Omalizumab as Monotherapy and as Adjunct Therapy to Multi-Allergen OIT in Food Allergic Children and Adults ("OUtMATCH")

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TITLE OF CLINICAL RESEARCH STUDY

Omaliz**u**mab as **M**onotherapy and as **A**djunct **T**herapy to Multi-Allergen OIT in Food Allergic **Ch**ildren and Adults ("OUtMATCH")

PART 1

This study is sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) through the Consortium for Food Allergy Research (CoFAR).

Protocol Number: CoFAR-11

PRINCIPAL INVESTIGATOR: Robert Wood, MD

Johns Hopkins Institutional Review Board Protocol Number: IRB00203850

In addition to Dr. Wood, the Study Principal Investigator, each site will have a Principal Investigator. Site Principal Investigators will be listed in the second part of the consent form that includes information specific to the study site where you are being asked to enroll.

YOUR PARTICIPATION IS VOLUNTARY

We will explain this research study to you. You may ask questions at any time.

- Your participation in this study is your decision. Research studies include only people who choose to take part.
- You may change your mind at anytime.
- We will give you a signed copy of this consent form for your records.

This study is a multi-site study, meaning it will take place at several different locations. Because this is a multi-site study, this informed consent form includes two parts. The first part of this document includes information that applies to all study sites. The second part of the consent form has information specific to the study site where you are being asked to enroll, such as HIPAA privacy language, payment, research related injury, language for pregnancy results, and contact information.

Key Information:

The first few pages of this document include a summary of this study to help you decide whether or not to participate. Detailed information is provided after the summary/key information.

Why am I being asked to take part in this research study?

We are asking you to be a part of this research study because you are between 18 to 55 years old and may be allergic to multiple foods including peanut and at least 2 other foods. Participation is voluntary and you may change your mind at any time.

Why is this research being done?
We would like to learn if omalizumab injections alone or in combination with Multi-allergen oral immunotherapy (OIT) will help people who are allergic to multiple foods, including peanut, eat the foods to which they are allergic.

How long will the research last and what will I need to do?

- This research project has 3 stages. Your participation will last up to 3 years and 3 months.
- If you agree to be in the study, you will complete screening procedures that include physical exams, blood collections, and feeding tests called oral food challenges (OFCs). There will be OFCs to peanut and at least 2 other foods to qualify for the study. If you qualify for the study, you will start out by getting injections that may or may not have the medicine omalizumab. The injections that do not have any medicine are called placebo.

There are 3 stages in this study.

Stage 1: We would like to learn if 16-20 weeks of omalizumab (Xolair) stops or reduces allergic reactions to peanut and other foods. Omalizumab is given as an injection under the skin in either the arm or thigh. Study visits will be scheduled every 2 or 4 weeks for 16-20 weeks so we can give you the omalizumab.

Stage 1 will also have an extra part called Stage 1 Open Label Extension (OLE). The first 60 participants who complete Stage 1 will move directly into Stage 1 Open Label Extension. They will receive omalizumab for an extra 24-28 weeks. There are no placebo injections during this part of the study. This is why it is called the Open Label Extension. This part of the study will help us learn if there is any difference when the omalizumab is given for a longer period of time compared to the shorter time.

All other participants will move directly to Stage 2.

Stage 2: Participants will start OIT along with omalizumab in this stage. Some participants will get OIT that will have the foods to which they are allergic. Others will get OIT that is placebo that will not have any of the foods to which they are allergic. We would like to compare an 8-week course of omalizumab combined with OIT to a longer course of omalizumab in decreasing allergic reactions to foods. Study visits will be scheduled every 2 or 4 weeks for 2 months, then every 2 weeks for up to 6 months. Visits will be every 2 or 4 weeks from month 6 through month 12-13.

Stage 3: We would like to see if people who have completed omalizumab or Multi-allergen OIT with omalizumab can eat peanut and 2 other foods. Study visits will be different. Visits may be every 2 weeks for up to 6 months and then every 8 weeks from month 6 through month 11.

Stage 1 and 2 of the study will involve OFCs to peanut and 2 other foods from the following list: milk, egg, wheat, cashew, hazelnut, or walnut.

In **all stages**, we would like to learn:

- How safe and effective the treatments are
- How the OIT and omalizumab affects the immune system

Is there any risk from being in this study?
The risks to participating in this study include reactions to the omalizumab injections, which includes a small risk of anaphylaxis (severe allergic reaction) and reactions to the Multi-allergen OIT.

When you are allergic to multiple foods, eating Multi-allergen OIT or anything that has the food(s) to which you are allergic could cause you to have an allergic reaction. These allergic reactions include sneezing, runny nose, rash, swelling, flushing, flares of eczema, nausea, vomiting, abdominal discomfort, cough, wheezing, shortness of breath, or itchy eyes, nose, mouth, and/or throat. There is a small risk of severe anaphylaxis (a potentially life-threatening allergic reaction that can cause a sudden drop in blood pressure and severe breathing problems). The likelihood that you will experience any allergic symptoms will be lessened by starting OIT dosing with very small amounts and slowly increasing the dose. There is a chance that you could get Eosinophilic Esophagitis (EoE). An eosinophil is a type of white blood cell that is normally in the blood in small amounts. EoE happens when this type of white blood cell increases in the esophagus, the tube that connects the mouth to the stomach.

The risks are discussed in more detail under the heading, "**RISKS AND/OR DISCOMFORTS**."

Will being in this study help me in any way?
You may or may not directly benefit from being in this study. But the information we learn from this study may help those who have food allergies in the future.

What other choices do I have besides taking part in this research study?
You do not have to take part in this research study. You can still get treated for your allergies by your allergist.

Detailed Consent Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

1. INTRODUCTION/BACKGROUND

Food allergy affects about 15 million people in the United States. This includes 6 million children. The current treatment for food allergy is to avoid eating the foods that may cause an allergic reaction and have medications such as epinephrine (adrenaline) in case of a reaction. But accidental exposures can be very difficult to avoid, especially if you are allergic to multiple foods. The risks of accidental exposures and life-threatening reactions can place a large burden on participants and their families.

2. PURPOSE OF THE STUDY

We would like to learn if omalizumab injections alone or in combination with Multi-allergen OIT will help people with multiple food allergies eat foods to which they are allergic. Oral means that you will take the food allergen (peanut and 2 other foods to which you are allergic) by mouth. If you are allergic to more than 3 foods, this study will only provide OIT for peanut and 2 other foods. You and the study doctor from this site will discuss and decide which 2 other foods will be part of your treatment.

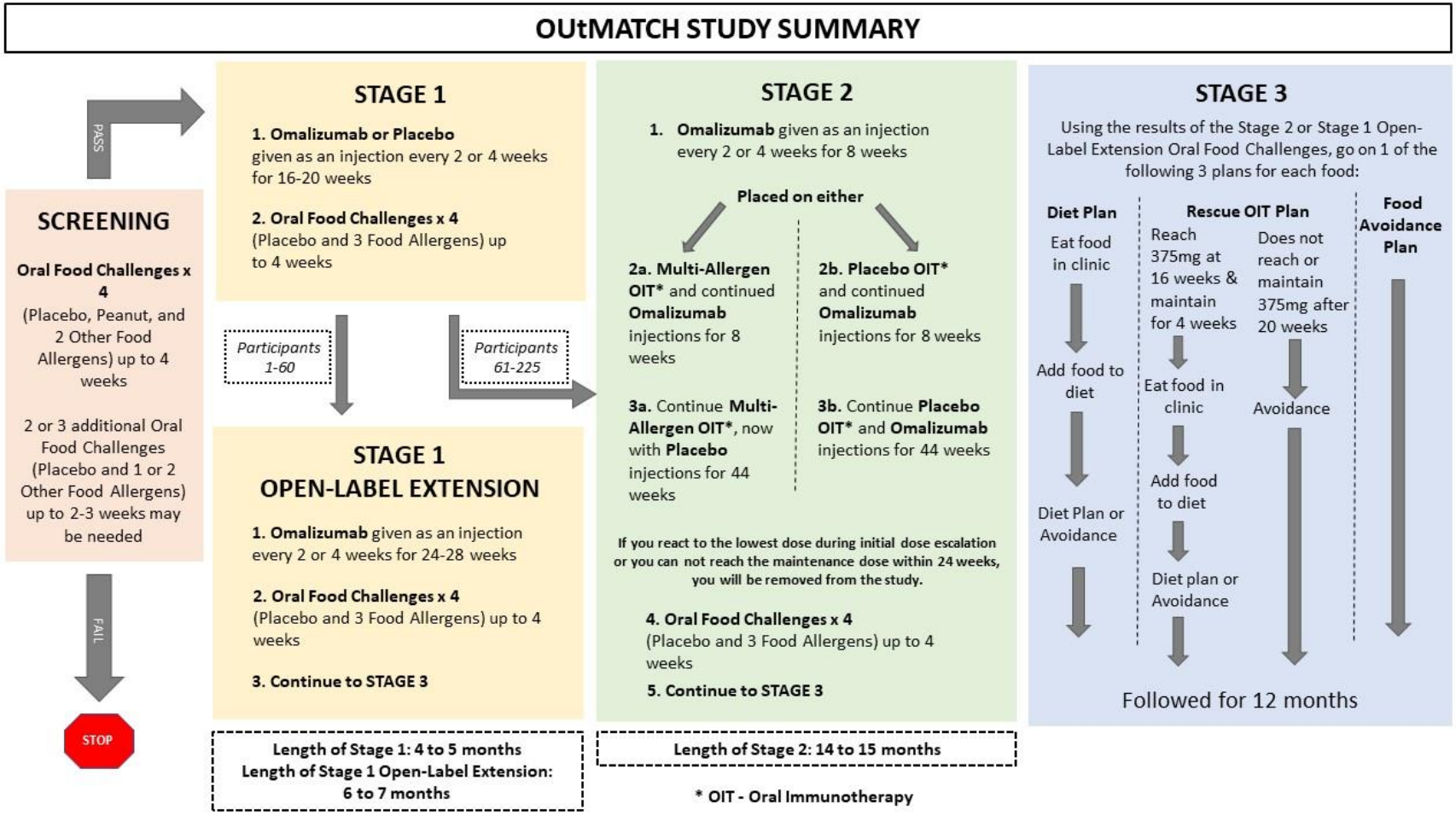
Are there any investigational drugs/devices/procedures?

Omalizumab is a drug that blocks the action of IgE, a type of antibody that causes allergies. Omalizumab is approved by the Food and Drug Administration (FDA) and European Commission for use in patients 6 years of age and older who have moderate to severe asthma. It is also approved for treatment of chronic hives with no known cause in patients 12 years and older, and for treatment of chronic rhinosinusitis with nasal polyps in patients 18 years and older.

As of 16 February 2024, Omalizumab is approved for food allergy in adults and children 1 year and older for reducing allergic reactions, including anaphylaxis, that may occur with accidental exposure to one or more foods. Omalizumab does not prevent food allergies, but it is to be used along with avoiding the foods. Omalizumab is not to be used for emergency treatment of allergic reactions, including anaphylaxis.

The use of the OIT in this research study is investigational. The word “investigational” means that it is not approved for marketing or regular treatment by the Food and Drug Administration (FDA). The FDA is allowing its use in this study. If we decide that you will receive rescue OIT in Stage 3, it will be an option for 6 months after you finish Stage 2.

The drawing on the next page gives the overall view of all the stages of the study.


OUtMATCH STUDY SUMMARY
SCREENING
Oral Food Challenges x 4
(Placebo, Peanut, and 2 Other Food Allergens) up to 4 weeks
2 or 3 additional Oral Food Challenges (Placebo and 1 or 2 Other Food Allergens) up to 2-3 weeks may be needed
PASS
FAIL
STOP
STAGE 1
1. Omalizumab or Placebo given as an injection every 2 or 4 weeks for 16-20 weeks
2. Oral Food Challenges x 4
(Placebo and 3 Food Allergens) up to 4 weeks
Participants 1-60
Participants 61-225
STAGE 1 OPEN-LABEL EXTENSION
1. Omalizumab given as an injection every 2 or 4 weeks for 24-28 weeks
2. Oral Food Challenges x 4
(Placebo and 3 Food Allergens) up to 4 weeks
3. Continue to STAGE 3
Length of Stage 1: 4 to 5 months
Length of Stage 1 Open-Label Extension: 6 to 7 months
STAGE 2
1. Omalizumab given as an injection every 2 or 4 weeks for 8 weeks
Placed on either
2a. Multi-Allergen OIT* and continued Omalizumab injections for 8 weeks
3a. Continue Multi-Allergen OIT*, now with Placebo injections for 44 weeks
2b. Placebo OIT* and continued Omalizumab injections for 8 weeks
3b. Continue Placebo OIT* and Omalizumab injections for 44 weeks
If you react to the lowest dose during initial dose escalation or you can not reach the maintenance dose within 24 weeks, you will be removed from the study.
4. Oral Food Challenges x 4
(Placebo and 3 Food Allergens) up to 4 weeks
5. Continue to STAGE 3
Length of Stage 2: 14 to 15 months
* OIT - Oral Immunotherapy
STAGE 3
Using the results of the Stage 2 or Stage 1 Open-Label Extension Oral Food Challenges, go on 1 of the following 3 plans for each food:
Diet Plan
Eat food in clinic
Add food to diet
Diet Plan or Avoidance
Rescue OIT Plan
Reach 375mg at 16 weeks & maintain for 4 weeks
Eat food in clinic
Add food to diet
Diet plan or Avoidance
Does not reach or maintain 375mg after 20 weeks
Avoidance
Food Avoidance Plan
Followed for 12 months

3. STUDY COMPONENTS

This study is sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH). The drug in the study, omalizumab, is made by Genentech/Novartis. Representatives from both companies worked with NIAID staff and principal investigators of the study in writing the protocol. Both companies under NIAID's lead will be able to review your research information at the end of each stage of the study. They also may examine the results from some of your blood samples. Your personal information, such as your name, birthdate and anything that could identify you, is removed before sharing blood samples with these companies. Your samples and information will have a code and only the study staff from this site will have the key to the code.

The following procedures are done over the course of the study:

- **Consent:** You will read and sign the consent form before any study procedures are done.
- **Questionnaires:** We will ask you questions about your allergies. This includes your family history, diet, general health, and quality of life. Your age will determine the questions we ask you. You may ask the study staff to explain any questions you do not understand.
- **Diaries:** You will keep a daily diary in Stage 2, and a daily or weekly diary in parts of Stage 3 based on assigned treatment plans. For the daily diaries, you will make a note of the doses taken each day and any reactions. You will also need to let us know of any changes to your health in the diary. Keeping track of any reactions to doses will be done either electronically or by paper.
- **Vital Signs, Height, and Weight:** We check your temperature, pulse, breathing rate, blood pressure, height, and weight.
- **Physical Examination**
- **Spirometry (Lung function test)**: We measure how much air is blown out of the lungs and how fast.
- **Peak Expiratory Flow ("Peak Flow"):** We measure how fast you can blow air out through your mouth using a small tube with a mouthpiece.
- **Medication Review:** We ask you about any medications you may have recently taken or treatments you may have used.
    - If you are taking any antihistamines like Benadryl or Zyrtec, they will need to be stopped for a short period of time before skin prick testing and OFCs. This is so they do not interfere with the results of the tests.
    - If you use a rescue inhaler like albuterol, we will ask you not to use it for four hours before visits that we evaluate your lung function. But if you need your rescue inhaler, please use it, and let us know.
- **Skin Prick Test:** You are tested to foods and environmental allergens. Small drops of liquid will be placed on your arm. Each drop is lightly pricked under the skin to see if there is a reaction. If there is a reaction, you will get a raised, red, itchy bump that may

look like a mosquito bite. The test takes about 15-20 minutes.

- **Oral Food Challenge:** An OFC is a feeding test. We slowly feed you increasing amounts of the food. We start with very small amounts of the food to lessen the chance of a severe reaction. The food challenges may be double blind placebo-controlled or an open challenge. During the food challenge, we may put a small tube called an I.V. in your arm inside the vein before starting the food challenge. The I.V. will help give medications quickly if needed.
    - The **double-blind placebo-controlled food challenge (DBPCFC)** means that neither you nor the study staff giving you the challenge will know which part is active or placebo.
    - The DBPCFC has parts that will have the foods to which you are allergic (active) and one part will just be oat (placebo). The placebo looks and tastes the same as the active parts but does not have any active ingredient.
- **Multi-allergen OIT or Placebo:** You eat small amounts of flour of the foods you are allergic to or placebo. The placebo is just oat flour and does not have any of the foods to which you should react. It will look and taste the same as the flour with foods to which you are allergic. Each dose of the food (the small amounts of flour) will be in single soufflé cups with lids. Each dose is to be mixed with something like applesauce or pudding and then eaten. We watch you for signs or symptoms like itching, rashes, stomach pain, or trouble breathing. If you tolerate the first small dose, we will gradually increase the amount of the foods to which you are allergic or placebo. Depending on how you do with each dose, we will either slowly increase the dose or decrease the dose, if it is not tolerated.
- **Omalizumab or Placebo Injections:** We will give you 1 to 4 injections subcutaneously. This means the injection is given in the fatty tissues under the skin in either the arm or thigh. The injections will be given every 2 or 4 weeks. Placebo for omalizumab does not have the omalizumab medication. The dose and how often you receive the injections will depend on your weight and a blood test that tells us the level of IgE in your blood. IgE is a type of antibody that the immune system makes and is usually higher in people with allergic diseases. We watch you for at least 2 hours after the first 3 injections in Stage 1. We will also watch you for any reaction for at least 2 hours after the first 3 injections in Stage 1 Open Label Extension and in Stage 2. For the rest of the injections, we will watch you for at least 30 minutes after the injections.
- **Epinephrine Autoinjector:** We will give you a prescription for an epinephrine autoinjector if you do not have one. The study staff also reviews the use of an injectable epinephrine device used to treat severe allergic reactions. We will teach you how to use it. <u>You must bring your epinephrine device to each visit. The epinephrine autoinjector should be taken everywhere with you</u>. You must sign an Epinephrine Autoinjector Training Form before you will receive study product.

- **Sample Collections**
  - **Blood:** The most amount of blood that we collect during a visit is a little over 1 teaspoon per pound of your weight. During any 8-week period, we will not collect over 550 milliliters (mL) (a little more than 2 cups and 4 tablespoons) or about one teaspoon per pound of body weight, whichever is smaller.
  - **Stool:** We give you a kit with instructions on how to collect stool that includes how to return the sample. You will fill out a questionnaire about changes in bowel movements. You will need to include what you ate or drank before collecting the sample, and how you stored the sample at home. You can bring the sample to the next clinic visit.
  - **Urine:** We collect a small amount of urine from you.
  - **Saliva:** We collect a small amount of saliva from you while in the clinic.

We may ask you to have blood and urine tests done to look at safety before you come to a clinic visit. You may have these tests done at a local laboratory or your doctor's office. You will not be billed for these tests.

Identifiers might be removed from the information or biospecimens collected as part of the research study. Only after such removal, the information or specimens could be used for future research studies or shared with another investigator for future studies without additional informed consent being obtained.

We may share results from some of the research tests that might help you learn more about your food allergies. These include results from some of the food challenges, skin prick tests, or blood tests that may be shared with you during or after study visits.

In this study, we do not plan to use your samples for genetic cloning, paternity testing, or other personal identification. This study will not look at all of your DNA at once ("whole genome testing") nor large chunks of your DNA (whole exome testing).

While in this study, it is very important that you do not eat any foods to which you are allergic. You should only eat what the study doctor tells you is okay.

STUDY VISITS

SCREENING

- **Screening Visit**
  A Screening Visit is done to make sure you qualify for the study. The following procedures are done at this visit:

- Informed Consent
- Medical History
- Diet and Allergy Questionnaires
- Vital Signs, Weight, and Height
- Full Physical Exam
- Evaluation of eczema
- Spirometry
- Peak Flow - for those participants who are unable to complete spirometry
- Medication Review
- Skin Prick Test to food and environmental allergens
- DBPCFC – up to 444 mg to include peanut protein and 2 to 4 other foods. **If you do not react to peanut and 2 other food challenges, you will not qualify for the study.** Each part of the DBPCFC may be done on different days.
- Blood Collection – for safety, to look at antibodies in the immune system and other potential causes related to food allergy.
- Evaluation of abdominal symptoms (**during each Screening DBPCFC Visit**)
- Urine Collection – for safety
- Urine pregnancy test for women capable of becoming pregnant
- Stool collection kit and questionnaire given **(first Screening DBPCFC Visit only)**

The Screening Visit takes place over several days. You must have an epinephrine autoinjector in case of any severe reactions. We will give you a form to sign that confirms you understand how to use an epinephrine autoinjector. You will need to sign this form to stay in the study. We will also review what to do if you have a reaction. This is a Food Allergy Action Plan.

If you qualify for the study, you will be randomly assigned to either receive omalizumab or placebo injections. Neither you nor the study doctor can choose which group you are assigned. You will be randomly assigned like flipping a coin or picking numbers out of a hat.

After the Screening Visit, we collect blood and urine every 3 months throughout Stage 1, Stage 1 Open Label Extension, Stage 2, and Stage 3 (while receiving study product from the previous stage) for safety. If you are a woman capable of becoming pregnant, we will do monthly urine pregnancy tests while you are receiving study product or before certain procedures. The study doctor may decide more urine pregnancy tests are needed.

STAGE 1

- **Randomization Visit**
  If you qualify for the study after the Screening Visit, we ask you to return to the clinic at a later date for the Randomization Visit. During this visit, you receive an injection of omalizumab or placebo. The following procedures are also done at this visit:
    - Vital Signs, Weight, and Height
    - Brief Medical History
    - Diet, Allergy (including your family history), and Quality of Life Questionnaires
    - Evaluation of any abdominal symptoms
    - Brief Physical Exam
    - Medication Review
    - Samples
        - Stool collection kit and questionnaire returned (if not returned before this visit)
        - Collection of saliva and urine samples

- **Omalizumab or Placebo Injection Visits – Every 2 or 4 weeks (depending on weight and results of blood tests)**
  You return to the clinic every 2 or 4 weeks for 14 weeks during Stage 1. At these visits, you receive injections of omalizumab or placebo. We watch you for any reactions for 2 hours after the first 3 injections and 30 minutes after future injections. Additionally, the following procedures are done at these visits:
    - Vital Signs, Weight, and Height
    - Brief Medical History
    - Diet and Allergy Questionnaires
    - Evaluation of any abdominal symptoms
    - Brief Physical Exam
    - Medication Review

- **Double-Blind Placebo-Controlled Food Challenge Visits – Week 16-20**
  After 16 weeks, you return to the clinic for blinded food challenges up to 6044 milligrams (mg) protein of each food. We will not give you the results of these challenges. You continue to receive omalizumab or placebo injections during the blinded food challenge period, which will last up to 4 weeks. You may have injections on the same day as a food challenge or on a different visit. Additionally, the following procedures are done at these visits:
    - Vital Signs, Weight, and Height
    - Brief Medical History
    - Diet and Allergy Questionnaires
    - Quality of Life Questionnaire **(Week 16 only)**

- Evaluation of any abdominal symptoms
- Full Physical Exam
- Evaluation of eczema **(Week 16 only)**
- Peak Flow
- Medication Review
- Skin Prick Test to peanut and 2 other food allergens **(Week 16 only)**
- Samples **(Week 16 only)**
  - Collection of saliva and urine samples
  - Blood collection

STAGE 1 OPEN LABEL EXTENSION

- **Omalizumab Injection Visits – Every 2 or 4 weeks the same schedule as Stage 1**
  Omalizumab injections will be given every 2 or 4 weeks for about 5 and ½ months (24-28 weeks). We watch you for any reactions for 2 hours after the first 3 injections and 30 minutes after future injections. The first Injection Visit in the Open Label Extension will be 2 or 4 weeks after your last injection in Stage 1. Additionally, the following procedures are done at these visits:
  - Vital Signs, Weight, and Height
  - Brief Medical History
  - Diet and Allergy (including your family history) Questionnaires
  - Quality of Life Questionnaire **(first Injection Visit of the Stage 1 Open Label Extension only)**
  - Evaluation of any abdominal symptoms
  - Brief Physical Exam
  - Medication Review

- **Double-Blind Placebo-Controlled Food Challenge (DBPCFC) Visits– Week 24-28**
  After 24 weeks, you return to the clinic for a DBPCFC up to 8044 mg protein of each food. The food challenges will be done over 4 visits (within 4 weeks). You continue to receive omalizumab injections during the blinded food challenge period. Injections may be given on the same day as a food challenge or on a different visit. Additionally, the following procedures are done at these visits:
  - Vital Signs, Weight, and Height
  - Brief Medical History
  - Full Physical Exam
  - Evaluation of eczema **(Week 24 only)**
  - Diet and Allergy Questionnaires
  - Quality of Life Questionnaire **(first DBPCFC Visit and last DBPCFC Visit)**
  - Evaluation of any abdominal symptoms
  - Peak Flow

- Medication Review
- Skin Prick Test to food allergens to peanut and 2 other foods **(Week 24 only)**
- Blood collection **(Week 24 only)**

Participants who complete the Stage 1 Open Label Extension will move directly to Stage 3 of the study. They will skip Stage 2. We will give you the results of your food challenge in this stage.

Change in the study after review of study results from the first 168 participants

- We planned to enroll up to 225 participants from 10 clinical centers across the United States.
- However, after we looked at the results of the first 168 people who entered stage 1, we learned that the study drug, omalizumab, is more effective than placebo for increasing the amount of peanut, milk, egg, and cashew that can be eaten without a reaction, although it was not effective in every participant.
- After reviewing the information from the first 168 participants, we stopped enrollment into Stage 1. Stage 1 of the study was completed in March 2023.
- After enrollment stopped, participants were given options to enter directly into Stage 2 or leave the study.

STAGE 2

- **Omalizumab Injection Visits – Every 2 or 4 weeks (same schedule as Stage 1)**
  We will give you omalizumab injections every 2 or 4 weeks for 8 weeks. We watch you for any reactions for 2 hours after the first 3 injections in Stage 2, then for 30 minutes for the rest of the injections. Additionally, the following procedures are done at these visits:
  - Vital Signs, Weight, and Height
  - Brief Medical History
  - Diet and Allergy (including your family history) Questionnaires
  - Quality of Life Questionnaire **(first Injection Visit only)**
  - Evaluation of any abdominal symptoms
  - Brief Physical Exam
  - Medication Review
  - Stool collection kit and questionnaire given (at the Injection Visit before the Initial Dose Escalation Visit)

  After 8 weeks of getting omalizumab injections, you will be randomly assigned like before to 1 of 2 different groups below to receive:
  - Omalizumab and Multi-allergen OIT for 8 weeks (2 months). After 2 months, you will receive placebo for omalizumab and Multi-allergen OIT for 44 weeks (a little more than 10 months); **or**

- Omalizumab and placebo for Multi-allergen OIT for 52 weeks (1 year).

Most participants will not know what treatment they are receiving until all participants have completed Stage 2 of the study. But it is possible that toward the end of Stage 2, a few participants may learn of their Stage 2 treatment to decide if Stage 3 rescue OIT is needed.

Initial Dose Escalation Visit – Multi-allergen or Placebo OIT

During this visit, we give you a mixture of small amounts of Multi-allergen OIT (peanut and 2 other foods), or placebo mixed in food to eat. The dose will be increased about every 15 minutes up to 375 mg of each food allergen. **You must be able to take at least 9 mg of Multi-allergen OIT or placebo during this visit to stay in the study.** Additionally, the following procedures are done at this visit:

- Vital Signs, Weight, and Height
- Brief Medical History
- Diet and Allergy Questionnaires
- Evaluation of any abdominal symptoms
- Review diaries
- Full Physical Exam
- Peak Flow
- Medication Review
- Omalizumab injections, if needed
- Samples:
  - Stool collection kit and questionnaire returned (if not returned before this visit)
  - Collection of saliva and urine samples
  - Blood collection

- **Multi-allergen OIT or Placebo OIT Build-Up Phase Visits – Every 2 weeks**

  After the Initial Dose Escalation Visit, we ask you to return to the clinic the next day to start the Build-Up Phase. You start at the last dose that was tolerated the day before. We watch you for any reactions. If there are no reactions, we will give you this dose to take at home every day for the next 2 weeks. Each dose will be in a small soufflé cup with a lid. The dose is to be mixed with something like applesauce or pudding at home, and then eaten every day. If you are unable to return to the clinic within 2 days after the Initial Dose Escalation Visit, the Initial Dose Escalation Visit will need to be repeated.

  Visits to the clinic will be every 2 weeks for up to 24 weeks during the Build-Up Phase. At these visits, we increase the dose of Multi-allergen OIT or placebo. We

watch you for any reactions. You go home on the increased dose unless you have reactions. If you have reactions, we may ask you to return to the clinic. Your dose may be changed.

Additionally, the following procedures are done at these visits:

- Vital Signs, Weight, and Height
- Brief Medical History
- Diet and Allergy Questionnaires
- Evaluation of any abdominal symptoms
- Review diaries
- Brief Physical Exam
- Peak Flow
- Medication Review
- Injections with omalizumab **(until Week 14) or**
- Injections with omalizumab/placebo **(after Week 16)**

You continue build-up until you reach the maximum tolerated dose. At this point, you will enter the Maintenance Phase. **If you do not reach a dose of at least 250 mg of each food allergen (a total of 750 mg), then you will not continue in the study.**

- **Initial Maintenance Dose Visit**
  Once you reach the maximum tolerated dose, you return to the clinic 2 weeks later for the first Maintenance Dose Visit. The following procedures are done at this visit:
  - Vital Signs, Weight, and Height
  - Brief Medical History
  - Diet and Allergy Questionnaires
  - Evaluation of any abdominal symptoms
  - Review diaries
  - Brief Physical Exam
  - Peak Flow
  - Medication Review
  - Dose administration for OIT/placebo
  - Injections with omalizumab/placebo
  - Blood collection

- **Follow-Up Maintenance Dose Visits – Every 8 weeks**
  During this phase, you return to the clinic every 8 weeks for 28-44 weeks. You take the same dose daily during this phase. The following procedures are done at these visits:
  - Vital Signs, Weight, and Height
  - Brief Medical History

- Diet and Allergy Questionnaires
- Evaluation of any abdominal symptoms
- Review diaries
- Brief Physical Exam
- Peak Flow
- Medication Review
- If you haven't taken a dose of the OIT/placebo at home, we may give you a dose while in the clinic
- Injections with omalizumab/placebo
- Stool collection kit and questionnaire given **(visit before the first DBPCFC Visit only)**

- **<u>Double-Blind Placebo-Controlled Food Challenge Visits – Week 60-64</u>**
  At 60 weeks after the start of Stage 2, you return to the clinic for blinded food challenges up to 8044 mg protein of each food. You continue to receive injections of omalizumab/placebo every 2 or 4 weeks during the blinded challenges. The food challenges may be done over 4 visits (within 4 weeks). Do not take the Multi-allergen OIT dose on days that you have a food challenge in the clinic. Additionally, the following procedures are done at these visits:
  - Vital Signs, Weight, and Height
  - Brief Medical History
  - Diet and Allergy Questionnaires
  - Quality of Life Questionnaire **(first DBPCFC Visit and last DBPCFC Visit)**
  - Evaluation of any abdominal symptoms
  - Review diaries
  - Full Physical Exam
  - Omalizumab/placebo injections if needed
  - Evaluation of eczema **(Week 60 only)**
  - Peak Flow
  - Medication Review
  - Skin Prick Test to peanut and 2 other food allergens **(Week 60 only)**
  - Samples **(Week 60 only)**
    - Stool collection kit and questionnaire returned (if not returned before this visit)
    - Collection of saliva and urine samples
    - Blood collection

Participants who complete Stage 2 will move to Stage 3 of the study.

We will give you the results of your food challenge in this stage.

STAGE 3 – Long-Term Follow-Up

Stage 3 includes a treatment plan for each food that you are being treated for in this study. We may give you the foods to eat or try OIT again. You may also avoid the foods for which you were being treated. The treatment plan for each food may change throughout Stage 3, depending on how well you respond to each food.

Long-Term Follow-Up with the Inclusion of Food(s) in Diet

If you tolerate a single dose of at least 600 mg of food during the food challenge for a food in Stage 1 Open Label Extension, Stage 2, or you tolerate 375mg of rescue OIT in Stage 3, you will be invited to move to Long-Term Follow-Up to include the food in the diet.

- **Long-Term Follow-Up with Inclusion of the Food(s) in Diet: In-Clinic Feeding Visits**
  During this part of the study, you return to the clinic so we can watch the first time you eat a small amount of the food as part of the diet. You will continue your treatment from the last stage until all in-clinic feeding visits are finished. After all visits with in-clinic feeding are finished, we give you instructions on how to include the food safely in your diet. The food will need to be eaten regularly to keep protecting you from allergic reactions. Additionally, the following procedures are done at these visits:
    - Vital Signs, Weight, and Height
    - Brief Medical History
    - Diet and Allergy (including your family history) Questionnaires
    - Evaluation of any abdominal symptoms
    - Review diaries
    - Full Physical Exam **(first time feeding of food only)**, then brief physical exams
    - Medication Review
    - Injections with omalizumab (if needed) or
    - Injections with omalizumab/placebo (if needed)

- **Long-Term Follow-Up with Inclusion of the Food(s) in Diet: Calls/Emails**
  After all visits with in-clinic feeding are finished, we call or email you weekly for the first 4 weeks, then every 2 weeks for the next 10 weeks. After that we call or email you every 2 months until you have completed 6 months of including the food in your diet. After you have completed 6 months, you may stop your daily diaries. Starting at 7 months, we will call or email you every month for about 1 year.

  During each call or email, we ask you about the following:
    - Progress with including food(s) in the diet
    - Current medications
    - Brief medical history

- Any reactions to the food(s), any abdominal symptoms, and overall health
- Diet and Allergy Questionnaires
- Review diaries, as applicable

- **Long-Term Follow-Up with Inclusion of the Food(s) in Diet: Follow-Up Visits**
  During this phase of the study, visits to the clinic are every 6 months for about 1 year. The following procedures are done at these visits:
  - Vital Signs, Weight, and Height
  - Brief Medical History
  - Diet and Allergy Questionnaires
  - Quality of Life Questionnaire **(first visit only)**
  - Evaluation of any abdominal symptom
  - Brief Physical Exam
  - Evaluation of eczema **(first visit only)**
  - Medication Review
  - Skin Prick Test to peanut and 2 other food allergens **(first visit)**
  - Blood collection **(first visit only)**
  - Review diaries, as applicable

Rescue OIT: Dose Escalation, Build-Up, and Maintenance

You may have another chance to take OIT again if any of the following happen:

- You completed Stage 1 Open Label Extension (OLE) or Stage 2 within the last 14 days and did not tolerate a single dose of at least 600 mg of the food during your last blinded food challenge or
- You completed the blinded food challenge at the end of Stage 1 OLE or Stage 2 within the last 14 days but refused the 600 mg dose, even if the lower dose was tolerated.

Toward the end of Stage 2, if one of the above occur and in the rare case we learn of your treatment, you may be offered OIT.

- **Rescue OIT: Initial Dose Escalation (IDE) Visit**
  If you did not tolerate or refused a single dose of at least 100 mg of the food allergen during your last blinded food challenge in Stage 1 Open Label Extension or Stage 2, you will again complete an Initial Dose Escalation Visit. You will continue the same treatment from the last stage until the Initial Dose Escalation Visit is complete.

  The dose of OIT will be increased about every 15 minutes up to 375 mg of each food allergen. **If you do not tolerate 3 mg protein of the food, you will receive long-term follow-up calls and visits while avoiding the food.** Additionally, the following procedures are done at this visit:

- Vital Signs, Weight, and Height
- Brief Medical History
- Diet and Allergy (including your family history) Questionnaires
- Evaluation of any abdominal symptoms
- Review diaries
- Full Physical Exam
- Peak Flow
- Medication Review
- Blood collection 6 months after starting rescue OIT
- Urine pregnancy test, if capable of becoming pregnant and one was not done within the last month
- Open label omalizumab or placebo/omalizumab injection may occur on the same day of the IDE

- **<u>Rescue OIT: Dose Build-Up Phase Visits – Every 2 weeks (up to 16 weeks)</u>**

  If you completed the Initial Dose Escalation Visit during rescue OIT, you will return to the clinic the next day to start the Build-Up Phase. You start at the last dose tolerated at the Initial Dose Escalation Visit. We watch you for any reactions. If there are no reactions, we give you this dose to take at home every day for the next 2 weeks. If you are unable to return to the clinic within 1 day, we will ask you to repeat the Initial Dose Escalation Visit.

  If you do not need to complete another Initial Dose Escalation Visit the starting dose of OIT will be determined by the results of your last blinded food challenge.

  Clinic visits will be every 2 weeks for up to 16 weeks during the Build-Up Phase. At these visits, we increase the dose. We watch you for any reactions. You go home on the next dose unless you have reactions. If this happens, you go home on the last dose tolerated for 2 more weeks.

  Additionally, the following procedures are done at these visits:
  - Vital Signs, Weight, and Height
  - Brief Medical History
  - Diet and Allergy Questionnaires
  - Evaluation of any abdominal symptoms
  - Review diaries
  - Brief Physical Exam
  - Peak Flow
  - Medication Review
  - Urine pregnancy test, if capable of becoming pregnant and one was not done

within the last month

You continue build-up until you reach the maximum required dose. Once you reach the maximum required dose, you will enter the Maintenance Phase. **If you do not reach a maximum tolerated dose of at least 375mg of the food, you will receive long-term follow-up calls/emails and visits while avoiding the food or be referred to an allergist.**

- **Rescue OIT: Initial Maintenance Dose Visit for Transition to Long-Term Follow-Up with Inclusion of the Food(s)**
  Once you reach the maximum tolerated dose, you return to the clinic 2 weeks later for the first Maintenance Dose Visit. The following procedures are done at this visit:
  - Vital Signs, Weight, and Height
  - Brief Medical History
  - Diet and Allergy Questionnaires
  - Evaluation of any abdominal symptoms
  - Review diaries
  - Brief Physical Exam
  - Peak Flow
  - Medication Review
  - Dose administration for OIT
  - Urine pregnancy test, if capable of becoming pregnant and one was not done within the last month

- **Rescue OIT: Transition to Long-Term Follow-Up with Inclusion of Food(s) in Diet - Calls/Emails**
  If you tolerate the maintenance dose required to transition to inclusion of the food in the diet, we will call or email you 2 weeks after the Initial Maintenance Dose Visit.

  During each call or email, we ask you about the following:
  - Progress with rescue OIT
  - Current medications
  - Brief medical history
  - Any reactions to the rescue OIT, any abdominal symptoms, and overall health
  - Diet and Allergy Questionnaires
  - Review diaries

  You will return to the clinic 4 weeks after the Initial Maintenance Dose Visit for a Follow-Up Maintenance Dose Visit

- **Rescue OIT: Transition to Long-Term Follow-Up with Inclusion of Food(s) in Diet - Follow-Up Maintenance Dose Visit**
  You will return to the clinic 4 weeks after your Initial Maintenance Dose Visit. The following procedures are done at this visit:
  - Vital Signs, Weight, and Height
  - Brief Medical History
  - Diet and Allergy Questionnaires
  - Evaluation of any abdominal symptoms
  - Review diaries
  - Brief Physical Exam
  - Peak Flow
  - Medication Review
  - Urine pregnancy test, if capable of becoming pregnant and one was not done within the last month

  If you do not tolerate the minimum target maintenance dose of 375mg during this 4 week period, you will be instructed to avoid the food or be referred to an allergist.

  If you tolerate the target maintenance dose visit during this 4 week period, you will transition to Long-Term Follow-Up with Inclusion of Food(s) in the Diet. You will have been on Rescue OIT for a total of 20 weeks.

- **Rescue OIT: Transition to Long-Term Follow-Up with Inclusion of the Food(s) in Diet: In-Clinic Feeding Visits**
  During this part of the study, you return to the clinic so we can watch the first time you eat a small amount of the food as part of the diet. You will continue your rescue OIT until all in-clinic feeding visits are finished. After all visits with in-clinic feeding are finished, we give you instructions on how to include the food safely in your diet. The food will need to be eaten regularly to keep protecting you from allergic reactions. Additionally, the following procedures are done at these visits:
  - Vital Signs, Weight, and Height
  - Brief Medical History
  - Diet and Allergy (including your family history) Questionnaires
  - Evaluation of any abdominal symptoms
  - Review diaries
  - Quality of Life Questionnaire **(6-month visit only)**
  - Full Physical Exam **(first time feeding of food only)**, then brief physical exams
  - Medication Review
  - Blood collection **(6-month visit only)**

- **Rescue OIT: Long-Term Follow-Up with Inclusion of the Food(s) in Diet: Calls/Emails**
  After all visits with in-clinic feeding are finished, we call or email you weekly for the first 4 weeks, then every 2 weeks for the next 10 weeks. After that we call or email you every 2 months until you have completed 6 months of including the food in your diet. After you have completed 6 months, you may discontinue your daily diaries and we will call you every month for about 1 year.

  During each call or email, we ask you about the following:
  - Progress with including food(s) in the diet
  - Current medications
  - Brief medical history
  - Any reactions to the food(s), any abdominal symptoms, and overall health
  - Diet and Allergy Questionnaires
  - Review diaries, as applicable

- **Rescue OIT: Long-Term Follow-Up with Inclusion of the Food(s) in Diet: Follow-Up Visits**
  During this phase of the study, visits to the clinic are every 6 months for about 1 year. The following procedures are done at these visits:
  - Vital Signs, Weight, and Height
  - Brief Medical History
  - Diet and Allergy Questionnaires
  - Quality of Life Questionnaire **(first visit only)**
  - Evaluation of any abdominal symptom
  - Brief Physical Exam
  - Evaluation of eczema **(first visit only)**
  - Medication Review
  - Skin Prick Test to peanut and 2 other food allergens **(first visit)**
  - Blood collection **(first visit only)**
  - Review diaries, as applicable

Long-Term Follow-Up with Avoidance

You may avoid including a food in your diet if you:

- Do not tolerate 3 mg protein of the food at the Initial Dose Escalation Visit, do not reach at least 375 mg of rescue OIT for 4 weeks;
- Do not tolerate the food during Long-Term Follow-Up and had rescue OIT for that food; or
- Do not want to include the food in your diet.

During this part of the study, you will be asked to avoid eating the food.

- **Long-Term Follow-Up with Avoidance: Calls/Emails**
  For the first 6 months you will complete a weekly diary to document any foods accidentally eaten that you are avoiding. You will need to write down any reactions to the food and any medications taken. After you have completed 6 months of avoiding the food, we will call or email you every month for about 6 months.

During each call or email, we ask you about the following:

- Progress with avoiding food(s) in the diet
- Current medications
- Brief medical history
- Any reactions to the accidental ingestion of food(s), any abdominal symptoms, and overall health
- Diet and Allergy Questionnaires

- **Long-Term Follow-Up with Avoidance: Follow-Up Visits**
  During this phase of the study, you return to the clinic every 6 months for about 1 year. The following procedures are done at these visits:
  - Vital Signs, Weight, and Height
  - Brief Medical History
  - Diet and Allergy (including your family history) Questionnaires
  - Quality of Life Questionnaire **(first visit only during this phase)**
  - Evaluation of any abdominal symptom
  - Brief Physical Exam
  - Evaluation of eczema **(first visit only during this phase)**
  - Medication Review
  - Review diaries, as applicable
  - Skin Prick Test to peanut and 2 other food allergens **(first visit)**
  - Blood collection **(first visit only)**

Unscheduled Visit(s)

We may ask you to return to the clinic for the following reasons:

- If you have symptoms with OIT doses taken at home
- If you miss OIT doses repeatedly because of illness
- If you have symptoms more than 2 hours after taking an OIT dose
- If samples need to be collected again or if any tests need to be repeated
- If you miss an omalizumab/placebo injection
- If you have any symptoms or tests the study doctor would like to follow-up on

If there is an unscheduled visit, procedures and samples that need to be collected at that time will be determined by the study doctor.
Unscheduled visits may be done during any part of the study.

Early Discontinuation Visit

If you decide to stop your participation in the study or the study doctor determines it is not in your best interest to continue, we ask you to return to the clinic for a final visit. Depending on where you are in the study, the following procedures may be done at this visit:

- Vital Signs, Weight, and Height
- Brief Medical History
- Brief Physical Exam
- Diet and Allergy Questionnaires
- Evaluation of any abdominal symptoms
- Monthly Long-Term Follow-up Questionnaires (as needed for the Stage)
- Review diaries (as needed for the Stage)
- Medication Review
- Urine pregnancy test, if capable of becoming pregnant

In addition, if you are in Stages 1 or 2, or the first 6 months of Stage 3 and the following procedures have not been completed within the last 8 weeks before this visit, they will be completed at this visit:

- Skin Prick Test to food allergens
- Blood collection
- Urine sample collection

4. RISKS AND/OR DISCOMFORTS

Treatment and procedures in this research study may involve risks that are not possible to predict. The most serious risks involve reactions to food challenges, OIT, and omalizumab, and developing EoE. You will be informed of any new risks that may be identified during the course of the study.

Below is a description of the risks we know about for each study procedure. Please ask the study doctor or study staff to explain any procedures or risks that you do not understand.

- **Questionnaires:** You may find that some of the questions are too personal. You may refuse to answer any questions that make you feel uncomfortable. There is a possibility that your answers may be read by others outside of the study. We do not put your name on the questionnaires. We only write identification numbers on the questionnaires.

- **Vital Signs, Height & Weight:** There are no known risks for having your vital signs, height, and weight evaluated.

- **Physical Exam:** There are no known risks for the physical exam.

- **Stopping Medications:**
  - Stopping allergy medications before skin prick testing or food challenges may cause worsening of allergic symptoms. You will be able to take the medications right after the test is finished or during the test if needed for an allergic reaction.
  - Stopping asthma medications before the lung function test may cause worsening of asthma symptoms. If your asthma symptoms worsen, take your rescue medication such as albuterol as prescribed and let the us know.

- **Skin Prick Testing:**
  - Skin testing may cause discomfort at the site, slight pain from the needle prick, itching, swelling, redness, and/or bleeding at the site. These symptoms usually go away shortly after the test.
  - Less often skin testing causes hives (itchy rash), "hay fever-like" symptoms such as sneezing/runny nose, and/or watery itchy eyes, "asthma-like" symptoms such as chest tightness, bruising at the site, or a skin infection.
  - Rarely, you could have a serious or life-threatening reaction (anaphylaxis). This involves the whole body. This could lead to a drop in blood pressure, difficulty breathing or swallowing, loss of consciousness, or death. In some cases, you may need to be hospitalized overnight during an anaphylactic reaction. A study doctor will always be close by when you are being tested and trained study staff will have medications close by to treat you if you have any of these reactions.

- **Oral Food Challenges:** Food challenges, both blinded and open, may cause allergic reactions. We expect that you may experience an allergic reaction to the food challenges.
  - You may experience mild itchy lips/mouth, mild lip swelling, face/body itching, mild abdominal pain, mild nausea, throat itchiness/irritation, a few hives (itchy rash), occasional cough, runny nose, stuffy nose, sneezing. Medications will be available to treat these reactions.
  - Less often OFCs cause a lot of hives (itchy rash), widespread lip/face swelling, tongue swelling, throat tightness, moderate or severe abdominal pain/cramping, moderate or severe nausea, vomiting, diarrhea, constant cough, wheezing, shortness of breath, chest discomfort/tightness. Medications will be available to treat these reactions.
  - Rarely, you could have a serious or life-threatening reaction (anaphylaxis). This

involves the whole body. This could lead to a drop in blood pressure, difficulty breathing or swallowing, loss of consciousness, or death. In some cases, you may need to be hospitalized overnight during an anaphylactic reaction. The risk of allergic reactions is lessened by starting the challenge with very small amounts of the food and slowly increasing the dose. The study doctor and trained study staff are always close by during an OFC. Medication and equipment will be immediately available in case of an anaphylactic reaction. Participation may end for anyone who has severe reactions during an OFC.

- **OIT (Initial Dose Escalation, Build-Up, and Daily OIT):** OIT may cause allergic symptoms.
    - You may experience itchy lips/mouth, body itching, abdominal pain/cramps, nausea, vomiting, throat itchiness/irritation, hives (itchy rash). In past studies using OIT, people described these symptoms the most.
    - Less often, OIT causes sneezing, runny nose, stuffy nose, itchy nose, itchy eyes, itchy ears, or itchy body. You could get lip and tongue swelling, mouth/throat discomfort or pain, mouth numbness, cough, wheezing, shortness of breath, throat tightness, chest discomfort/tightness, or worsening of eczema.
    - There is a small risk you may have a serious or life-threatening reaction (anaphylaxis). This involves the whole body. This may lead to a drop in blood pressure, difficulty breathing or swallowing, loss of consciousness, or death. In some cases, you may need to be hospitalized overnight during an anaphylactic reaction. The likelihood of a participant experiencing any allergic symptoms will be lessened by starting OIT dosing with very small amounts and slowly increasing the dose. Each time a dose is increased it is done in clinic so the study doctor and study staff can watch you for any reaction.
    - There is also a small chance that you could get Eosinophilic Esophagitis (EoE). An eosinophil is a type of white blood cell that is normally in the blood in small amounts. In EoE, this type of white blood cell increases in the esophagus. The esophagus is a tube that goes from the throat to the stomach. **This increase in eosinophils can cause belly aches, trouble swallowing, and vomiting. If you have EoE symptoms, we may stop your participation in the study. The symptoms of EoE may or may not stop after exposure to OIT ends.**

- **Food products used for Oral Food Challenges and OIT:** The food products used in this study for OIT and oral food challenges are made from commercially available food flours. The flours are not treated in any way (such as additional baking or sterilization) so that the allergens within them are not changed. As natural products, these flours probably contain small amounts of bacteria and mold picked up from the environment. As with any food, there is a risk of mold growth if the products become damp, are not stored properly, or are kept too long. Mold has been seen in food products packaged for

this study. While ingesting mold is usually harmless, it is possible that it could cause an allergic reaction. Allergy symptoms would include watery eyes, runny nose, sneezing, itching or asthma symptoms. Mold may also cause symptoms of food poisoning, such as nausea, vomiting, and diarrhea.

- **Omalizumab:**
  - You may feel faint, have headaches, upper abdominal pain, fever, and injection site reactions (including pain, swelling, redness, bruising, and itching of the skin around the injection site). At least 3 in 100 people may experience one of these side effects.
  - There is a small risk (around 1 in 1,000 people) that you may have a serious or life-threatening reaction (anaphylaxis) involving the whole body, which may lead to a drop in blood pressure, difficulty breathing or swallowing, loss of consciousness, or death. In some cases, you may need to be hospitalized overnight during an anaphylactic reaction. Each time a dose is given, it is done in clinic so the study doctor and study staff can watch you for any reaction. Participation may end for anyone who has severe reactions.
  - There is also a small risk (the exact frequency is unknown) of you developing:
    - Serum sickness, which includes the following symptoms joint pain, rash, fever, and lymph nodes that may be abnormal in size, number, or consistency.
    - A rare blood disorder that causes inflammation in the wall of blood vessels of the body and/or an increase in eosinophils in the blood.
    - A reduced number of platelets in the blood. Platelets are blood cells that help blood clot. Symptoms of reduced platelets include easy bruising, prolonged bleeding, nose bleeds, blood in urine or stool. Blood will be collected every 3 months to evaluate this potential side effect. If you have any of these problems, your participation in the study may be stopped.
  - **Potential side effects include:**
    - Events related to clots in the blood vessels including stroke, transient ischemic attack (mini-strokes), heart attack, unstable angina or discomfort caused by poor blood flow in the heart, and sudden death caused by loss of heart function.
    - Increased risk of malignancies (cancer).
    - Risk of you developing antibodies to omalizumab. Antibodies are proteins in blood that recognizes foreign substances in the blood.

- **Open Feedings:** Open feeding of a food allergen may cause allergic reactions.
  - You may experience mild itchy lips/mouth, mild lip swelling, face/body itching,

mild abdominal pain, mild nausea, throat itchiness/irritation, a few hives (itchy rash), occasional cough, runny nose, stuffy nose, or sneezing. Medications will be available to treat these reactions.

- Less often you may experience a lot of hives (itchy rash), widespread lip/face or tongue swelling, throat tightness, moderate or severe abdominal pain/cramping, moderate to severe nausea, vomiting, diarrhea, constant cough, wheezing, shortness of breath, or chest discomfort/tightness. Medications will be available to treat these reactions.
- There is a small risk you may have a serious or life-threatening reaction (anaphylaxis). This involves the whole body. This could lead to a drop in blood pressure, difficulty breathing or swallowing, loss of consciousness, or death. In some cases, you may need to be hospitalized overnight during an anaphylactic reaction. The open feedings are done in the clinic, so that the study doctor and trained study staff are always close. Medication and equipment will be immediately available in case of an anaphylactic reaction.

- **Other Medications:** If you have any allergic reactions during Multi-allergen OIT therapy, you may be treated with other medications. Risks of these common medications are summarized below:
  - Antihistamines: drowsiness, dizziness, constipation, stomach upset, blurred vision, or dry mouth/nose/throat.
  - Epinephrine: rapid heart rate, strong or irregular heart rate, nervousness, sweating, nausea, vomiting, trouble breathing, headache, dizziness, anxiety, shaking, or pale skin.
  - Medications like albuterol: nervousness, shaking, headache, or dizziness.
  - Oral steroids: nausea, vomiting, loss of appetite, heartburn, trouble sleeping, increased sweating, or acne.
  - Topical steroids: itching, burning, reddening of the skin, loss of skin pigment or coloring, skin thinning, stretch marks, bruising, or spider veins.

- **Spirometry and Peak Flow Measurements:** Spirometry and peak flow are tests to measure lung function. They may cause coughing or lightheadedness that go away shortly after the test is finished.

- **Blood Collection/Intravenous (I.V.) Catheter Insertion:** The risks of having blood taken or getting an I.V. catheter inserted may include pain, bleeding, bruising, or infection. Lightheadedness and fainting rarely happen. A numbing cream may be placed on the skin before the blood draw to reduce the pain of the stick if you choose this option. Side effects of this cream (mainly skin rash) are unlikely but may happen.

- **Stool, Saliva, and Urine Sample Collections:** There are no known risks for the collection of the stool, saliva, and urine samples.

- **The Genetic Information Nondiscrimination Act (GINA):** GINA is a federal law that helps reduce the risk of discrimination by health insurers or employers based on your genetic information. GINA does not protect you from discrimination if you apply for other types of insurance (such as life, disability or long-term care). GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.
    - Health insurance companies and group plans may not request genetic information from this research
    - Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums
    - Employers with 15 or more employees may not use your genetic information when deciding to hire, promote, or fire you when setting the terms of your employment.
    - The law will not stop health insurance companies from using genetic information to decide whether to pay claims. The law does not apply to other types of insurance (such as life, disability or long-term care).

- Your privacy and the confidentiality of your data are very important to us. We will make every effort to protect them, but we cannot make guarantees. Confidentiality is described under the heading, "**CONFIDENTIALITY".**

5. POTENTIAL BENEFITS

If you agree to take part in this study, there may or may not be direct medical benefit to you. The information we learn from this study may someday help those who have food allergies.

6. ALTERNATIVES TO PARTICIPATION

Before you decide to take part in this study, the study doctor from this site will talk with you about the treatment options available to you. You may choose not to take part in this research study. You can still be treated for allergies or other medical problems at this site.

7. NEW FINDINGS

The study doctor will tell you about any new information or significant findings that may affect your willingness to continue in this study.

8. VOLUNTARY WITHDRAWAL FROM STUDY

- You may decide not to take part in this study.
- You can decide to leave the study at any time. If you decide to leave the study, there will

not be any penalty or loss of benefits in your routine medical care or any other benefit(s) that you are otherwise entitled to receive.
- In addition, you should talk to the study doctor from this site, who will discuss future treatment and procedures for your continued care.

9. REASONS WHY YOU MAY BE TAKEN OFF STUDY WITHOUT YOUR CONSENT

You may be removed from the study without your consent at any time. Reasons why you may be removed from the study include, but are not limited to, the following:

- The study doctor from this site determines it is not in your best interest to continue in the study.
- You are unable to complete required study treatments and examinations.
- You are diagnosed with a serious illness or other condition that requires treatments that are not allowed for study participants.
- You start taking a treatment that is not allowed in the study.
- The study is stopped by the Institution, the Sponsor, or by the FDA or other health authorities.
- You become pregnant.

If you are removed from the study, the study doctor from this site will contact you to discuss stopping procedures and your future care.

10. PREGNANCIES, BREASTFEEDING, AND BIRTH CONTROL

You cannot take part in this study if:

- You are currently pregnant or breastfeeding.
- You plan to get pregnant in the next 37 months.

Treatments and procedures involved in this research study may involve unexpected risks to your unborn or nursing child. If you are a woman capable of becoming pregnant, a pregnancy test will be done before to enrollment and periodically during this study.

The effects of omalizumab on an unborn child are unknown and may be harmful; therefore, you should not become pregnant or father a child while in this study. If you are capable of becoming pregnant, you must agree to use an effective method of birth control to prevent pregnancy during the study and 60 days after omalizumab. Females who are capable of becoming pregnant will be required to take a pregnancy test before entry into this study. If you become pregnant or if there is any chance that you are pregnant (late menstrual period), please contact the study personnel immediately so that we may provide medical assistance and counseling. If you are male and your partner becomes pregnant during the study, you should also notify the study doctor immediately. You should not nurse (breast feed) a baby while on this study because omalizumab may enter breast milk and possibly harm the baby.

The study doctor from this site will discuss acceptable methods of birth control.
If you or your partner should become pregnant while participating in this study, or if you suspect that you are pregnant, you must contact the study doctor from this site immediately. If you become pregnant during the treatment phase, omalizumab and OIT dosing will be stopped. You will no longer receive omalizumab and/or Multi-allergen OIT. You will be followed until the end of the study and/or pregnancy outcome.

11. COSTS TO THE PARTICIPANT (YOU)

There is no charge to you or your health plan/insurance company for any costs which are directly related to study procedures.

The study does not provide epinephrine autoinjectors. You must have epinephrine autoinjectors to participate in the study. If you do not have an epinephrine autoinjector, you will be given a prescription for this medication. You and/or your health plan/insurance company will be billed for the epinephrine autoinjectors. The cost of an epinephrine autoinjector two dose kit without insurance ranges from approximately $150 to $900 depending on the brand and pharmacy. If you have a health plan/insurance, the amount you might pay is based on your specific health plan/insurance plan or eligibility for a patient assistance program.

The study does not provide routine care or any medications/treatments for your general health or allergic problems. You and/or your health plan/insurance company will be billed for some or all the costs of any routine medical care for your condition provided outside of the study. Visits to the doctor outside of the study visits, emergency room, urgent care visits, or hospitalizations during the study will be billed to your health plan/ insurance company.

12. SHARING YOUR HEALTH-RELATED INFORMATION WITH RESEARCHERS OF THIS STUDY

As part of this study, the researchers may ask to see your medical records from your other health care providers. Specifically, we may look any IgE results that were done in the 3 months before the Screening Visit.

13. EMERGENCY UNBLINDING

During this study, you will not have access to certain medical information. You will not know if you are receiving active or placebo treatment. If an emergency happens while you are in the study, there is a procedure in place to share medical information needed for your treatment with your study doctor and other physicians who treat you.

14. CONFIDENTIALITY

Your medical and research records will be confidential to the extent permitted by law. Efforts

will be made to keep your personal information private. But we cannot guarantee complete confidentiality. You will be identified by a code, and personal information from your records will not be released without your written permission. You will not be identified in any publication or in the sharing of data about this study.

When the study is finished, information and samples from the study may be placed in a central storage location. Information will not be included that can identify you. The purpose is to make study data available to other researchers. Your privacy is protected whenever this information is used. We will keep your samples indefinitely, unless you tell us differently. The purpose is to make study data available to other researchers.

Information from this study may be put into databases along with information from other studies. There are different kinds of databases; some are publicly accessible, and some are restricted. Anyone on the internet can access publicly accessible databases. Only researchers who apply and are approved can access restricted databases. Traditionally used identifying information about you (such as name, phone number, address) will NOT be included or shared with others. Information collected about you in this study could be placed in both publicly accessible and restricted databases.

Your privacy is important to us and we will use safety measures to protect your privacy. In spite of all the safety measures that we use, we cannot guarantee that your identity will never become known. Although your genetic information is unique to you, you share some genetic information with your children, parents, brothers, sisters, and other blood relatives. Consequently, it may be possible that genetic information from them could be used to help identify you. Similarly, it may be possible that genetic information from you could be used to help identify them.

While we will not use information that is traditionally used to identify you, people may develop ways in the future that would allow someone to link your genetic or medical information in our databases back to you. For example, someone could compare information in our databases with information from you (or a blood relative) in another database and be able to identify you (or your blood relative). It is also possible there could be violations to the security of the computer systems used to store the codes linking your genetic and medical information to you. There may also be other privacy risks that we have not foreseen.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- NIAID, sponsor of the research
- NIAID representatives, agents, employees, contractors, and other persons assisting in conducting, monitoring, or analyzing the study

- The US Food and Drug Administration
- Other Health Authorities
    - Local and state US health authorities
- Pharmaceutical or Device Companies and their commercial partners may review your medical and research records for regulatory purposes.

15. WHAT DOES A CONFLICT OF INTEREST MEAN TO YOU AS A PARTICIPANT IN THIS STUDY?

A researcher has a financial or other interest in this study.

In some situations, the results of this study may lead to a financial gain for the researcher and/or Johns Hopkins University. This financial interest has been reviewed in keeping with Johns Hopkins' policies. It has been approved with certain conditions, which are intended to guard against bias and to protect participants.

If you have any questions about this financial interest, please talk to Dr. Jennifer Dantzer at (410) 955-5883. This person is a member of the study team, but does not have a financial interest related to the study. You may also call the Office of Policy Coordination 410-361-8667 for more information. The Office of Policy Coordination reviews financial interests of researchers and/or Johns Hopkins.

16. WHAT IS A CERTIFICATE OF CONFIDENTIALITY?

As this is a NIH funded study, you are further protected through a policy that prevents the study doctor from releasing any sensitive information about you that may identify you, unless you say it is okay. This does not prevent you or a family member from voluntarily releasing information about you or your involvement in this research.

This policy does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by US law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

17. FUTURE USE OF YOUR DATA/BIOLOGIC MATERIALS

Information about you, including your biospecimens, collected for this study may be shared

with other researchers. It may also be used for other research studies. We will make sure that your identity cannot be linked to the information we share. We will not ask you for additional permission before sharing the information.

We are asking your permission to store unused/extra samples of biological specimens such as blood, tissue, and urine collected during this study to be used in the future for research studies that are not yet planned. These studies may or may not be related to the study of food allergy or other allergic conditions.

Your stored samples will be used to obtain knowledge about genetic information in relation to your immune system. Genetic tests study an individual's inherited characteristics, found in DNA, which is present in each of the cells of his/her body. DNA contains information needed to construct and operate the human body.

The results of research studies performed on stored samples or reports resulting from the analysis of your samples will not be given to you or your doctor and they will not be put in your medical record. They will not identify you and will not affect your routine medical care.

There is no benefit to you from the storage of samples and information. But the use of your samples and information may help researchers learn more about your disease or the genetics related to a specific condition. The purpose of storage and sharing data is to make information available for use in health research and to share what is stored with other researchers. Collecting, storing, sharing information, and making it available for other studies may help people in the future. Coded information put into databases, together with other stored information from many studies conducted in different places, allow researchers to study the combined information and learn even more about health and many different diseases.

Samples will be stored at The University of North Carolina – Chapel Hill and Stanford University. If you decide to allow storage of your samples and information, they may be stored for an unknown length of time.

Although your stored research samples will not be sold, the information obtained from the research performed on your samples may in the future lead to the development of commercial products. You will not receive any money from research using your stored samples and information.

There may be unknown risks associated with the storage of samples and information. For example, if future research involves genetic testing, it is possible that it could be traced back to you because your genes are specific to you. We will make every attempt to protect your confidentiality and to make sure that your personal identity does not become known.

If you decide to leave the research study, already collected information may not be removed from the research database and will continue to be used to complete the research analysis. Your previously collected blood samples will still be used as planned.

You may decide to change your mind about storing samples for future use at any time and ask to have your samples destroyed after planned use. This request should be made in writing to the study doctor. If you make this request, all remaining stored samples will be destroyed. But the results of any previous tests using your stored samples will be used. Your decision regarding the storage of samples or the information resulting from the analysis of your samples will not affect your ability to take part in this study. The future use of your samples and information may contribute to learning more about disease or help to study the genetics related to a specific condition.

Please indicate your response below:
I agree to the storage and sharing of samples (blood, stool, and urine) for genetic studies not currently planned.

Yes ☐ No ☐

_____
Initials of Research Participant

I agree to the storage and sharing of samples (blood, stool, saliva, and urine) and information resulting from the analysis of my samples for other studies not currently planned.

Yes ☐ No ☐

_____
Initials of Research Participant

OTHER PARTICIPANT AUTHORIZATIONS
Please read and indicate your response below:

Future Contact:

- I agree to be contacted in the future as a follow-up to the OUtMATCH study.

  ☐ Yes ☐ No

  _____
  Initials of Research Participant

- I agree to be contacted about future research studies.

  ☐ Yes ☐ No

  _____
  Initials of Research Participant