USP Section 21 – Compounding Allergenic Extracts

***Final 2019 standards for allergen extract compounding under USP Chapter 797.**

Allergenic extract prescription sets must follow standards at least as stringent as those in this section:

Personnel Qualifications

- A designated person with training and expertise in allergen immunotherapy is responsible for ensuring that personnel who will be preparing allergen immunotherapy are trained, evaluated and supervised.
- Before beginning to independently prepare allergenic extracts, all compounding personnel must complete training and be able to demonstrate knowledge of principles and skills for sterile compounding.
- Annual personnel training and competency must be documented. Personnel must demonstrate proficiency in these procedures by passing written or electronic testing before they can be allowed to compound allergenic extract prescription sets.
- Before being allowed to independently compound, all compounders must successfully complete gloved fingertip and thumb sampling on both hands (see USP Chapter <797>; Box 2-1 and Table 1), no fewer than 3 separate times. Each fingertip and thumb evaluation must occur after performing separate and complete hand hygiene and garbing procedure. After the initial competency evaluation, compounding personnel must successfully complete gloved fingertip and thumb sampling at least every 12 months thereafter.
- Compounding personnel must have their sterile technique and related practices evaluated every 12 months as demonstrated by successful completion of a media-fill test (see USP Chapter <797>; Box 2-2).
- Personnel who fail competency evaluations must successfully pass reevaluations in the deficient area(s) before they can resume compounding of allergenic extract prescription sets. The designated person(s) must identify the cause of failure and determine appropriate retraining requirements.
- Personnel who have not compounded an allergenic extract prescription set in more than 6 months must be evaluated in all core competencies before resuming compounding duties.

Personnel Hygiene and Garbing

- Before beginning compounding of allergen immunotherapy prescription sets, personnel must perform hand hygiene (see USP Chapter <797>; Box 3-1 and garbing procedure according to facility SOPs.
- The Minimum garb requirements include:
  - Low-lint garment with sleeves that fit snugly around the wrists and that is enclosed at the neck (e.g., gowns or coveralls).
  - Low-lint, disposable covers for head that cover the hair and ears and, if applicable, disposable cover for facial hair.
  - Face mask.
  - Sterile powder-free gloves.
- Compounding personnel must rub sterile 70% IPA onto all surfaces of the gloves and allow them to dry thoroughly throughout the compounding process.

Facilities

- The compounding process must occur in an ISO Class 5 PEC or in a dedicated allergenic extract compounding area (AECA). The PEC or AECA used to compound prescription sets must be located away from unsealed windows, doors that connect to the outdoors, and traffic flow, all of which may adversely affect the air quality. Neither a PEC nor an AECA may be located where environmental control challenges (e.g., restrooms, warehouses, or food preparation areas) could negatively affect the air quality. The PEC or the work surfaces in the AECA must be located at least 1 meter away from a sink. The impact of activities that will be conducted around or adjacent to the PEC or AECA must be considered carefully when designing such an area.
  - If used, the PEC must be certified every 6 months (see 5. Certification and Recertification).
  - If used, a visible perimeter must establish the boundaries of the AECA.
    - › Access to the AECA during compounding must be restricted to authorized personnel.
    - › During compounding activities, no other activity is permitted in the AECA.

› The surfaces of walls, floors, fixtures, shelving, counters, and cabinets in the AECA must be cleanable.

› Carpet is not allowed in the AECA.

› Surfaces should be resistant to damage by cleaning and sanitizing agents.

› The surfaces in the AECA upon which the allergenic extract prescription sets are prepared must be smooth, impervious, free from cracks and crevices, and non-shedding to allow for easy cleaning and disinfecting.

› Dust-collecting overhangs such as utility pipes, ledges, and windowsills should be minimized. If overhangs or ledges are present, they must be easily cleanable.

› The AECA must be designed and controlled to provide a well-lit working environment, with temperature and humidity controls for the comfort of compounding personnel wearing the required garb.

Cleaning and Disinfecting

- In a PEC, all interior surfaces of the PEC must be cleaned and disinfected daily and when surface contamination is known or suspected. Apply sterile 70% IPA to the horizontal work surface between each prescription set.
- In an AECA, all work surfaces in the AECA where direct compounding is occurring must be cleaned and disinfected daily and when surface contamination is known or suspected. Apply sterile 70% IPA to the horizontal work surface between each prescription set.
  - If present, walls, doors, and door frames within the perimeter of the AECA must be cleaned and disinfected monthly and when surface contamination is known or suspected.
  - Ceilings within the perimeter of the AECA must be cleaned and disinfected when visibly soiled and when surface contamination is known or suspected.
- Vial stoppers on packages of conventionally manufactured sterile ingredients must be wiped with sterile 70% IPA to ensure that the critical sites are wet and allowed to dry before they are used to compound allergenic extracts prescription sets.

Establishing BUDs

- The by-use-date (BUD) for the prescription set must be no later than the earliest expiration date of any allergenic extract or any diluent that is part of the prescription set, and the BUD must not exceed 1 year from the date the prescription set is mixed or diluted.

Labeling

- The label of each vial of an allergenic extract prescription set must display the following prominently and understandably:
  - Patient name.
  - Type and fractional dilution of each vial, with a corresponding vial number.
  - BUD.
  - Storage conditions.

Shipping and Transport

- If shipping or transporting allergenic extract prescriptions sets, compounding personnel must select modes of transport that are expected to deliver properly packed prescription sets in an undamaged, sterile, and stable condition.
- When shipping or transporting allergen extract prescriptions sets that require special handling, personnel must include specific handling instructions on the exterior of the container.

Documentation

- All facilities where allergenic extract prescription sets are prepared must have and maintain written or electronic documentation to include, but not limited to the following:
  - SOPs describing all aspects of the compounding process.
  - Personnel training records, competency assessments, and qualification records including corrective actions for any failures.
  - Certification reports of the PEC, if used, including corrective actions for any failures.
  - Temperature logs for the refrigerator(s).
  - Compounding records for individual allergenic extract prescription sets (see USP Chapter <797>; Box 21-1).
  - Information related to complaints and adverse events.
  - Investigations and corrective actions.

*Adapted from USP General Chapter <797> Pharmaceutical Compounding-Sterile Preparations; Section 21. Compounding Allergenic Extracts

Box 2-1. Gloved Fingertip and Thumb Sampling Procedures

- Use one sampling device per hand (e.g., plates, paddles, or slides) containing general microbial growth agar [e.g., trypticase soy agar (TSA)] supplemented with neutralizing additives (e.g., lecithin and polysorbate 80) as the agar supports both bacterial and fungal growth.
- Label each sampling device with a personnel identifier, whether it was from the right or left hand, and the date and time of sampling.
- Do not apply sterile 70% isopropyl alcohol (IPA) to gloves immediately before touching the sampling device because this could cause a false-negative result.
- Using a separate sampling device for each hand, collect samples from all gloved fingers and thumbs from both hands by rolling finger pads and thumb pad over the agar surface.
- Incubate the sampling device at a temperature of 30°- 35°for no less than 48 hours and then at 20°- 25° for no less than 5 additional days. Store media devices during incubation to prevent condensate from dropping onto the agar and affecting the accuracy of the cfu reading (e.g., invert plates).
- Record the number of cfu per hand (left hand, right hand).
- Determine whether the cfu action level is exceeded by counting the total number of cfu from both hands.

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Table 1. Action Levels for Gloved Fingertip and Thumb Sampling[a]

Gloved Fingertip and Thumb Sampling	**Action Levels** (total number of cfu from both hands)
Initial sampling after garbing	>0
Subsequent sampling after media-fill testing	>3

[a]Action levels are based on the total cfu count from both hands.

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Box 2-2. Media-Fill Testing Procedures

- If all of the starting components are sterile to begin with, manipulate them in a manner that simulates sterile-to-sterile compounding activities, and transfer the sterile soybean – Casein digest medium in non-bacteriostatic water to make a 3% nonsterile solution. Manipulate it in a manner that simulates nonsterile-to-sterile compounding activities. Prepare at least 1 container as the positive control to demonstrate growth promotion, which is indicated by visible turbidity upon incubation.
- Once the compounding simulation is completed and the final containers are filled with the test media, incubate them in an incubator for 7 days at 20°- 25° followed by 7 days at 30°- 35° to detect a broad spectrum of microorganisms.
- Failure is indicated by visible turbidity or other visual manifestations of growth in the media in one or more container-closure unit(s) on or before 14 days.

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Box 3-1. Hand Washing Procedures

- Remove visible debris from underneath fingernails under warm running water using a disposable nail cleaner.
- Wash hands and forearms up to the elbows with soap and water for at least 30 seconds.
- Dry hands and forearms to the elbows completely with low-lint disposable towels or wipers.

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Box 3-2. Hand Sanitizing Procedures

- Apply an alcohol-based hand rub to dry skin following the manufacturer's instructions for the volume of product to use.
- Apply product to one hand and rub hands together, covering all surfaces of hands and fingers, until hands are dry.
- Allow hands to dry thoroughly before conning sterile gloves.

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Box 21-1. Compounding Records for individual Allergenic Extract Prescription Sets

Compounding Records must include at least the following information:

- Name, concentration, volume, vendor or manufacturer, lot number, and expiration date for each component.
- Date and time of preparation of the allergenic extract.
- Assigned internal identification number.
- A method to identify the individuals involved in the compounding process and verifying the final CSP.
- Total quantity compounded.
- Assigned BUD and storage requirements.
- Results of QC procedures (e.g., visual inspection, second verification of quantities).

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