



Immunotherapy Vaccine Preparation — Practical Issues

After undergoing allergy testing, either in vivo or in vitro, a patient may elect to pursue subcutaneous allergy immunotherapy. Once prescribed, the immunotherapy vaccine vials may be formulated in physician's office, under sterile conditions.

Diagnostic services including allergy testing codes are generally assigned a level of physician supervision to be covered by Medicare when the service is not personally performed by a physician. There are 3 levels of supervision—personal, direct, and general defined as follows:

General Supervision—means the procedure is furnished under the physician's overall direction and control, but the physician's presence is not required during the performance of the procedure. Under general supervision, the training of the nonphysician personnel who actually perform the diagnostic procedure and the maintenance of the necessary equipment and supplies are the continuing responsibility of the physician.

Direct Supervision—in the office setting means the physician must be present in the office suite and immediately available to furnish assistance and direction throughout the performance of the procedure. It does not mean the physician must be present in the room when the procedure is performed.

Personal Supervision—means a physician must be in attendance in the room during the performance of the procedure.

Codes 95004, 95024 and 95027 are all assigned a direct supervision status indicator.

Most therapeutic services including immunotherapy injections such as Codes 95115 and 95117 and

preparation of a vial (95144 and 95165) are as "incident to" service and not as diagnostic tests. Incident to services require direct supervision meaning the physician is in the office suite when the service is performed.

Allergy vaccines prepared for the delivery of immunotherapy must include additives for bacteriostasis and potency preservation. There are three available diluents and additives presently used in the preparation of immunotherapy vaccines used for either subcutaneous or sublingual routes. It is recommended that agent or agents that are bacteriostatic and act as antigen stabilizers be utilized. These options include glycerin (10 or 50%), which can act as both a bacteriostatic agent and antigen stabilizer in higher concentrations; phenol, which is bacteriostatic; and human serum albumin (HSA), which acts as a stabilizer and decreases antigen adherence to the glass vial; or combinations of these agents.^{1, 2, 3, 4, 5}

A marked decrease in antigen potency was noted when phenolated saline was used alone.^{2, 5, 6} Phenolated saline can be used with HSA, and also has an additive effect on preservation when used with 10% glycerin.⁴ When preparing immunotherapy vials for sublingual therapy one should consider using 50% glycerin as the diluent, to incorporate the bacteriostatic and stabilizing properties and improve palatability.

In addition, it is recommended that allergy practitioners maintain consistency with antigen lots and antigen suppliers as much as possible to reduce variation of potency and dose.⁵ However, the Academy recognizes the need to switch antigen suppliers under certain circumstances. Caution should be used when changing

Note: American Academy of Otolaryngic Allergy's (AAOA) Clinical Care Statements attempt to assist otolaryngic allergists by sharing summaries of recommended therapies and practices from current medical literature. They do not attempt to define a quality of care for legal malpractice proceedings. They should not be taken as recommending for or against a particular company's products. The Statements are not meant for patients to use in treating themselves or making decisions about their care. Advances constantly occur in medicine, and some advances will doubtless occur faster than these Statements can be updated. Otolaryngic allergists will want to keep abreast of the most recent medical literature in deciding the best course for treating their patients.



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lots of individual antigens, and especially when changing antigen suppliers, as potency can vary significantly, even in well-characterized or standardized extracts. The clinical implication of changing lots of antigen supplier should also be determined by the clinician as the patient's risk factors and history with immunotherapy should be incorporated into the decision.

If an antigen supplier switch is necessary, options include:

1. Re-testing the affected patient with the antigens from the new antigen supplier to establish new endpoints for immunotherapy thereby establishing a new safe initial dose.
2. Implementing the recommendations of the antigen supplier for conversion.

In all circumstances, a new vial test is highly recommended whenever new lots of antigen or new antigen suppliers are used.

Also, several clinical scenarios have been identified in which a single treatment vial for immunotherapy may not be adequate. It is recommended to consider separation into more than one vial antigens with known high proteolytic activity from antigens that are sensitive to proteases or antigens with low proteolytic activity to preserve their potency over the course of immuno-

therapy treatment.^{6,7} In addition, at least temporary separation of antigens into more than one vial may be considered when there are antigens to which a patient is highly sensitized and antigens to which the patient is less sensitized, in order to minimize the risk of reaction as well as avoid hindering advancement of less sensitive antigens during escalation.^{6,7,8} Also, separation may be necessary if the number of antigens included in the patient's vaccine exceeds what is allowable based on the total volume of the treatment vial.^{6,7}

1 Cox L, et al. *Allergen Immunotherapy: A practice parameter third update*. J Allergy Clin Immunol. 27(1): S1-S55. 2010.

2 Nelson HS. *Effect of preservatives and conditions of storage on the potency of allergy extracts*. J Allergy Clin Immunol. 67(1): 64-69, Jan 1981.

3 Nelson HS, et al. *Studies of allergen extract stability: The effects of dilution and mixing*. J Allergy Clin Immunol. 98(2): 382-388, Aug 1996.

4 Gilbert KC, et al. *Antibacterial properties of additives used in injection immunotherapy*. International Forum Allergy Rhinology, 2(2): 135-8, Mar-Apr 2012.

5 Bosquet J, Lockey R, Malling H-J. *Allergen immunotherapy: Therapeutic vaccines for allergic diseases—A WHO position paper*. J Allergy Clinical Immunology. 102(4):558-62. Oct 1998. Benefit Policy Manual, sections 60 to 60.4 <http://cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf>

6 King HC, et al. *Allergy in ENT Practice, second edition*. Theme Medical Publishers, Inc. New York, NY, 2005: 226-229, 273-79

7 Haydon RC III, Gordon BR. *Aeroallergen immunotherapy*. In: Krause HF, et al., ed. *Allergy and immunology: an otolaryngic approach*. Philadelphia: Lippincott Williams & Wilkins, 2002; 170-1.

8 Ward WA Jr. *Skin endpoint immunotherapy*. In: Krause HF, ed. *Otolaryngic allergy and immunology*. Philadelphia: WB Saunders, 1989; 155-62.

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