Standards of Practice
For The
Specialty Sterile Pharmaceutical Society

Preamble

Member companies of the Specialty Sterile Pharmaceutical Society are dedicated to compounding sterile preparations for client institutions ensuring the safety, identity, strength, purity and quality of those preparations. Their goal is to set high standards for compounding to assure the client institutions and the final end user of the preparation's quality and suitability for use.

The member companies currently find themselves in the unique position of potentially being held accountable for meeting the standards and regulations of the United States Pharmacopeia and the United States Food and Drug Administration. In this environment it is important for the Specialty Sterile Pharmaceutical Society to set forth Standards of Practice that will meet the specifications, standards and regulations of those agencies. Those standards and regulations that are directly applicable to the special environment in which member companies operate are incorporated into its Standards of Practice. The adopted Standards of Practice are those that are necessary and sufficient to assure the safety and quality of the final compounded preparation. In those cases where it appears that direct compliance with the regulations found in 21 CFR Part 211 have not been achieved, suitable alternatives to those regulations have been incorporated into the Standards of Practice to obtain the desired objective.

Source Documents

USP <795> Pharmaceutical Compounding – Non Sterile Preparations

USP <797> Pharmaceutical Compounding – Sterile Preparations

USP <1163> Quality Assurance in Pharmaceutical Compounding

21 CFR Part 11 - Electronic Records; Electronic Signatures

21 CFR Part 210 – Current Good Manufacturing Practice in Manufacturing, Processing, Packing, or Holding of Drugs; General - §210.3 Definitions

21 CFR Part 211 – Current Good Manufacturing Practice For Finished Pharmaceuticals

Guidance for Industry – Electronic Records; Electronic Signatures – Scope and Application

Guidance for Industry – Sterile Drug Products Produced by Aseptic Processing – Good Manufacturing Practice

Standards of Practice

Specialty Sterile Pharmaceutical Society member companies shall comply with appropriate sections of USP <795> as they may apply to compounding sterile preparations, and the requirements of USP <797>.

Specialty Sterile Pharmaceutical Society member companies shall comply with the sections of the Food, Drug and Cosmetic Act pertaining to company registration, and reporting adverse events.

The following sections provide further guidance to the Standards of Practice for member companies as they apply to the special environment in which they operate.

Electronic Records; Electronic Signatures

There shall be written procedures describing in sufficient detail to control those activities associated with the following elements of electronic records and signatures:

- Limiting access to authorized personnel
- Provision for operational system checks
- Provision for authority limits
- Use of device checks
- Documentation that the individuals maintaining or using the electronic systems have the education, training and experience to carry out their assigned duties
- Accountability for actions taken under an individual's electronic signature
- Controls over system documentation

Quality Control

- Procedures shall be written and maintained detailing the function of the Quality Control Unit
- There shall be written specifications for all materials, components, containers, closures and devices used in compounding sterile preparations.
- Procedures shall be written and maintained for examining the various materials used in the compounding the sterile preparation to ensure that they are appropriate for use.
- The Quality Control unit shall have the responsibility for:

    - Review and approval of all compounding procedures, testing procedures and acceptance criteria.
    - Release or rejection of each lot of compounded sterile preparation following a review of compounding documentation and test results.
    - Investigating unexpected results or errors resulting from compounding or testing.
    - Initiating corrective or preventative action plans resulting unexpected results, errors, or complaints from client institutions.
- The Quality Control Unit shall have sole authority independent of executive management to accept or reject all materials, components, containers, closures and devices used in compounding sterile preparations and to accept or reject the finished compounded sterile preparation.

Quality Assurance

- There shall be a written Quality Assurance plan explaining the organizational structure, responsibilities, policies, procedures, and processes needed to implement the quality assurance program for member companies.
- There shall be procedures written and maintained for:
    - Trending of non-conformances and/or out-of-specification (OOS) results
    - Initiating investigations and root cause analysis into questionable trends and OOS results.
    - Developing corrective or preventative action plans for unexpected results, errors, OOS results or complaints from client institutions
- Procedures shall be written and maintained to recall compounded sterile preparations resulting from:
    - Notice of recall by manufacturers of commercial product, materials or devices used in compounding sterile preparations
    - Failure of a sterile compounded preparation to meet its established specifications throughout its beyond-use date.

Personnel

- All personnel shall have the education, training and experience to carry out their assigned duties.
- A formal written training program shall be implemented for all compounding pharmacists and technicians to ensure they have a basic understanding of the principles and practice of aseptic compounding.
- The training program shall contain on-the-job segments to ensure development of proficiency in aseptic processes and procedures specific to the member company's operating environment.

- Pharmacists and Technicians shall demonstrate their proficiency in compounding sterile preparations using written testing procedures to test and document their ability to successfully carry out aseptic procedures.
- No pharmacist or technician shall compound a sterile preparation without having successfully demonstrated their ability to successfully carry out aseptic procedures.
- Failure to meet and maintain proficiency requirements shall result in additional training, testing or disqualification from compounding sterile preparations at the discretion of the Quality Assurance unit.
- Technicians compounding sterile preparations shall be licensed by the state in which the member company operates.
- The compounding activities of Technicians shall be supervised by Pharmacists licensed by state in which the member company operates.
- Quality Control shall establish and maintain a list of pharmacists and technicians qualified to compound sterile preparations.

Facilities and Equipment

- There shall be adequate work areas and equipment for compounding sterile preparations.
- The areas shall be suitable for preventing the introduction of ingredients and components into the sterile compounding process prior to their release for use by the Quality Control unit.
- There shall be adequate processes in place for continuous monitoring and recording of temperature and humidity in all clean rooms.
- There shall be written procedures for environmental monitoring including surface and air testing of all clean rooms where aseptic processes take place.
- Adequate verification processes such as QC checks, use of microbial indicators, and integrity testing shall be followed to ensure adequate performance of all sterilizing equipment including dry heat ovens, steam sterilizers, and filters.
- Adequate space shall be provided for washing and depyrogenation of glassware.
- Water generating systems shall be monitored to ensure that water of the appropriate classification is produced if applicable.
- Areas shall be of sufficient size to prevent mix up of ingredients, components and devices used in sterile compounding during staging, while in-process, and inspection prior to release and dispensing.
- Utensils used in compounding shall be clean to prevent the contamination of the sterile preparation.
- Equipment shall be suitable for maintaining an air cleanliness classification appropriate for the stage of compounding being conducted in the area.
- Testing of air cleanliness standards shall be conducted on a periodic basis and documented.

Use of Commercial Product and Bulk Active Pharmaceutical Ingredients

- Use of commercial product currently on the market may be used to compound sterile preparations having strengths or packaging configurations requested by client institutions that are not available from the manufacturer.
- Certificates of Analysis for commercial product shall be obtained whenever possible and kept on file in keeping with applicable record retention requirements.
- Bulk active pharmaceutical ingredients also may be used under the following conditions:
    - The bulk ingredient shall be procured only from an FDA registered manufacturer or repackager.
    - The vendor of the bulk ingredient shall be qualified through a written vendor qualification program.
    - The original manufacturer's certificate of analysis shall be obtained providing evidence that the bulk ingredient meets all predetermined specifications and shall be kept on file in keeping with applicable record retention requirements.
    - The bulk ingredient shall undergo independent testing by an FDA registered laboratory or by qualified in-house test procedures for those specifications set forth in the original manufacturer's certificate of analysis.
    - After test results for a sufficient number of different lots of the bulk ingredient meeting the specifications set forth by the manufacturer have been obtained from an FDA registered laboratory or by appropriate in-house testing, lots may be released thereafter for use in compounding solely on the basis of an acceptable manufacturer's certificate of analysis.

Control of Components, Containers, Closures, and Devices

- There shall be written specifications for components, containers, closures, and devices used in compounding sterile preparations.
- There shall be written procedures for the review and acceptance of components, containers, closures and devices used in compounding sterile preparations.
- Procedures shall be in place to enable traceability of each component, container, closure and device used in compounding a sterile preparation from its receipt, allocation to a specific lot, and distribution to client institutions.
- Certificates of Analysis where appropriate shall be obtained from the manufacturer and reviewed for each component, container, closure, and device to ensure its suitability for use.

Formulation and Compounding Records

- There shall be a written procedure for establishing a formulation record including appropriate steps for review and approval.
- The formulation record shall contain each step in the process for compounding the sterile preparation to provide documented evidence that the process was carried out successfully and met predetermined specifications and acceptance criteria.
- The formulation record shall contain sufficient detail to ensure that approved ingredients, components and devices are used in the compounding process.
- There shall be specifications set forth in the formulation records for theoretical yields at appropriate stages of the compounding process including in-process yields and yield of the final preparation.
- Labels printed or issued shall be reconciled at the end of the labeling process.
- There shall be acceptance specifications for the label reconciliation.
- A compounding record shall be made and authenticated prior to initiating the compounding process.
- A record of any deviation from the approved compounding procedure along with the rationale for the deviation shall be submitted to Quality Control for review and approval prior to release of the sterile compounded preparation.
- The completed compounding record shall be reviewed and approved by a compounding pharmacist before submitting to Quality Control for final review and approval.
- Testing of a representative sample of the sterile compounded preparation shall be conducted prior to release of the preparation to ensure that the preparation meets predetermined specifications for sterility, potency, and other such quality attributes.
- The Quality Control Unit shall maintain a file of each completed compounding record along with all supporting documentation and information such as calculations, actual yields, specifications, test results, approved deviations, and research to establish the entire history of the compounded preparation from the set up and preparation for compounding through final release for distribution.

Compounding Sterile Preparations

Assurance of sterility of the final compounded preparation is a critical element of the compounding process. Therefore procedures shall be established and maintained for the following:

- Proper hand washing and garbing for aseptic compounding.
- Specifications for personnel monitoring to establish proficiency in garbing.
- A training plan for compounding technicians and pharmacists on proper aseptic technique and manipulations, and clean room processes.
- Cleaning and sanitizing equipment.

- Cleaning and sanitizing floors, walls and ceilings.
- Operation of laminar flow hoods, autoclaves, depyrogenation ovens, vial washers, mixers, pumps, sterilizing filters, labelers, baggers and any other equipment utilized in compounding as appropriate for the member company's particular processing requirements.
- Cleaning and maintaining a sterile environment in the device or room that provides the ISO 5 environment for compounding
- Ensuring that ISO 7 and ISO 8 areas are clean and acceptable for use.
- Conducting a room or area clearance to prevent mix ups by ensuring that all materials, components, devices and labels of previous lots are removed from the compounding room or area.
- Completion of the compounding record making appropriate entries for lot numbers, weights, measures, checks and verifications.
- Provision for 100% visual inspection of the final preparation at appropriate stages of compounding for particulate matter, color, clarity, integrity of the container and closure, and label accuracy.
- Obtaining an appropriate number of representative samples of each lot based on the volume and lot size of the compounded sterile preparation for conducting test necessary for approval and release of the final preparation.
- Ensuring that every lot of compounded sterile preparation having an extended beyond use date is tested for sterility prior to release for distribution.
- Reserving a sufficient number of representative samples to allow for retesting if necessary.

Laboratory Testing

- Laboratory tests shall be conducted in-house using validated test methods on representative samples of the compounded preparation.
- In lieu of in-house testing, representative samples may be submitted to an FDA registered laboratory for analysis.
- The testing shall be designed to ensure the identity, strength, purity and sterility of the final compounded preparation.

Packaging and Labeling

- The compounded sterile preparation shall be packaged in such a manner as to protect the final preparation from alteration, contamination or damage during storage, handling and shipping.
- The compounded sterile preparation shall be labeled to indicate at a minimum the drug name, concentration, strength, volume or quantity, beyond use date, storage conditions, route of administration, DEA designation if any, NDC number if available, and company name, address and phone number.

- Other labeling specifications required by a regulating agency shall be met as appropriate for the regulatory environment in which the member company operates.

Dispensing and Distribution

- Compounded sterile preparations shall be dispensed and distributed only to client institutions and are not for resale by those institutions.
- There shall be written procedures in sufficient detail to ensure that each lot of compounded sterile preparation can be traced to the client institution and recalled if necessary.

Maintenance of Compounding and Testing Records

Complete records shall be maintained for the following for a period of time that meets all appropriate record retention regulations:

- Equipment maintenance and calibrations
- Compounding records for each lot of compounded sterile preparation
- Analytical test records and results
- Environmental monitoring of personnel and facilities
- Cleaning and sanitizing of equipment and clean rooms.
- Records of each ingredient, component, or device used in the compounding process
- Deviations and investigations
- Complaints
- Recalls