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**YOUNG PARTICIPANT INFORMATION SHEET 14-16 years- OPIA STUDY**

**Oral Peanut Immunotherapy with dietary starch adjuvant for peanut allergy**

HREC/16/SCHN/372

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**Information Sheet – Young people (14-16 years)**

You are being invited to take part in a research study. Before you decide whether you would like to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others. Ask us if there is anything that is not clear or if you would like more information.

Take time to decide whether or not you wish to take part.

**What is the study about?**

You are being asked to participate in this study because you have a peanut allergy. Peanut allergy is common and affects up to 3-5% of Australian children and is likely to persist. There is no current cure for peanut allergy, and strict avoidance is the current standard of care. To avoid allergic reactions, people with peanut allergy are advised to avoid peanuts in their diet. We know that this has a negative impact on quality of life, limiting their choice of food, affecting shopping and social life, and causing anxiety around the potential for severe reactions from accidental exposure.

Recent research has shown that gradual exposure to low doses of peanut over months (under strict medical supervision) can allow people to eat peanut safely. This is called desensitization or oral immunotherapy (OIT).

We are interested in trying to develop improved and safer ways of desensitising children and teenagers to peanut. Currently oral desensitisation studies have shown that short term desensitisation can be achieved in many individuals, but getting more permanent tolerance to peanut has not been possible.

We want to try and improve this situation by adding in a dietary starch supplement to a standard peanut desensitisation (OIT) regime. We have some very promising information from studies in mice that some types of starch (like the HAMSB we are using in this study) help to prevent allergic reactions to peanuts in mice. We believe that this starch and its product butyrate help promote a special type of immune cell, called a Tregulatory cell. These cells have been shown to be very important in determining allergy and tolerance to foods.

This type of starch (HAMSB) has been developed by the CSIRO and has been used in Australian human studies of gut diseases with no safety concerns, and these studies are ongoing. In this modified starch, a short chain fatty acid called butyrate is attached to starch with links that are broken by chemicals in the gut releasing the butyrate. It is taken as a granular powder and will come in a small tub. It can be mixed in with other food.

**Who can participate in the study?**

Children and teenagers aged 10-16 years with a history of peanut allergy are considered potentially eligible. If you have very severe asthma, other serious health issues, are pregnant or have been admitted to the intensive care unit because of your allergy to peanuts, you can’t participate in the study.

**Do I have to take part?**

It is up to you to decide whether or not you want to take part. You should also talk to your parents about this. If you do decide to take part, then you will be given this information sheet to keep. Both you and your parents will be asked to sign a consent form. You are free to withdraw from the study at any time and without giving a reason. A decision to withdraw, or a decision not to take part, will not affect the care you receive in the future.

**What will the study involve?**

**What does the study involve in terms of time commitment?**

This study lasts 2 years, with an active study period of 58 week. It involves you visiting the Allergy Research Unit at Children’s Hospital at Westmead for 5 day visits, at least 15 updosing visits (where each increase in peanut dose is first taken under supervision at hospital) and 2 short visits over that 58 week period:

• The day visits will last approximately 6 hours. These are for allergy tests (including peanut challenge tests) and questionnaires (for screening eligibility and then ongoing assessment).

• In addition, you will need to attend the Research Unit every 2-3 weeks (at least 15 visits) when the dose of peanut is increased. These ‘updosing’ visits will last 2 hours. The exact number of visits depends on how allergic you are to the peanut. Where possible, we will offer late-afternoon clinic slots to minimize time away from school for these visits. We will provide an information sheet for you to give to your school, so they are aware of your participation and potential impact on schooling.

If you are allocated to one of the two active groups, you will need to eat a dose of peanut every day. You will also need to avoid strenuous activity for 2 hours following an OIT dose. You will need to eat their fibre dose at a different time each day from the peanut dose. You (and your parents) will need to complete a brief daily diary to confirm that doses are given and any problems experienced.

**What will happen to me during the study?**

Following consent (and agreement from you), there are 3 main stages to the study:

**Stage 1**: **Screening to assess eligibility and initial allergy tests**:

Allergy screening (2-4 hrs), including a full history and clinical examination, Lung Function testing, Skin Prick Tests and a test to see if you can tolerate soy. We will also ask you and your parents to complete a questionnaire assessing the impact your allergy has on quality of life. This will be repeated at 3, 6, 12, and 14 months.

**A food challenge test to roasted peanut** (see “tests” below), which will take place over 2 separate visits (5-6 hrs each). This test is to prove you still have a peanut allergy and determine how much peanut they need to eat to cause symptoms.

**A single visit for a food challenge re-test tolerance** to the starting dose of the peanut therapy. This visit will take 2-3 hours. Only if you are able to tolerate at least 10mg of peanut (around 1/12th of a peanut) can you start the therapy.

If you can, we will then find out if you start the OIT immediately (**active group**) or have been randomly selected (by a computer generated code) to the **control group**. The control group will continue with normal peanut avoidance and will have an opportunity to commence the treatment at the end of the current study period of 58 weeks.

Neither you, your parents nor the research team can choose which group you will be in. For every 4 children in the active groups there will be 1 child in control group.

**The active group** will be divided into two further groups. Both will take peanut therapy each day. One group (half of the active group) will be randomly assigned the CSIRO fibre supplement (HAMSB) and the other group will take an identically appearing starch (called a placebo) each day – thus, you have a 4 in 5 chance of starting the active treatment immediately and a 2 in 5 chance of being assigned the peanut and HAMSB . Neither you, your parent nor the research team will know which fibre supplement you are receiving. Only the statistician and the clinical trials pharmacist will know this until the end of the study.

**Stage 2**. If you are in the active group (Group A or B) you will take the daily fibre supplement (or placebo fibre supplement) and take a daily dose of peanut. Every 2-3 weeks you will return to the Allergy Research Unit to have your dose of peanut increased under observation. You should not eat any other peanut during this time, apart from the peanut OIT doses.

If you have been randomly allocated to the **control group**- you will continue to avoid peanut for the duration of the study, and will be retested for peanut allergy at 58 weeks. We will regularly call to see how you are going, and if you have had any accidental ingestion of peanut and, if so, if this caused an allergic reaction. At this stage you will have the opportunity to start the active therapy with the peanut and HAMSB for a 12 month period.

**You will be provided with full dietary advice**; an allergy management plan; and a kit containing medicines to use in the event of an allergic reaction, and how/when to use them. All families will have access to a 24 hour advice line staffed by the research team. On the visits to the hospital you will also be given tailored anaphylaxis education to meet your, and your parents’, needs.

**Stage 3.** After 1 year, everyone in the active groups will stop eating peanut and the fibre supplement for 6 weeks. All participating children and teenagers- (ACTIVE and CONTROL groups) will then be invited back for a further peanut challenge which will be conducted in the same way as the two peanut challenges at the start of the study. By comparing the three groups, this will tell us how effective the therapy has been. The therapy may not work in some children and teenagers – if this is the case, you will need to stop the treatment and avoid all peanut in the future.

Children and teenagers who:

• pass this challenge will be able to reduce their peanut doses to once weekly.

• have an allergic reaction will recommence daily peanut doses, and will undergo a second ‘tolerance check’ at 24 months.

Children and teenagers in the control group will be offered the opportunity to start the immunotherapy for 12 months, following the same protocol as described above. At the end of the study, you will be offered the opportunity for a further tolerance check, prior to being re-integrated into the routine allergy clinic at Children’s Hospital Westmead.

**What allergy tests will I have?**

A summary table of all the study visits and tests can be found at the end of this document.

**Skin Prick Tests** (SPT) are routine in allergy clinics - you have probably had one before. A small drop of food extract is placed on the skin (usually the forearm) and a small prick is made in the skin, through the drop. Most children do not find SPT to be painful, and describe it as “being pressed with a sharp pencil”. If allergic, an itchy lump or “hive” will form at the site of the test after 10-15 minutes. The skin tests will be repeated at 3, 6, 12, and 14 months later.

**Peanut Challenge**: In order to prove you have peanut allergy (and determine how much peanut is needed to cause symptoms), we will perform a “**double-blind placebo-controlled” food challenge** at the start and end of the 12 month OIT period. Each challenge consists of two visits, one week apart – one visit we will use peanut, the other a placebo (or ‘dummy food’). To prepare for the challenge you must not have taken any antihistamines for at least 72 hours prior to the day.

We will give you small but increasing doses of peanut or placebo every 30 minutes, until you develop symptoms of an allergic reaction (or reach the final dose). Any symptoms are generally mild and respond readily to treatment. We will carefully monitor you, measuring heart rate and blood pressure. Neither you nor the medical team will know on which day you are eating peanut or placebo, so that no-one can influence the result of the test. The challenge will take several hours, so be prepared to spend most of the day at the hospital.

**For the double-blind challenges**, we will insert a short plastic tube (called a cannula) into a vein, to allow us to take blood samples and give medicines in the event of a serious reaction. The maximum amount of blood taken on any one day will be 50mls (about 10 teaspoons). Blood will be collected during the challenge at the start of the study, for all children and teenagers, and at 3,6 and 12 and 14 months after starting OIT. We’ll use these samples to help us understand how the therapy works, and predict those children and teenagers in whom the therapy might be more successful.

We will also ask you to collect your stool at the first food challenge, after taking the fibre supplement for 2 weeks (if you are in the peanut oral immunotherapy groups), 6 months, 12 months and at the last food challenge 14 months after starting the study. We will provide you with a special kit with instructions on how to do this.

During the study we will collect urine samples at 4 different times from girls who have started their period. This will be used for a **pregnancy test**. It is a way to make sure that it is safe for their body to take treatments or have investigations that may affect an unborn child (such as possible anaphylaxis in food challenges). It is standard in any study involving females who may be able to fall pregnant.

**Are there any benefits for me participating in the study?**

We hope that using fibre with the peanut immunotherapy will increase the amount of roasted peanut that you are able to eat without having an allergic reaction, and without needing to take a daily dose of peanut after the therapy finishes. Ultimately our aim is to reduce the risk of you having an allergic reaction to peanut due to accidental exposure, and to treat the peanut allergy without you needing to take a daily peanut dose to remind the body to be tolerant to peanut. We hope results from this study will help us understand more about food allergy.

**Are there any side-effects and risks associated with this study?**

During the food challenges, you will eat peanut which we expect to cause an allergic reaction: this will generally be mild (e.g. itchy rash or hives, tummy pains). We will give you an antihistamine to relieve these symptoms. You may experience more significant symptoms (such as cough, wheezing) consistent with anaphylaxis - this has been reported to occur in up to half of reactions at food challenges in previous, similar studies. If this happens, we will give you an injection of adrenaline into the leg muscle. Safety is our primary concern, so the study will happen on a Paediatric Allergy Research Unit under the supervision of a Consultant in Paediatric Allergy.

Allergic reactions can also happen at home following a peanut dose - this is why all increases in the peanut dose will happen in hospital Research unit. At the beginning of the study, we will check that you know how to spot these symptoms and manage them safely. We will provide regular anaphylaxis education tailored to your needs when you come to hospital. You and you parents will be able to contact the research team 24 hours per day to get advice in the event of a reaction. This risk is greater if you miss a dose of OIT. If you develop a cough/cold or become unwell, you need to let us know as we may have to adjust the OIT dose.

The OIT may not work in all children and teenagers. If necessary, we may need to withdraw you from the study, in which case you should continue to avoid ALL peanut. Ongoing clinical care in the routine allergy clinic at Children’s Hospital at Westmead will be offered.

To minimize discomfort during blood tests which are not taken from the small plastic tube (cannula), we shall offer local anaesthetic cream or numbing spray (“cold spray”).We will need to collect 50mls of blood (around 10 teaspoons) from a vein in your arm. This can be painful and bruising can occur. The dietary supplements used in this study have been used by the CSIRO in 5 other clinical trials. There is no suggestion or evidence that these supplements are unsafe. In studies to date there have not been any issues with abdominal (tummy) pain, diarrhoea or bloating with using these fibre supplements. They are designed to feed the healthy bacteria already living in the gut and to release a naturally occurring chemical called butyrate, which is a product made naturally by the bacteria that live in the lower gut.

**What if I change my mind about the study?**

Participation in this project is voluntary and if you decide not to take part or decide to withdraw at any time. This will not otherwise affect your care at the Hospital.

**What if new information becomes available?**

Sometimes during the course of a research project, new information becomes available about the study. If this happens, your research doctor will tell you about it and discuss whether you should continue in the study. If you decide to withdraw, or the research team consider it to be in your best interests to be withdrawn from the study, then we will make arrangements for your care to continue. If you decide you can continue in the study you may be asked to sign an updated consent form.

**Will my taking part in this study be kept confidential?**

All information collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the hospital will have your name and address removed so that you cannot be recognised from it. With your permission, we will notify your GP of your participation in the study.

The clinical information you provide, and the blood tests results will be kept anonymous to persons other than the CHW researchers. Data may be published in medical journals and/or at medical conferences, but only anonymous group data will be reported. Your parents will be provided with your results and will be notified of any study related publications. The data will be securely kept for at least 15 years as required by NSW and Federal Law, and then destroyed according to hospital guidelines.

**What will happen to the results of the research study?**

The results of this study will be used to develop new therapies for food allergy. They may be published in a scientific journal and presented at scientific medical conferences. You will not be identified in any report or publication.

**What if something goes wrong?**

The Sydney Children’s Hospital’s Network holds insurance policies which apply to this study. If you experience harm or injury as a result of taking part in this study, you will be eligible to claim compensation without having to prove fault. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Chief Investigator, Professor Dianne Campbell or the SCHN human ethics office (contact details are at the top of the first page of this form).

**Who is organising and funding the research?**

The study sponsor is Sydney Children’s Hospital’s Network and the study is funded by a grant from the National Medical Research Council of Australia (NHMRC).

**Other information**

If you have any concerns about the conduct of this study please do not hesitate to discuss them with Professor Dianne Campbell or Dr Melanie Wong (T 02 9845 3420) or with the research ethics manager (98453066), secretary of the Ethics Committee that has approved this project and quote HREC/16/SCHN/372.

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Visit | Study week | Duration of OIT dose at visit | Informed consent | Assessment/Procedure | | | | | | | | | | | | | | | | | |
|  | Anaphylaxis education | Demographic  information | Randomisation | Stool sample | Blood collection | Peak flow | Spirometry | Clinical assessment | Open soy challenge | DBPCFC Food challenge | Initial peanut OIT | Updosing peanut OIT | Commence supplement  supplement | Cease all intervention | Iv cannula | Skin prick test | Pregnancy test | QOL questionnaire | |
| Screening | -1 |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | |
| V1 (DBPCFC1) | 0 |  |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | |
| V2(DBPCFC2) randomisation | 1 |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | |
| V3 commence OIT (step 1) | 3 | 0 |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  |  |  |  | |
| V4 (step 2) | 5 | 2 |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  |  |  | |
| V5 (step 3) | 7 | 4 |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  |  |  | |
| V6 (step 4) | 9 | 6 |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  |  |  | |
| V7 (step 5) | 11 | 8 |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  |  |  | |
| V8 (step 6) | 13 | 10 |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  |  |  | |
| V9 (step 7)  3 months OIT | 15 | 12 |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | |
| V10 (step 8) | 17 | 14 |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  |  |  | |
| V11 (step 9) | 19 | 16 |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  |  |  | |
| V12 (step 10) | 21 | 18 |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  |  |  | |
| V13 (step 11) | 23 | 20 |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  |  |  | |
| V14 (step 12) | 25 | 22 |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  |  |  | |
| V15 (step 13) | 27 | 24 |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  |  |  | |
| V16 (step 14)  6 months OIT | 29 | 26 |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | |
| V17 (step 15)  9 months OIT | 41 | 38 |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | |
| V18  12 months OIT | 55 | 52 |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | |
| V19 (DBPCFC1) | 61 |  |  |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | |
| V20 (DBPCFC2) | 61 |  |  |  |  |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | |
| V21 end study | 62 |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png |  |  |  |  |  |  |  |  |  | C:\Users\Michelc5\AppData\Local\Microsoft\Windows\INetCache\IE\GBESNQW9\Tick-green[1].png | |

**Timetable for OPIA trial**