

AAOA



PRACTICE RESOURCE TOOL KIT

Section 21. Compounding Allergenic Extracts from USP General Chapter <797> Pharmaceutical Compounding — Sterile Preparations

Materials presented in this tool kit are intended as resource only and should not be construed as guidance



Section 21. Compounding Allergenic Extracts from USP General Chapter <797> Pharmaceutical Compounding – Sterile Preparations

Excerpted below is section 21. Compounding Allergenic Extracts from USP General Chapter <797> Pharmaceutical Compounding – Sterile Preparations. For the full document, please go to www.usp.org

21. COMPOUNDING ALLERGENIC EXTRACTS

Licensed allergenic extracts are mixed and diluted into prescription sets for an individual patient, even though these allergenic extract combinations are not specified in the approved licenses for the licensed biological products [e.g., Biological License Applications (BLA)]. Because patients must be maintained on a maintenance dose of prepared concentrated allergenic extracts for a period of time longer than the BUDs specified for Category 1 and Category 2, longer BUDs are required for prescription sets to achieve effective therapy.

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

Personnel Qualifications

1. 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.
2. 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.
3. 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.
4. Before being allowed to independently compound, all compounders must successfully complete gloved fingertip and thumb sampling on both hands (see 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.
5. 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 Box 2-2).
6. 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.
7. 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

8. Before beginning compounding of allergen immunotherapy prescription sets, personnel must perform hand hygiene (see Box 3-1) and garbing procedures according to facility SOPs.
9. 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
10. Compounding personnel must rub sterile 70% IPA onto all surfaces of the gloves and allow them to dry thoroughly throughout the compounding process.

Facilities

11. The compounding process must occur in an ISO Class 5 PEC or in a dedicated allergenic extracts 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-lighted working environment, with temperature and humidity controls for the comfort of compounding personnel wearing the required garb.

Cleaning and Disinfecting

12. 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.
13. 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.
14. 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

15. The 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

16. 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

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

Documentation

19. 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 Box 21-1)
 - Information related to complaints and adverse events
 - Investigations and corrective actions

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)

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 this 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.

Table 1. Action Levels for Gloved Fingertip and Thumb Sampling*

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 (every 6 months)	>3

*Action levels are based on the total cfu count from both hands.

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 media into the same types of container–closure systems commonly used at the facility. Do not further dilute the media unless specified by the manufacturer.
- If some of the starting components are nonsterile to begin with, use a nonsterile soybean–casein digest powder to make a solution. Dissolve nonsterile commercially available soybean–casein digest medium in nonbacteriostatic 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.

Glossary*

Allergenic extract prescription set: Combinations of licensed allergenic extracts which would be mixed and diluted to provide subcutaneous immunotherapy to an individual patient, even though these allergenic extract combinations are not specified in the approved BLAs for the licensed biological products.

Allergenic extracts: Biological substances used for the diagnosis and/or treatment of allergic diseases such as allergic rhinitis, allergic sinusitis, allergic conjunctivitis, bee venom allergy, and food allergy.

Allergenic extracts compounding area (AECA): A designated, unclassified space, area, or room with a visible perimeter that is suitable for preparation of allergenic extract prescription sets.

Aseptic processing: A method by which separate, sterile components (e.g., drugs, containers, or closures) are brought together under conditions that maintain their sterility. The components can either be purchased as sterile or, when starting with nonsterile components, can be separately sterilized prior to combining (e.g., by membrane filtration, autoclave).

Aseptic technique: A set of methods used to keep objects and areas free of microorganisms and thereby minimize infection risk to the patient. It is accomplished through practices that maintain the microbe count at an irreducible minimum.

Compounding: The process of combining, admixing, diluting, pooling, reconstituting, repackaging, or otherwise altering a drug or bulk drug substance to create a sterile medication.

Garb: Items such as gloves, garments (e.g., gowns, coveralls), shoe covers, head and facial hair covers, masks, and other items designed to reduce particle-shedding from personnel and minimize the risk of contamination of CSP(s).

Gloved fingertip and thumb sampling: Process to evaluate a compounder's competency in correctly performing hand hygiene and garbing.

Media-fill test: A simulation used to qualify processes and personnel engaged in sterile compounding to ensure that the processes and personnel are able to prepare CSPs without contamination.

* Glossary descriptions extracted from the 2019 release of the USP General Chapter <797> Pharmaceutical Compounding -Sterile Preparations.