetric
- Melting Point
- Freezing Point
- Boiling Point
- Density
- Refractive Index
- Optical Rotation (Polarimetry)
- Thermal Analysis
- Color Change
- Precipitate Formation
- Viscosity Change
- Particle Size
- Light Scattering
- Zeta Potential
- Light Obscuration
- Microscopic Examination
- Interaction of Electromagnetic Radiation
- Ultraviolet/Visible Spectroscopy
- Infrared Spectroscopy
- Fluorescence/Phosphorescence Spectroscopy
- Raman Spectroscopy
- X-ray Spectroscopy
- Flame Emission and Atomic Absorption Spectroscopy
- Polarimetry
- Refractometry
- Interferometry
- Conductance Methods
- pH
- Ion Selective Electrodes
- Polarography
- Immunoassay
- Radioimmunosassay
- Enzyme Multiplied Immunoassay Technique (EMIT)
- Enzyme Linked Immunosorbent Assay (ELISA)
- Fluorescent Immunoassay (FIA)
- Separation Techniques

Back to Top

- High Performance Liquid Chromatography (HPLC)
- Gas Chromatography (GC)
- Thin-Layer Chromatography (TLC)
- Paper Chromatography (PC)
- Column Chromatography (CC)
- Others
- Osmolality
- Microbiological Methods
- Sterility Testing
- Microbial Limit Testing
- Endotoxin Testing
- Preservative Effectiveness Testing

Section 7.5 - Microbiological Testing

Section 7.5.1: Microbiological testing for Compounding Pharmacy includes sterility, endotoxin, and microbial limit testing. Preservative effectiveness may also be considered.

Section 7.5.2: Sterility Testing — Sterility tests can be conducted using commercial kits or by developing and validating USP sterility testing protocols, which are more detailed than the commercial sterility-testing kits. Standards and procedures are explained in USP <71> Sterility Tests.

Section 7.5.3: Endotoxin Testing — Endotoxin tests can be conducted using commercially available kits or by purchasing the components separately. Endotoxin testing endpoints can be difficult to interpret and in-house testing should only be done after obtaining training and experience. See USP <85> Bacterial Endotoxins Test.

Section 7.5.4: Microbial Limit Testing — Microbial limit testing can be conducted to provide an estimate of the number of viable aerobic microorganisms and for freedom from designated microbial species. See USP <61> Microbial Enumeration Tests and USP <62> Tests for Specified Microorganisms.

Section 7.6 - Continuous Quality Improvement (CQI)

Section 7.6.1: The Pharmacy must actively participate in Continuous Quality Improvement (CQI) by implementing a quality improvement plan and documenting Quality Related Events (QREs) (formerly known as Adverse Events).

Section 7.6.2: At a minimum, a CQI program shall include provisions to:

- Designate an individual or individuals responsible for monitoring CQI Program compliance
- Identify and document QREs
- Minimize impact of QREs on patients

Back to Top

- Analyze data collected in response to QREs to assess causes and any contributing factors
- Use the findings of the analysis to formulate an appropriate response and develop pharmacy systems and workflow processes designed to prevent QREs
- Provide ongoing education at least annually in the area of CQI to pharmacy personnel

Section 7.6.3: Identification and Documentation of QREs is maintained including a description of the event that is sufficient to permit categorization and analysis of the event.

- Pharmacy will collect data on QREs during all hours of pharmacy operation and will collect data including, but not limited to:
  - Where detected
  - Where made
  - Type of QRE
  - Reception by patient
- If a patient was effected by the QRE, (1) notification to the patient or patient's representative and the prescriber (if indicated in the professional judgment of the Pharmacist); (2) directions for correcting the error; and (3) instructions for minimizing the negative impact to the patient.

Section 7.6.4: Root Cause Analysis/Investigative Analysis is conducted to determine the “Root Cause” of the QRE. The PIC, Peer Review, or a Patient Safety Organization (PSO) may conduct this investigation. The investigation is to take in account:

- a consideration of the effects on quality assurance related to workflow processes, technological support, personnel training, and staffing levels
- any recommended remedial changes to pharmacy policies, procedures, systems, or processes

Section 7.6.5: The final step of a Root Cause Analysis (RCA) is a process of improvement(s) that must be incorporated in Policy and Procedures, SOPs, workflow processes, environmental factors, technological factors, and/or training.

Section 7.6.6: BOC strongly recommends the Pharmacy enroll into a Patient Safety Organization (PSO) and report all QREs to this organization. If the Pharmacy does, most documentation and meetings minutes are considered “Patient Safety Work Product — Privileged & Confidential, Inadmissible as Evidence, not Subject to Discovery.”

Back to Top