

**ALLERGEN THERAPY AND THE ESTABLISHMENT OF ALLERGEN
IMMUNOTHERAPY CLINICS**

- 1. REASON FOR ISSUE:** This Veterans Health Administration (VHA) directive was developed to ensure safe and proper administration of allergen immunotherapy.
- 2. SUMMARY OF CONTENT:** This revised directive establishes policy for minimum requirements for the storage of allergen extracts and the establishment of allergen immunotherapy clinics in the Department of Veterans Affairs (VA) medical facilities.
- 3. RELATED ISSUE:** None.
- 4. RESPONSIBLE OFFICE:** The Assistant Deputy Under Secretary for Health for Patient Care Services is responsible for the content of this directive. Questions may be directed to Specialty Care Services at 202-461-7120.
- 5. RESCISSIONS:** VHA Directive 2012-010, dated March 12, 2012, is rescinded.
- 6. RECERTIFICATION:** This VHA directive is due to be recertified on or before the last working day of December 2021. This VHA directive will continue to serve as national VHA policy until it is recertified or rescinded.

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Under Secretary for Health

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ALLERGEN THERAPY AND THE ESTABLISHMENT OF ALLERGEN IMMUNOTHERAPY CLINICS

1. PURPOSE

This Veterans Health Administration (VHA) directive provides policy for minimum requirements for establishment of allergen immunotherapy clinics in Department of Veterans Affairs (VA) medical facilities and addresses compounding for allergen extracts within VHA allergy clinics. **AUTHORITY:** Title 38 United States Code (U.S.C.) 7301(b).

2. BACKGROUND

Allergen extracts are biologics that contain allergenic proteins that are used to test for allergy and to treat allergic disease through allergen immunotherapy. Allergy divisions/sections at VA medical facilities are responsible for the ordering, management, procurement, tracking, inspection, storage, and disposition of allergen extract formulations in VHA allergen clinic areas. Allergen immunotherapy is an effective, evidence-based treatment widely utilized in the practice of Allergy and Immunology. An established VA sharing agreement with the Department of Defense, United States Army Centralized Allergen Extracts Laboratory (USACAEL), facilitates the availability of uniform diagnostic and therapeutic extracts in standardized formulations for VA patients receiving immunotherapy.

3. POLICY

- a. It is VHA policy that allergen extracts must be administered by qualified personnel as determined by the allergist/immunologist and facility privileging.
- b. Allergen extracts must be stored on site at the administering facility or the administering facility agrees to initiate a process to provide storage. Patients are not permitted to store or carry extracts to a facility and under no circumstances will allergen extracts be self-administered.

4. RESPONSIBILITIES

a. **Assistant Deputy Under Secretary for Health for Patient Care Services and Chief Consultant for Specialty Care Services.** The Assistant Deputy Under Secretary for Health for Patient Care Services and Chief Consultant for Specialty Care Services are responsible for:

(1) Appointing a qualified board-certified allergist/immunologist as National Director of the VHA Allergen Extract Program, and

(2) Defining the policy for the administration of allergen immunotherapy and the establishment of allergy and immunology clinics in VHA. The Assistant Deputy Under Secretary for Health for Patient Care Services and Chief Consultant for Specialty Care Services are the final authority.

b. **National Program Director for Allergen Extract Program.** The National Director for Allergen Extract Program is responsible for ensuring that:

(1) VA medical facilities requesting immunotherapy clinics have, available for overseeing the ordering and administration of allergen immunotherapy, either directly or remotely within the assigned VISN(s), board-certified or board-eligible allergists and/or immunologists or practitioners defined as those with training in immunotherapy, as determined by the National Program Director for Allergen Extract Program, and are informed that they are eligible to enroll in the VHA Allergen Extract Program. In addition, the allergists should be provided with a trained LPN, RN or medical assistant who is familiar with administration of allergen immunotherapy.

(2) Allergen extracts for testing and therapy are supplied by:

(a) The VHA Allergen Extract Program through the USACAEL, or

(b) A recognized high-quality manufacturer. **NOTE:** *Established facilities may continue to obtain immunotherapy from a qualified private allergen company if they are already doing so. However, any newly established allergy programs will be required to enroll in the VHA Allergen Extract Program as specified under paragraph 4.b.(2)(a) of this policy.*

(3) VA medical facilities are required to demonstrate competency to safely provide immunotherapy services. This includes ensuring that:

(a) The facility has a designated board-certified or board-eligible allergist and/or immunologist or practitioner, as defined in paragraph 4.b.(1) of this policy, who is trained in immunotherapy and who has oversight, either directly or remotely over allergy and immunotherapy clinics provided within the medical facility or remote care outpatient site,

(b) Immunotherapy prescriptive orders will only be prescribed by the allergist/immunologist or allergy practitioner responsible for those patients within the designated Veteran Integrated System Network (VISN) initially evaluated and receiving immunotherapy at approved remote sites,

(c) Credentials of prescriptive allergy providers, including their Scope of Practice (SOP) privileges supporting VISN prescriptive authority, are available upon request and fall within the scope approved by the VHA local Director, Credentialing and Privileging. Their prescriptive authority will also include patients they are following who are being administered immunotherapy at the remote site,

(d) All allergen testing and treatment is administered by trained personnel (both providers and nursing), as determined by the board-certified or board-eligible allergist and/or immunologist or practitioner defined in paragraph 4.b.(1) of this policy, in a setting with access to adequate measures to treat an anaphylactic reaction,

(e) Allergists/immunologists or practitioners, as defined in paragraph 4.b.(1) of this policy, certified in prescribing immunotherapy are held responsible for ensuring the safe administration of immunotherapy. This includes ensuring the appropriate location, supplies, and adequately trained personnel are available.

(f) Immunotherapy may be administered at any VA medical facility, including VA medical centers, Community Based Outpatient Clinics (CBOC) and satellite clinics as long as the criteria in paragraphs 4.b.(3)(a)-(e) of this policy are met.

(4) Billing for each participating VA medical facility involved in the USACAEL extract program is accurate through reviewing quarterly billing statements sent from the USACAEL.

(5) Ensuring that an updated sharing agreement between the Department of Defense (DoD) and VA is active.

(6) Ensuring that all allergy clinics interested in administering immunotherapy submit a "Restructuring of VHA Allergy/Immunology Shot Clinics USACAEL Allergens" request for approval.

c. **VA Medical Facility Director.** The Director of a VA medical facility administering immunotherapy to qualified patients is responsible for ensuring that the facility has:

(1) A designated board-certified or board-eligible allergist and/or immunologist or practitioner, as defined in paragraph 4.b.(1) of this policy, overseeing the ordering and administration of allergen immunotherapy either directly or remotely within the assigned VISN(s),

(2) Qualified personnel demonstrate competency in the administration of immunotherapy that follow the immunotherapy guidelines. (See paragraph 5.c.),

(3) An appropriately staffed Allergen Immunotherapy Clinic that should include a provider trained in treating anaphylaxis and other complications from allergen immunotherapy administration.

(4) Personnel involved in administration of allergen immunotherapy who have undergone allergen immunotherapy competency training determined by the supervising allergist, and who have no or limited other duties scheduled at the time the immunotherapy clinic is in session,

(5) When immunotherapy is administered at a remote site, a primary care provider who agrees to provide medical oversight during allergy immunotherapy administration. It is recommended to have service agreements between the facilities and specific directions on administering immunotherapy.

(6) Appropriate facilities for the compounding of allergen extracts. **NOTE:** VA medical facilities must refer to Appendix A for guidance on compounding allergen

extract formulations when needed in compliance with United States Pharmacopeia Chapter 797 (USP <797>) "Pharmaceutical Compounding-Sterile Preparations," and must adhere to local VA medical facility policy on labeling, storage recommendations, and expiration dating for diluted formulations.

5. REFERENCES

- a. VHA Handbook 1108.06, Inpatient Pharmacy Services.
- b. Allergen immunotherapy: A practice parameter third update. *Journal of Allergy and Clinical Immunology*. 2011; 127(1):S1-S55.
- c. The diagnosis and management of anaphylaxis practice parameter: 2010 update. *Journal of Allergy and Clinical Immunology*. 2010; 126(3):477-80.e1-42.
- d. Nelson, M, Cox, L. 2012. Chapter 9. In AAAAI Practice Management Resource Guide, 2012 edition 1.
- e. United States Pharmacopeia (USP) Chapter 1075 "Good Compounding Practices."
- f. United States Pharmacopeia General Chapter 797; "Pharmaceutical Compounding-Sterile Preparations"; The United States Pharmacopeia, 35th rev., and The national formulary, 30th ed. Rockville, MD: United States Pharmacopeial Convention; 2012.
- g. Walter Reed Army Medical Center Immunology and Allergy Specialty Course Manual. 200-Y8 Army. SEI 453 and 454 Air Force Updated Dec 2010.

COMPOUNDING OF ALLERGEN EXTRACTS

1. VA allergy clinics administer antigens that are prepared as patient specific formulations. Patient specific allergen extract formulations are ordered from the USACAEL or purchased from a recognized high quality manufacturer to minimize the requirement for VA personnel to compound (dilute) antigens for a patient.
2. Occasionally compounding of diluted allergen extract formulations will need to be performed at the allergy clinic site when less concentrated doses are needed for individual patient use. There are two options that can be utilized: Compounding by a health care provider or qualified personnel in the allergy clinic or compounding by qualified allergy clinic personnel within the pharmacy service (under United States Pharmacopeia Chapter 797 (USP <797>) "Pharmaceutical Compounding-Sterile Preparations" compliance standards). Allergy clinic personnel are responsible to notify the chief of pharmacy service should there be a necessity to prepare allergen extract dilutions in the pharmacy service. Allergy clinic personnel must be specially trained in allergen extract formulation preparations and comply with standards in the USP <797> section on "Allergen Extracts as CSPs" and the Joint Council for Allergy, Asthma, and Immunology (JCAAI) recommendations as discussed in the Physician Instruction Guide for Preparation of Allergen Extracts. If allergen extract formulations are diluted and stored as additional doses by allergy clinic personnel, they must comply with USP <797> standards under the section on "Personnel Training and Competency Evaluation of Garbing, Aseptic Work Practices and Cleaning/Disinfection Procedures." Allergy clinic personnel must also contact the Chief of Pharmacy Service in order to perform the applicable media fill sampling procedures annually in the pharmacy service USP <797> compliant environment when needed.
3. Allergy clinic personnel are required to follow the Allergen Immunotherapy Extract Preparation Guidelines as stated in the practice parameters developed by the American Academy of Allergy, Asthma, and Immunology (AAAAI) and the American College of Allergy Asthma and Immunology (ACAAI) as follows:
 - a. Compounding personnel must pass a written test on aseptic technique and extract preparation.
 - b. Compounding personnel must be trained in the preparation of allergenic products.
 - c. Compounding personnel must annually pass a media-fill test, as described in Addendum A of JCAAI Allergen Immunotherapy Extract Preparation Guidelines.
 - d. Compounding personnel who fail written or media-fill tests would be reinstructed and re-evaluated.
 - e. Compounding personnel must be able to demonstrate understanding of antiseptic hand cleaning and disinfection of mixing surfaces.

f. Compounding personnel must be able to correctly identify, measure, and mix ingredients.

g. Compounding personnel should be appropriately trained health professionals, including but not limited to, registered nurses, licensed practical nurses, medical technicians, medical assistants, physicians' assistants, advanced practice nurses, and physicians.

4. Physician Responsibility. A physician with training and expertise in allergen immunotherapy is responsible for ensuring that compounding personnel are instructed and trained in preparation of immunotherapy with aseptic techniques as described in paragraph 4.k. below and that they meet the requirements of these guidelines. Evidence of such compliance must be documented and maintained in personnel files. The physician is responsible for providing general oversight and supervision of compounding.

5. Bacteriostasis. Allergen extract dilutions must be bacteriostatic, meaning that they must contain phenol concentrations of at least 0.25 percent, or if the phenol concentration is less than 0.25 percent, the extract must have a glycerin concentration of at least 20 percent.

6. Allergen extracts must be diluted in accordance with the antigen manufacturer's instructions.

7. Potency. The manufacturer's expiration dates must be followed. Beyond-use dates for allergy extract dilutions should not exceed the expiration date of the reference stock allergen extract formulation from the USACAEL.

8. Mixing of Extracts with High and Low Proteolytic Enzymes. Cross-reactivity of antigens: separation of aqueous extracts with high proteolytic enzyme activities from other extracts is recommended.

9. Storage. Extracts should be stored at 2° – 8°C (36° – 46°F) to reduce the rate of potency loss or according to the manufacturer's directions. Extracts stored beyond the expiration date of the manufacturer are to be discarded. Storage must be in a designated refrigerator for medications and not used for food or specimens.

10. Subcutaneous Injection. Allergen extracts can only be administered through subcutaneous injection.

11. Aseptic Technique. Preparation of allergy immunotherapy must follow aseptic manipulations defined as follows:

12. The physician must designate a specific site, such as a countertop, within the VA medical facility, where personnel traffic is restricted and activities that might contribute to microbial contamination (e.g., eating, food preparation, and placement of used diagnostic devices and materials and soiled linens) are prohibited.

13. The extract preparation area must be sanitized with 70 percent isopropanol that does not contain added ingredients, such as dyes and glycerin.
14. Extract preparation personnel must thoroughly wash hands to wrists with detergent or soap and potable water. Substitution of hand washing by means of treatment with sanitizing agents containing alcohol, 70 percent isopropanol, or both is acceptable.
15. Necks of ampules to be opened and stoppers of vials to be needle punctured must be sanitized with isopropanol.
16. Direct contact contamination of sterile needles, syringes, and other drug-administration devices and sites on containers of manufactured sterile drug products from which drugs are administered must be avoided. Sources of direct contact contamination include, but are not limited to, touch by personnel and non-sterile objects, human secretions, blood, and exposure to other non-sterile materials.
17. After mixing is complete, visual inspection is to be performed for physical integrity of the vial.
18. Labeling. Immunotherapy vials are to be clearly labeled with the patient's name and the beyond-use date of the vial and include information described in paragraph p.(4).
19. Mixing Log. A mixing log is to be kept with information on the patient's name, extract used for mixing, mixing date, and expiration date and lot numbers. The mixing log may be maintained in the patient's immunotherapy record.
20. Policy and Procedure Manual. VA medical facilities preparing allergy extracts must maintain a policy and procedure manual for the procedures to be followed in the mixing, diluting, or reconstituting of sterile products and for the training of personnel in the standards described in this handbook.
21. Example of a Media-fill Test Procedure:
 - a. This or an equivalent test is performed at least annually by each person authorized to compound allergen immunotherapy extracts under conditions that closely simulate the most challenging or stressful conditions encountered during compounding of allergen immunotherapy extracts. Once begun, this test is completed without interruption.
 - b. A double-concentrated medium, such as from Valiteq, is transferred in ten 0.5-mL increments with a sterile syringe to a sterile 10-mL vial. Five milliliters of sterile water (preservative free) is added. This is the "concentrate." The vial is incubated within a range of 20°C to 35°C for 14 days. Failure is indicated by visible turbidity in the medium on or before 14 days.
22. Compounding in Clinic. When compounding in the allergy clinic, it is imperative that personnel follow standards to comply with USP <797>, under the section on

“Allergen Extracts as CSPs”, which establishes VHA policy standards of quality and sterility for compounded sterile preparations (CSPs), and the Allergen Immunotherapy: A Practice Parameter Third Update 2011. The preparation of allergenic extracts and dilutions following USP <797> must ensure that these products meet their purported characteristics of acceptable sterility, purity, quality, identity, and strength. **NOTE:** *A compounded dilution of the allergen formulation must be administered to the patient by qualified allergy clinic personnel within 1 hour from time of preparation.* Any remaining amount of the compounded dilution that is present in a multi-dose vial must be labeled appropriately in accordance with this Handbook and local VA medical facility policy and include at a minimum the patient’s name, diluted formulation name and concentration, name of preparer and, expiration dating (beyond-use-date) that is not to exceed the expiration date of the reference stock allergen extract formulation from the USACAEL. The recommended steps to ensure that allergen extracts are acquired from USACAEL or appropriately prepared for dilution as needed by the allergy clinic are described as follows:

a. First Method (preferred). For multi-dose allergen formulation: Acquisition of allergy formulations from USACAEL (as first option) or alternative source (pharmaceutical manufacturer or university facility).

b. Second Method (Acceptable).

(1) For single-dose allergen formulation dilution: Prepared by physician or staff trained in allergy formulation compounding (in compliance with standards described in Section A(2) and <USP 797> Section on “Allergy Extracts as CSPs”) or, by VA Pharmacy Service per USP <797> compliance standards.

(2) For multi-dose allergen formulation: Prepared by physician or staff trained in allergy formulation compounding (in compliance with standards in Section A(2) and, <USP 797> Section on “Allergy Extracts as CSPs”) or, by VA Pharmacy Service per <USP 797> compliance standards.

c. Ensure that allergen formulation dilutions prepared by VHA allergy clinic or by Pharmacy Service are adequately labeled per this Handbook and local VA medical facility policy to include, but not limited to: the allergen extract formulation’s identity, strength, storage recommendations, expiration date, and name or initials of preparer. Allergy clinic personnel are responsible to inspect all allergen extract formulations stored in the clinic at least monthly to ensure product labeling, dating and quality, and maintaining a log of allergen extract formulations in stock with an information record of the allergen extract formulation.

d. Allergen extract formulations that have been compounded by dilution for individual patients must not be given to patients for storage at home. The diluted formulation must be maintained at required storage conditions under refrigeration in the allergy clinic premises at all times.

e. Allergen extract formulations purchased from a pharmaceutical manufacturer or university that require further compounding for dilution by the allergy clinic must be labeled and inspected in accordance with USP <797>, and local VA medical facility policy for the specific patient with an expiration date (beyond-use-date) and storage recommendations that is assigned based on the pharmaceutical manufacturers' recommendations or peer-reviewed publications. It is imperative that the pharmaceutical manufacturer supplying the allergen extracts be contacted VA medical facility allergy clinic personnel to obtain the correct date of expiration for the compounded diluted allergen formulation.

23. Allergen Extract Delivery and Storage Allergy extracts may be mailed directly to the allergy clinic or Pharmacy Service depending on the VA medical facility site preference. Extracts must be refrigerated immediately upon receipt. Extracts must be stored at 2° – 8°C (36° – 46°F) to reduce the rate of potency loss and in accordance with manufacturer's directions. Allergen extracts stored beyond the expiration date of the manufacturer must be discarded. Storage must be in a designated refrigerator for medications and not used for food or specimens.