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USP <797>

LIST OF STANDARD OPERATING PROCEDURES

Standard operating procedures (SOPs) must be reviewed initially and at least every 12 months by the designated person(s) to ensure that the SOPs reflect current practices, and the review must be documented. Any changes or alterations to an SOP must be made only by a designed person(s) and must be documented. Revisions to SOPs must be communicated to all personnel involved in these processes and procedures, and personnel should document acknowledgement of the communication.

Total SOPs Required: 46

INTRODUCTION AND SCOPE (3)

- **Blood-Derived and Other Biological Materials**
  - When compounding activities require the manipulation of a patient's blood-derived or other biological material (e.g., autologous serum), the manipulations must be clearly separated from other compounding activities and equipment used in compounded sterile preparation (CSP) preparation activities, and they must be controlled by specific standard operating procedures (SOPs) to avoid any cross-contamination.
- **Immediate-Use CSPs**
  - Aseptic techniques, processes, and procedures are followed, and written SOPs are in place to minimize the potential for contact with nonsterile surfaces, introduction of particulate matter or biological fluids, and mix-ups with other conventionally manufactured products or CSPs.
  - Personnel are trained and demonstrate competency in aseptic processes as they relate to assigned tasks and the facility's SOPs.

PERSONNEL TRAINING AND EVALUATION (6)

- **Personnel Training and Evaluation**
  - Personnel who only perform restocking or cleaning and disinfecting duties outside of the primary engineering control (PEC) must complete ongoing training as required by the facility's SOPs.
  - Personnel compounding only immediate-use CSPs must complete training as required by the facility's SOPs (see 1.3 Immediate-Use CSPs).
  - This program must equip personnel with the appropriate knowledge and train them in the required skills necessary to perform their assigned tasks, and SOPs should specify the training required for such tasks.
- **Media-Fill Testing Procedures**
  - The order of the incubation temperatures must be described in the facility's SOPs.
- **Initial & Ongoing Training and Competency**
  - Training and competency must be defined by facility SOPs for the personnel who do not compound nor have direct oversight of compounding personnel.
  - Training and competency should supplement facility SOPs for the designated person(s), personnel who compound, and personnel with direct oversight of compounding personnel.

PERSONAL HYGIENE AND GARBING (5)

- **Hand Hygiene**
  - The order of garbing must be determined by the facility and documented in the facility's SOPs.
- **Garbing Requirements**
  - The required garb, manner of storage, and order of garbing must be determined by the facility and documented in the facility's SOPs.
  - Category 1 and 2: The facility's SOPs must describe disinfection procedures for reusing goggles, respirators, and other reusable equipment.
  - Category 3: The facility's SOPs must describe disinfection procedures for reusing goggles, respirators, and other reusable equipment.
  - The restricted-access barrier system (RABS) sleeves and gloves and the pharmaceutical isolator sleeves and gloves should be changed per the manufacturer's recommendations and as defined in the facility's SOPs.

FACILITIES AND ENGINEERING CONTROLS (2)

- **Facility Design and Environmental Controls**
  - The temperature and humidity readings must be reviewed as described in the facility's SOPs.
- **Placement and Movement of Materials**
  - The designated person(s) is responsible for addressing other areas of risk in the facility's SOPs.

CERTIFICATION AND RECERTIFICATION (1)

- **Total Airborne Particle Sampling**
  - All sampling sites and procedures must be described in the facility's SOPs.

MICROBIOLOGICAL AIR AND SURFACE MONITORING (3)

- **General Monitoring Requirements**
  - The microbiological air and surface monitoring program must be clearly described in the facility's SOPs, which must include a diagram of the sampling locations, procedures for collecting samples, frequency of sampling, size of samples (e.g., surface area, volume or air), time of day of sampling in relation to activities in the compounding area, and action levels that will trigger corrective action.
- **Viable Air Sampling Procedures**
  - The incubator temperature must be monitored during incubation, either manually or by a continuous recording device, and the results must be reviewed and documented as described in the facility's SOPs.
- **Monitoring Surfaces for Viable Particles:**
  - All sampling sites and procedures must be described in the facility's SOPs.

CLEANING, DISINFECTING, AND APPLYING SPORICIDAL DISINFECTS AND STERILE 70% ISOPROPYL ALCOHOL (4)

- All cleaning and disinfecting activities must be performed by trained and appropriately garbed personnel using facility-approved agents and procedures, which must be described in written SOPs.
- The frequency, method(s), and location(s) of cleaning, disinfecting, and applying sporicidal disinfectants must be established in written SOPs, in accordance with the manufacturer's instructions, and must be followed by all cleaning personnel.
- All cleaning, disinfecting, and application of sporicidal disinfectants must be documented according to the facility's SOPs.
- Once opened, sterile cleaning and disinfecting agents and supplies (e.g., closed containers for sterile wipers) and sterile 70% isopropyl alcohol may be reused for a time period specified as by the manufacturer or described in the facility's written SOPs.

EQUIPMENT, SUPPLIES, AND COMPONENTS (3)

- **Equipment**
  - » Compounding personnel must follow established SOPs for the calibration, maintenance, cleaning, and use of equipment based on the manufacturer's recommendations.
  - » Weighing, measuring, or otherwise manipulating components that could generate airborne chemical particles (e.g., active pharmaceutical ingredients, added substances, conventionally manufactured products) must be evaluated to determine if these activities must be performed in a PEC or other closed system processing device (e.g., single use containment glove bag) to reduce the potential exposure to personnel or contamination of the facility or CSPs (See 4.2.6 Facilities Preparing Category 2 or Category 3 CSPs from Nonsterile Starting Component(s)). The process evaluation must be carried out in accordance with the facility's SOPs and the assessment must be documented.
- **Components**
  - » Compounding personnel must follow the facility's SOPs, which must address the selection, receipt, evaluation, handling, storage, and documentation of all CSP components, including all ingredients and container closures.

STERILIZATION AND DEPYROGENATION (4)

- A description of the terminal sterilization and depyrogenation process, including temperature, pressure (if applicable), duration, permissible load conditions for each cycle, and the use of biological indicators and endotoxin challenge vials must be included in the facility's SOPs.
- SOPs must include training and competency of personnel on all sterilization methods and equipment used by the facility.
- The SOPs must include a schedule and method for establishing and verifying the effectiveness of the terminal sterilization and depyrogenation methods selected, as well as the methods for maintaining and cleaning the sterilizing and depyrogenation equipment.
- **Depyrogenation**
  - » The effectiveness of the depyrogenation cycle must be re-established if there are changes to the depyrogenation cycle described in SOPs (e.g., changes in load conditions, duration, or temperature).

MASTER FORMULATION AND COMPOUNDING RECORDS (1)

- **Creating Master Formulation Records (MFRs)**
  - » Any changes or alterations to the MFR must be approved and documented according to the facility's SOPs.

RELEASE INSPECTIONS AND TESTING (2)

- All release testing procedures (e.g., visual inspections and testing) must be included in the facility's documentation (see 17. SOPs).
- **Visual Inspection**
  - » Defects that indicate sterility or stability problems must be investigated to determine the cause according to the facility's SOPs.

LABELING (1)

- Labeling procedures must be followed as described in the facility's SOPs to prevent labeling errors and CSP mix-ups.

SOPS (2)

- Facilities that prepare CSPs must develop SOPs for the compounding process and other support activities.
- SOPs must include the types of CSPs that are prepared (i.e., Category 1, Category 2, Category 3).

QUALITY ASSURANCE AND QUALITY CONTROL (5)

- A facility's quality assurance (QA) and quality control (QC) programs must be formally established and documented in the facility's SOPs that ensure that all aspects of the preparation of CSPs are conducted in accordance with the requirements in this chapter (<797>) and the laws and regulations of the applicable regulatory jurisdiction.
- The facility's SOPs must describe the roles, duties, and training of the personnel responsible for each aspect of the QA program.
- **Notification about and recall of out-of-specification dispensed CSPs**
  - » An SOP for recall of out-of-specification dispensed CSPs must contain: (1) procedures to determine the severity of the problem and the urgency for implementation and completion of the recall, (2) procedures to determine the distribution of any affected CSP, including the date and quantity of distribution, (3) procedures to identify patients who have received the CSP, (4) procedures for disposal and documentation of the recalled CSP, and (5) procedures to investigate and document the reason for failure.
- **Complaint Handling**
  - » Compounding facilities must develop and implement SOPs for handling complaints.
- **Adverse Event Reporting**
  - » Adverse events potentially associated with the quality of CSPs must be reported in accordance with the facility's SOPs and all laws and regulations of the applicable regulatory jurisdiction.

CSP HANDLING, STORAGE, PACKAGING, SHIPPING, AND TRANSPORT (3)

- Processes and techniques for handling, storing, packaging, and transporting CSPs must be outlined in the facility's SOPs.
- Personnel who will be handling, storing, packaging, and transporting CSPs within the facility must be trained in accordance with the relevant SOPs, and the training must be documented.
- **Handling and Storing CSPs**
  - » The results of the temperature readings must be documented in a temperature log per facility SOPs or stored in the continuous temperature recording device and must be retrievable.

COMPOUNDING ALLERGENIC EXTRACTS (1)

- **Personnel Hygiene and Garbing for Compounding Allergenic Extract Prescription Sets**
  - » Before beginning compounding of allergenic extract prescription sets, personnel must perform hand hygiene (see Box 3) and garbing procedures according to the facility's SOPs.

Special acknowledgment to **Sarah Hall, PharmD (candidate)**, *UNC Eshelman School of Pharmacy, and* **Kevin Hansen, PharmD**, **MS, BCSCP**, *Director of Pharmacy, Compounding Services and Data Analytics, Cone Health, for the development of this resource, and to* **Patricia Kienle, RPh, MPA, BCSCP, FASHP**, *Director, Accreditation and Medication Safety, Cardinal Health, and* **Michael Ganio, PharmD, MS, BCSCP, FASHP**, *Senior Director, Pharmacy Practice and Quality, ASHP, for peer-review.*

Kevin and Patti are members of the USP Compounding Expert Committee, but this resource is not affiliated with or endorsed by USP.