

# Food Sublingual Immunotherapy Using Consistent, Cheaper and Customizable Oral Immunotherapy Solutions

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**Abstract:** Food SLIT (sublingual immunotherapy) is a food desensitization method with a daily maintenance dose of <10 mg for up to 5 years. Many protocols use commercially available skin test extracts. Oral immunotherapy (OIT) treatment solutions have consistent protein concentrations, are comparatively cheaper and customizable and therefore were adapted for use in a published SLIT dosing schedule.

**Keywords:** food allergy, immunotherapy, pharmacoeconomics, food allergy treatments, sublingual immunotherapy, desensitization

Food Sublingual Immunotherapy (SLIT) is a food desensitization method with a typical daily maintenance dose of <10 mg protein for up to 3–5 years, which has been shown to increase tolerance in hazelnut and peanut allergic patients in randomized, double-blind, placebo-controlled trials.<sup>1,2</sup> In SLIT, intact food protein is given sublingually to the tolerogenic antigen-presenting Langerhans cells, held for 2 minutes, and then swallowed or spat out. Starting doses are at the microgram level and increase to milligram doses by maintenance.<sup>3</sup> SLIT buffers against unintentional food exposure while maintaining a favorable safety profile with mostly transient oropharyngeal itching in less than 5% of peanut SLIT doses.<sup>4</sup> Many published SLIT protocols use commercially available skin test extracts.

Skin test extracts have relatively higher protein concentration variability and cost, and lower customizability in comparison to Oral Immunotherapy (OIT) solutions. Egg and milk skin test extracts contain 2–4 mg protein per milliliter, while peanut extract contains 4–8 mg protein per milliliter at an approximate price of 4 US dollars per mg protein.<sup>5</sup> Allergists collaborate to develop and refine OIT protocols which yield solutions with reasonable protein concentration consistency.<sup>6,7</sup> Since actual food is used to make OIT solutions, the cost is orders of magnitude less. Although OIT solutions have a shorter shelf life than skin test extracts, they can be frozen for future use.<sup>8</sup> An OIT solution can be made to approximate the protein concentration of a skin test extract and substituted for the skin test extract used in a published SLIT protocol<sup>4</sup> (Figure 1) and is found to dispense easily (Figure 2). If for any reason, the maintenance dose needs to be adjusted, the OIT solution can be customized without changing the protocol, which is difficult to do with skin test extracts which have variable, fixed protein concentrations (Table 1).

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#### Dilution 1 - 1:1

- To start out you will be taking one aliquot of food plus flavoring and adding distilled water (<25 ml) up to a final volume of 25 ml. This will be your Food SLIT Dilution 1, which you will use to make Dilutions 2, 3, and 4.
- To make vials for a 3-month supply renewal: you will be taking 2 aliquots of food and adding distilled water (<50 ml) up to a final volume of 50 ml. Shelf life is 2 weeks unless frozen.
- Patients will advance every 14 days and begin with 1 drop (0.05 ml x14), followed by 2 drops (0.10 ml x14), followed by 4 drops (0.20 ml x14), and finishing with 8 drops for 14 days (0.40 ml x14). This totals 10.50 ml needed.
- Then patients will be maintaining 8 drops daily which equals 0.40 ml, requiring 12 ml per month. (0.40 ml x 30days = 12 ml/month)

#### Dilution 2 - 1:10

- Take 1.5 ml from Dilution 1 (Stock) and place into 13.5ml distilled water. This is now dilution 2.
- Patients will advance every 14 days and begin with 1 drop (0.05ml x14), followed by 2 drops (0.10 ml x14), followed by 4 drops (0.20 ml x14), and finishing with 8 drops for 14 days (0.40 ml x14). This totals 10.50 ml needed.

#### Dilution 3 - 1:100

- Take 1.5 ml from Dilution 2 and place into 13.5 ml distilled water. This is now dilution 3.
- Patients will advance every 14 days and begin with 1 drop (0.05 ml x14), followed by 2 drops (0.10 ml x14), followed by 4 drops (0.20 ml x14), and finishing with 8 drops for 14 days (0.40 ml x14). This totals 10.50 ml needed.

#### Dilution 4 - 1:1,000

- Take 0.5 ml from Dilution 3 and place into 4.5 ml distilled water. This is now dilution 4.
- Patients will advance every 14 days and begin with 1 drop (0.05 ml x14 and finish with 5 drops (0.25 ml x14). This totals 4.2 ml needed.

**Figure 1** Food SLIT dilution protocol.



**Figure 2** Peanut dilution I – 1:1 5mg/mL plus flavoring.

**Table 1** Summary of Food Amounts Needed to Create a SLIT Maintenance Vial Using an OIT Dosing Protocol

Food	Maintenance Dose (mg Protein)	Aliquot of Food in 25mL Vial	Flavoring	Notes
Almond	2 mg	1/8 tsp almond butter	Kool-Aid 0.5 tsp	Barney Butter Almond Butter – Smooth
Cashew	2 mg	1/8 tsp cashew butter	Kool-Aid 0.5 tsp	Artisana Raw Organic Cashew Butter
Chickpea	2 mg	625 mg flour	Kool-Aid 0.5 tsp	Garbanzo Bean Flour Bob's Red Mill <a href="http://www.bobsredmill.com">www.bobsredmill.com</a>
Coconut	2 mg	3/8 tsp or 875 mg flour	Kool-Aid 0.5 tsp	Bob's Red Mill Organic Coconut Flour <a href="http://www.bobsredmill.com/organic-coconut-flour.html">http://www.bobsredmill.com/organic-coconut-flour.html</a>
Egg White	2 mg	1.1 mL egg white	Kool-Aid 0.5 tsp	All Whites 100% or Eggland's Best Liquid Egg Whites
Hazelnut	2 mg	15 mL milk or 875 mg flour	Kool-Aid 0.5 tsp for flour, Chocolate or strawberry syrup for milk	Elmhurst Hazelnut Milk or Bob's Red Mill <a href="http://www.bobsredmill.com/hazelnut-flour-meal.html">www.bobsredmill.com/hazelnut-flour-meal.html</a>
Milk	2 mg	3.75 mL milk	Chocolate or strawberry syrup	Use milk > 10 days from expiration date. Use organic or irradiated whole milk
Milk	7 mg	13.1 mL milk	Chocolate or strawberry syrup	Use milk > 10 days from expiration date. Use organic or irradiated whole milk
Peanut	2 mg	1/8 tsp peanut butter	Kool-Aid 0.5 tsp	Peanut Butter & Company, Santa Cruz Organic or Jif peanut butters. Stir for 2 hours
Rye	2 mg	938 mg flour	Kool-Aid 0.5 tsp	Organic Dark Rye Flour at <a href="http://www.nuts.com">www.nuts.com</a>
Sesame	1.7mg	1/8 tsp tahini	Kool-Aid 0.5 tsp	Max Sesame Tahini Spread
Shrimp		Consider dust mite SLIT		Eur Ann Allergy Clin Immunol. 2011 Oct;43(5):162–4
Soy	2 mg	3.75 mL soy milk	Chocolate or strawberry syrup	Use milk > 10 days from expiration date. Use Original Silk Soy Milk
Sunflower	2 mg	567 mg butter	Kool-Aid 0.5 tsp	Sunbutter
Walnut	1.7 mg	1/8 tsp walnut butter	Kool-Aid 0.5 tsp	<a href="http://www.fastachi.com">www.fastachi.com</a> Raw Walnut Butter
Wheat	2 mg	178 mg flour	Kool-Aid 0.5 tsp	Druids Grove Vital Wheat Gluten Flour

We hope that this adaption of OIT solutions for use in available SLIT protocols improves the access to consistent, economical, and customizable food desensitization.

## Disclosure

Dr Joshua Jacobs reports consultancy fees and contracted research from Aimmune, outside the submitted work. The authors report no other conflicts of interest in this work.

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