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PARTICIPANT INFORMATION SHEET – Group 1

Investigating the human biology of resident immunity in tissue via neoantigen challenge (INHABIT)

We'd like to invite you to take part in our research study. Before you decide, it is important that you understand why the research is being done and what it would involve for you. Please take time to read this information, and discuss it with others if you wish. If there is anything that is not clear, or if you would like more information, please ask us.

First, we want to introduce you to the study and key facts. Then we will go through the study in more detail. There will be time for you to ask us any questions, and to discuss your participation with friends, relatives, and you General Practitioner (GP), if you wish. **Taking part in this study is entirely your choice.**

Could I be eligible to take part?	
✓ You must	✗ You must not
Be aged 18-45 years old	Have any significant medical conditions
Be in good health	Be a current smoker, including vaping
Be willing to travel to our research facility in Oxford for a screening visit, and seven study visits over 91 days	

If you decide to join our study:

1. You will be given injections of keyhole limpet haemocyanin (KLH; trade name: Immucothel) into the muscle or skin, on four occasions, with or without a medicine ('adjuvant') which helps the immune response (Montanide ISA-51). All these products are used clinically and are manufactured to the standard of medicines.

2. You will have to attend a screening visit, where we will ask questions about your health, perform a physical examination, and take a blood sample. If you are eligible based on the screening assessment and decide to take part, you will have to attend the research facility a further 7 occasions over 91 days, for about 30 minutes to one hour per visit.

3. You will be closely monitored by the study team with a range of tests and procedures, including questionnaires, physical examinations, and blood tests.

4. On four of the visits (visits 1, 3, 5, and 7) we will take a tiny sample of skin (punch skin biopsy) from your forearm (four samples total), using local anaesthetic.

5. You will be free to withdraw from the study at any time you wish.

Contents

1. Introduction

The immune system is the body's defence system that protects from infections and illnesses. Faulty regulation of the immune system contributes to multiple diseases including inflammatory arthritis, cardiovascular disease, and cancer, and therefore represents a leading cause of disability and death worldwide. Whilst there have been revolutionary advances in our understanding of how to use drugs to treat abnormal immune responses, there remains huge unmet need for new, better medicines. Unfortunately, as many as 9 in every 10 promising drugs studied in humans ultimately do not succeed in becoming clinical treatments. A significant cause of failure is when information gained in the laboratory or in animal studies does not hold true when the drug is given to humans.

2. Why are we doing this study?

One approach to improve the efficiency of the drug development process is the use of human 'immune challenge' studies. In these studies, healthy volunteers are given small amounts of substances which are foreign to their immune system to provoke a temporary response: the 'challenge'. Depending on the nature and dose of the challenge, the body's immune system will react in a different but predictable way, elements of which mimic those seen in disease, thereby 'modelling' them. These models can help safely bridge the gap between animal experiments and people with disease, allowing us to test the effect of new drugs safely without exposing patients to risk. Sadly, whilst immune challenge models have been used in drug development for many years, this has been done in an unstructured manner, which greatly limits the usefulness of the approach.

The purpose of this research is to better understand, improve, and standardise a common method of immune challenge which uses a protein called 'Keyhole Limpet Haemocyanin' (KLH). KLH is available as a highly purified formulation, and because it is not usually encountered by the human immune system (it is derived from an inedible shellfish), it allows us to study the development of immune responses right from the time it is administered. We plan to give different groups of healthy volunteers KLH with an 'immune-boosting' agent (Montanide ISA™51, commonly referred to as an adjuvant), before measuring and comparing their response. We will then re-challenge all volunteers one, two, and three months later with a specific dose of KLH in the skin on their forearms. This is similar to an allergy test, where we will take images, blood samples and skin biopsies to understand the nature, time course, and variability of the immune response in each individual. The results will help us to characterise responses to repeated KLH challenge over time, which could be used to model better different diseases and test drugs with. In turn, this will allow earlier and better evaluation of new therapeutics.

3. Why have I been invited?

You have been invited because you are aged 18—45 years old (inclusive), are healthy, take no regular medications affecting the immune system and have mark-

free forearms (no skin damage, tattoos or scars on the hairless part of either arm). If you tell us you are healthy, don't take any regular medications and don't smoke, then you can participate.

4. Are there any advantages to taking part?

You will not gain any direct benefit from the study. We hope that the information we gather from this and future studies will help us to develop new treatments for diseases caused by, or affecting the immune system.

5. Do I have to take part?

- No, taking part is entirely your choice.
- You can withdraw at any time without giving a reason, without your legal rights being affected.

6. Can I take part?

To take part in the study, ALL of the following must apply to you:

- Be willing and able to give informed consent for participation in the study and able to comply with the study protocol.
- Be aged 18—45 years of age inclusive, at the time of signing the informed consent.
- Be healthy, based on a detailed medical history and a complete physical examination including vital signs and laboratory measurements.
- Have a body weight greater >= 50 kg, and body mass index (BMI) within the range 18 to 30 kilogram/meter squared (inclusive).
- If female, be of non-childbearing potential or if female and of childbearing potential not be pregnant (negative pregnancy test on the day of both screening and vaccination) and willing to use effective methods of contraception to prevent pregnancy from the time of first dose to 60 days afterwards. This should include two methods of contraception simultaneously (e.g. condoms and the oral contraceptive pill).
- If male and with a female partner of childbearing potential, agree to use effective methods of contraception from the time of the first dose of challenge agent to 60 days afterwards.
- Have sufficient English language ability to enable appropriate informed consent procedures to be conducted in English.

You CANNOT participate if any of the below exclusion criteria apply to you:

- Have had antibiotics or antiviral therapy after a serious illness within 30 days of study entry.
- Have any use of immunosuppressant or immunomodulatory agents (systemic or topical) in 3 months prior to study entry, including anti-coagulant or anti-platelet drugs.

- Have chronic medical conditions with potential effect on immune responses including diabetes, significant history of atopy, or any condition that, in the opinion of the investigator, would interfere with the study.
- Have any tattoos, moles or other skin abnormalities such as overgrown scars, called keloids (or history of keloids) that may, in the opinion of the investigator, interfere with study assessments or increase the risk of an adverse outcome from study procedures (e.g. skin biopsy healing).
- Pregnant or breastfeeding (lactating), where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive hCG laboratory test
- Have an allergy to KLH, Montanide ISA-51, related vaccine adjuvants, or components of the study challenge agents.
- Have an allergy to shellfish.
- Have resided in or have significant previous travel to areas endemic for schistosomiasis (due to potential cross-reactive immune responses to KLH).
- Have previous exposure to Keyhole Limpet Haemocyanin, e.g. in the context of a previous study, except for existing KLH-exposed participants who have been recalled for optional KLH rechallenge in the skin.
- Participate, within 60 days of screening, in recreational sun-bathing, or use of sun-bed, on the area of the skin from wrist to shoulder inclusive.
- Have a phobia of needles or minor surgical procedures.
- Are a current smoker (including vaping) or using nicotine replacement therapy.
- Have received any vaccinations within 30 days prior to screening visit, or will require vaccination prior to the end of study follow-up.
- Have any other significant disease, disorder, or finding, which, in the opinion of the investigator, may either put you at risk, affect your ability to participate in the study or impair interpretation of the study data.

7. Lifestyle restrictions during study

During the study, we will ask that you abstain from certain lifestyle activities, in case these affect the study results.

7.1. Caffeine, Alcohol, and Tobacco

- Participants will abstain from ingesting caffeine- or xanthine-containing products (e.g. tea, coffee, cola drinks, and chocolate) for 12 hours prior to each scheduled study visit, until the final immunological study assessment for that visit (i.e. tea / coffee etc. is permitted during a study visit once immunological assessments have taken place)
- Participants will abstain from alcohol for 24 hours before each study visit until discharge from the study facility for that visit.

- Participants will not be permitted to use nicotine containing products from 30 days prior to first visit until the final follow-up visit.

7.2. Activity

- Participants will not be permitted to use sun-beds from 60 days prior to screening until the final follow-up visit.
- Participants will be advised to avoid excessive sun exposure from screening through to final study visit, including recreational sunbathing.
- Participants will abstain from strenuous exercise (e.g., contact sports, weightlifting, or any other moderate/high intensity exercise) for 24h prior to and after each study visit. Participants may participate in light recreational activities during this time (e.g. mild intensity exercise for 30 minutes or less).

8. What will happen to me if I decide to take part?

We will assign you to a study group. You will receive an intramuscular (IM) injection of KLH with an adjuvant (Montanide ISA-51), into the deltoid muscle of the shoulder on day 0 of the study (see Table 1). You will be given 3 injections of KLH into the skin ('intradermal', ID) of the forearms, on 3 visits, over the course of 3 months in total. You will attend 7 study visits in total.

Table 1: Study Part A Group 1 treatment

Group	IM dose KLH 1000 mcg plus Montanide ISA-51	ID dose KLH 10 mcg
1	Day 0	Days 28, 56, 84

8.1. Pre-screening

If you are interested in the study we will ask you to complete a pre-screening questionnaire online – we will send you the link to this, or direct you to our website where the questionnaire can be accessed. The questionnaire should take about 10 minutes to complete. Prior to completing the questionnaire, we will ask you to ensure you have carefully read this information sheet. A link to this information sheet will be available at the top of the pre-screening questionnaire. The pre-screening questionnaire covers key criteria for participation in the study, your contact details, and medical history (including medications). As part of completing this pre-screening questionnaire you will be asked to indicate your consent (via electronic signature) to allow us to collect this data. If you are deemed ineligible based on any of the replies you give to the major inclusions and exclusions in the pre-screening questionnaire, the questionnaire will stop at this point and consent for personal identifiable data and medical history will not be collected. Personal data of individuals who complete the pre-screening

questionnaire, but do not enrol in the study, will be deleted. Non-identifying data (e.g., screening outcome, reason for non-participation where given) will be retained and aggregated for recruitment monitoring and Consolidated Standards of Reporting Trials (CONSORT) reporting.

If you are unable to complete the questionnaire online, you can communicate directly with the study team by phone or email and we can complete the questionnaire on your behalf. If you indicate that you agree to take part in the study over the phone, you will be asked to provide your written consent at the screening visit.

8.2. Screening phase

If you are eligible, and if you decide that you would like to proceed, a member of the study team will arrange a visit to the research facility for a physical examination, and blood tests. Face to face visits will take place at the Experimental Medicine Clinical Research Facility (EMCRF), based at the Churchill Hospital site, run by the University of Oxford. We will explain where you need to go before your visit.

Upon arrival you will have the opportunity to ask any further questions and, once you are happy that you fully understand what the study involves and before anything else takes place, the study doctor will ask you to sign a consent form. You will be given a copy of the consent form to take away and keep.

The study doctor will then go through a few administrative questions as well as detailed questions about your health. This will be followed by a physical examination and blood tests to see if you are suitable for this study (see more details below). You should allow approximately 1 hour for this first screening visit, and it will occur up to 90 days prior to enrolment in the study. You will receive financial compensation for this visit. We will ask to see some form of ID, such a driver's licence or passport.

<u>TOPS registration</u>

Healthy volunteers must not take part too often in trials of new medicines and other scientific studies (such as this one), for scientific, medical, and ethical reasons (i) if the gap between two studies is too short, or the studies overlap, the medicines might interact, (ii) taking too many blood samples could cause anaemia, (iii) it's unethical to expose healthy people too often to medicines they don't need.

So, to help research units, the Health Research Authority keep a database of healthy volunteers and when they take part in studies – this is called TOPS. We will enter into the database your National Insurance Number (if you're a UK citizen), or your passport number and country of origin (if you're not a UK citizen), and the date of your last dose of study medicine. We will ask you to indicate your consent for us to enter this personal identifiable information into the TOPS database when you sign the consent form for taking part in this study. If you withdraw from the study

before you receive any study medicine, the database will show that you never received a dose.

Medical examination and clinical observations

Medical examination of your skin, chest, abdomen, mouth and the lymph glands in your upper body will be performed. Your blood pressure, heart rate, and temperature will be recorded. We will record your weight and height. Additionally, for women of childbearing potential, a urine pregnancy test will be performed.

Questions on contraception use and menstrual cycle

As part of this study, we are interested in understanding whether biological sex and the use of different types of contraception influence immune responses.

If you were assigned female at birth, we will ask you some questions about your menstrual cycle and your contraceptive use. This will include the date of your most recent menstrual period and what form of contraception you are currently taking, such as the oral contraceptive pill, an intrauterine device (IUD), implant, injection, patch, or ring), and for how long you have been taking it. We will ask you to update this information at each study visit, as changes over time may be important for interpreting the study results. All information you provide will be kept confidential and handled in accordance with data protection regulations.

Blood tests

To check that you are suitable for the study and that it is safe to take part, we will take blood to test for anaemia (low red blood cells), problems with your immune system, kidney function, and prediabetes/diabetes. These tests will be performed by Oxford University Hospitals NHS Foundation Trust, and will be linked to your NHS record (so will be visible to other healthcare professionals, such as your GP). We will take approximately 10mL (two teaspoons) of blood for these tests. In addition, we will do a test to determine your ‘HLA type’ which is a genetically determined (inherited) characteristic which can influence an individual’s immune response.

What happens if any of the tests are abnormal?

Sometimes test results are outside the usual ranges for healthy individuals. Depending on the results, you may not be eligible for the study, and you may be advised to contact your GP for further tests or review. In some cases, the study doctor may simply recommend that the blood tests be rechecked on a later date, before deciding on eligibility. You will be compensated for this additional blood test on a pro-rata basis.

Optional consent for further blood donation

At this visit you will be asked whether you would be happy to be contacted in the future to give further blood samples once the study is over (i.e. after the final study visit), to better understand how the immune response to KLH changes over a longer period of time (up to 5 years). This is optional and does not oblige you to give a blood donation when contacted. If you do provide further blood donations, we will take up to 50mL of blood (approximately 3 tablespoons) per visit, and a maximum of 400mL (approximately two cups) in any 3 month period (similar to the limit used by the NHS blood and transplant service for regular blood donors). You will be compensated for the time and inconvenience of providing these additional blood samples. You will also be asked if you would be happy to be contacted in the future (up to 5 years) to undergo additional intradermal rechallenges in the skin (up to three total), that would be biopsied between 1 and 28 days later. On both visits, we would also take up to 33mL of blood (about 2 tablespoons). All additional rechallenges and blood donations are optional and do not affect your participation in the current study. If you agree to be contacted to provide a blood donation in the future for research related to this study, you will be compensated £20 to attend an appointment and provide this sample. If you agree to be contacted to undergo skin rechallenge and follow-up (within 5 years of joining the original study), you will be compensated £100 to attend both appointments and provide the samples.

What happens if I decide not to take part at this stage?

There is nothing else you need to do—taking part is entirely your choice. We may ask if you are willing to be contacted in the future to see if you are interested in taking part in any future studies—this is also optional.

8.3. Study Group 1

If you consent to take part in the study, you will be allocated to a group and invited to attend 7 further in-person visits. Figure 1 shows the visits you will need to attend if you join the study. The details of these visits are described below.

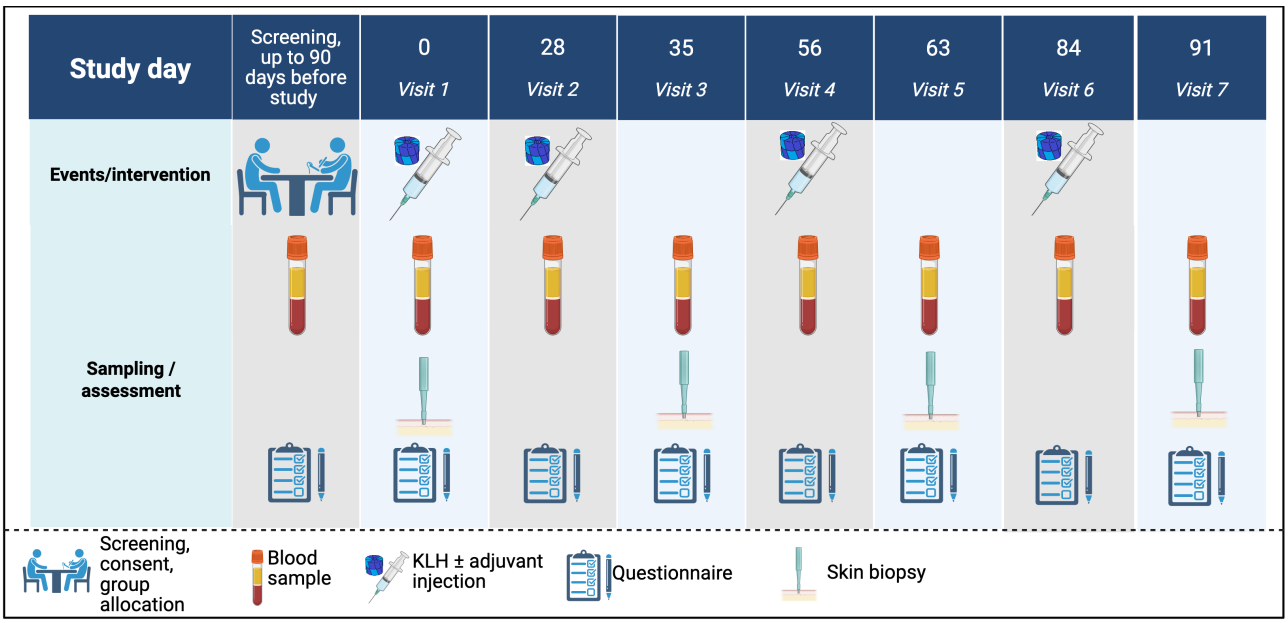

Figure 1 Timeline of study procedures

8.4. Study visit 1 (day 0)

When you arrive at the study site, we will ask you questions to confirm you are still healthy and suitable for the study. Your blood pressure, heart rate, and temperature will be recorded. For women of childbearing potential a urine pregnancy test will be performed. **This visit will take approximately one and a half hours.**

Blood tests

We will take blood samples to measure the status of your immune system, as a baseline prior to the first injection of the challenge agent. We will also do a test for evidence of a previous viral infection with cytomegalovirus, which very commonly infects people as children or in early adulthood, as this virus may affect the immune response to KLH, or provide additional insight into the way your immune system reacts to infection/inflammation. The total volume of blood taken on this occasion will be approximately 58mL (about 4 tablespoons).

Skin biopsy

We will take a sample of skin (a skin biopsy) to measure the immune cell types present there, using a special device called a punch biopsy, on your forearm (Figure 2). To take the biopsy we will clean the skin with antiseptic, and then give an injection of local anaesthetic to minimise discomfort. The punch biopsy takes a tiny circular amount of skin (4-6mm in diameter, about the size of 2-3 grains of rice side by side). We will then close the skin with either an absorbable or a non-absorbable stitch. We will then put a dressing over these biopsy sites, which can be left on until it falls off, or removed carefully after 48h. After the biopsy you will be asked to keep the area dry for 48h, then you can bathe/swim normally. If a non-absorbable stitch was used, you will be asked to attend an additional 15-minute visit, 10-14 days

following your biopsy, for a nurse to remove your stitch for you. If an absorbable stitch has been used, this will dissolve and fall out on its own in about 10 days. We will provide, and go through with you, a manual that will outline how to care for your biopsy.

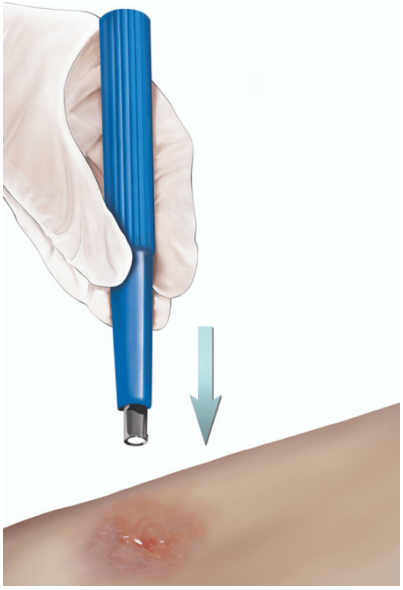

Figure 2 Skin punch biopsy procedure

From https://www.healthdirect.gov.au/surgery/punch-biopsy-of-a-skin-lesion

KLH administration

We will give you an injection into the deltoid muscle of the arm (see Figure 3) with KLH with an adjuvant.

Figure 3 Site of first study injection

After the injection, we will ask you to wait at the study site for 20 minutes, to check you do not have a reaction to the injection (this is very unlikely).

8.5. Study visits 2, 4, 6 (days 28, 56, 84)

On days 28, 56, and 84 you will attend the study site. ***These visits will take approximately 30 minutes***. We will ask questions about your current health and any possible reactions to the study agents. If necessary, we will do a brief physical examination or check your vital signs. We will take a blood sample to measure the immune response to KLH. On these visits we will take approximately 35 mL (about 2.5 tablespoons) of blood.

KLH re-challenge

On each of days 28, 56, and 84 of the study we will give you 1 small injection of KLH into the skin of the forearms, as shown Figure 4 (3 skin injections in total for the study). We will ask you to stay at the study site for a minimum of 20 minutes after the injections, to check you do not have a reaction to them. Around 2 days after the first KLH rechallenge in the skin (day 30), we will send you a link by email to a secure online questionnaire to ask you some questions about the rechallenge sites, and to upload a picture of the injected sites, to check for a positive immune response (redness, thickening of the skin). We will provide a paper ruler to place next to the injection sites on your forearm.

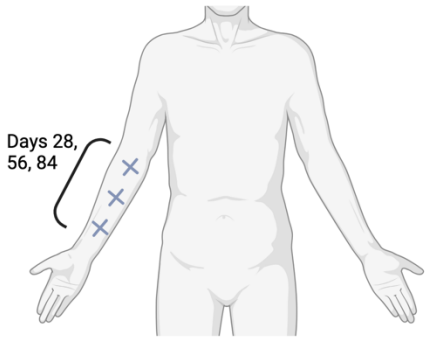

Figure 4: Sites of KLH re-challenge injections

8.6. Study visits 3, 5, 7 (days 35, 63, and 91)

On days 35, 63, and 91 we will perform the physical assessments also performed on visits 2, 4, and 6. ***These visits will each take approximately one hour.*** In addition, we will take a skin punch biopsy of the same place where KLH was injected 7 days previously (on days 28, 56, and 84). On these visits we will take approximately 35 mL (about 2.5 tablespoons) of blood.

Participant experience questionnaire

On your final visit (visit 7, day 91) We will ask you about your experience in the study to date, e.g. how you found the study procedures, and whether you would volunteer for similar studies in the future, based on your experience in this study.

End of the study

The study follow-up will end at the day 91 visit. You will have contact details for the study team in case there are any problems after this, such as any concern around the healing of the punch biopsy sites (this is very unlikely).

8.7. Flexibility for visits 4/5, and 6/7

Due to the extended nature of the study (91 days, or ~3 months), we anticipate that it may not be possible to attend the study visits on the exact study days set out above. Each rechallenge must have a 7-day follow-up at which we will take a skin punch biopsy and blood – that is, each of visits 3, 5, and 7 must occur 7 days after visits 2, 4, and 6, respectively). However, we will allow a flexibility window of 25 days to 3 months between each rechallenge visit (that is, between visits 2 & 4, and 4 & 6), to accommodate your availability. Following your consent to the study, we will agree on a set of study visit dates that works with your schedule.

9. What are my responsibilities?

It is important to consider whether you can commit to coming for all study visits, as far as possible.

If you take part in the study we will ask you to avoid the following activities, within 3 days of primary and re-challenge KLH doses:

- Sunbathing and use of sunbeds
- Contact sports, weight lifting, and any other moderate/high intensity exercise lasting >30 minutes
- Consumption of more than 3 units of alcohol per day
- Smoking of tobacco or cannabis, or use of vapes
- Consumption of non-steroidal anti-inflammatory drugs and antihistamines
- Use of topical creams, ointments, or gels containing corticosteroids or non-steroidal anti-inflammatory drugs.

Following the skin biopsy you will need to take care to not disturb the skin too much until the skin is healed.

You should not donate blood within 3 months of the study, as the total amount of blood donated during this study is similar to that of a standard blood donation.

Women of childbearing potential

For female participants, we consider you to be of childbearing potential unless you have had previous surgical sterilisation (e.g. hysterectomy, bilateral salpingectomy, bilateral oophorectomy). Female participants of childbearing potential are required to use a **two** effective forms of contraception from the day of first administration of KLH until 60 days after the last administration of KLH. Acceptable forms of contraception for participants of childbearing potential include:

- Established use of oral, injected or implanted hormonal methods of contraception
- Placement of an intrauterine device (IUD) or intrauterine system (IUS)
- Barrier methods of contraception (condom or occlusive cap with spermicide).
- Male sterilisation, if the vasectomised partner is the sole partner of for the subject.
- True abstinence (defined as refraining from heterosexual intercourse) when this is in line with the preferred and usual lifestyle of the subject. Periodic abstinence and withdrawal are not acceptable methods of contraception.

If you become pregnant during the study, we will ask you to inform your healthcare practitioner of your involvement with the study at the time of your booking visit. We would not anticipate any adverse effects from KLH exposure during pregnancy. However, if you do become pregnant at any point during the study, you will be withdrawn from the study.

10. Are there any possible disadvantages or risks from taking part?

The disadvantages of taking part relate to the inconvenience of attending for study visits, and the small risk of adverse effects of the study procedures. You should consider the following risks before agreeing to take part:

10.1. Potential risks of the challenge agents

Keyhole Limpet Haemocyanin (Immucothel)

KLH is a highly purified protein obtained from the blood of an inedible shellfish. It has been used for over 50 years for challenge studies similar to ours, at doses up to 5 times greater than those used in our study. The specific product we are using (Immucothel) is a registered medicine in some countries.

Expected common (more than 1 in 10 risk) adverse effects are limited to mild responses at the injection site e.g. pain, redness, warmth, swelling, tenderness or itching. Other potential (less than 1 in 10 risk) foreseeable risks would be similar to those seen with standard vaccinations, including mild systemic reactions e.g. flu-like illness with feverishness, fatigue, malaise, arthralgia, sore muscles and headache. In almost all cases we would expect these to last no more than a few days. In very rare cases (less than 10,000 risk), local reactions could be more severe. If this were to occur we would not give any further injections and would withdraw you from the study, while also providing any appropriate medical care that you might need, or referring you to your GP or other NHS service as required.

There are some very rare but serious adverse effects that can occur with commonly used vaccinations. Although KLH is not a vaccine, it is similar to a vaccine in that it is foreign to the body and provokes an immune response, and it is therefore reasonable to expect a similar potential for these adverse effects. These include severe allergy (anaphylaxis) and problems with nerves such as Guillain-Barre Syndrome. The risk of these is extremely low (1 to 2 in a million risk).

Montanide ISA-51

Montanide ISA-51 is a mineral oil-based adjuvant, extensively studied for enhancing vaccine responses. Montanide ISA-51 can cause transient local skin reactions, including swelling, redness, pain, and itch (approximately 1 in 10 risk). Occasionally (less than 1 in 100 risk) Montanide ISA-51 has been associated with systemic effects such as fatigue, and fever, which would be expected to disappear in no more than a day or two. In rare situations (less than 1 in 1000 risk), more severe local reactions have been observed. These side effects were not reported in the two previous studies which combined KLH with Montanide ISA-51 at the same doses used in this study, thus the risk of these more severe side effects is considered to be low (less than 1 in 1000 risk).

10.2. Potential risks of tests performed as part of the study

To minimise the risk of problems, all study procedures will be performed by experienced professionals using appropriate precautions and equipment.

Blood donation

If you take part in the study and complete all follow-up the total amount of blood taken will be about 268mL, which is under 2/3rd of a standard blood donation. As such it would not be expected to cause problems for an otherwise healthy volunteer. The blood donation itself requires the use of a needle into a vein of the arm, and this can cause minor bruising and tenderness in around 1 in 10 people, and occasionally feeling faint or actually fainting (in around 1 in 20 to 1 in 100 people). We will provide food and water following blood donation. Very rarely, in less than 1 in 10,000 people, sites of blood tests can become infected and require antibiotic treatment (we will provide these, unless you require treatment outside of normal working hours, at which point we would direct you to normal NHS services). The blood tests will be taken by experienced members of the study team which should minimize the risks of side effects.

Intramuscular injection

Intramuscular injection is a commonly performed procedure for the administration of medicines, including vaccines. The potential risks commonly include (1 in 10 risk) minor discomfort on injection, minor bruising, tenderness, and occasionally feeling faint or actually fainting (1 in 20 to 1 in 100 people). There can also be discomfort

for a few days afterwards due to bruising related to the injection, and due to the body's response to the KLH + adjuvant injection. Very rarely sites of injections can become infected and require antibiotic treatment (less than 1 in 10,000 risk). The injections will be performed by experienced members of the study team which should minimize the risks of side effects.

Intradermal injection

The risks of intradermal injection are similar to those of intramuscular injection. Intradermal injections can cause stinging at the time of injection. There can also be discomfort, redness, and itching for a few days afterwards. Very rarely (in less than 1 in 10,000 people) a small sore can form at the time of injection which can take longer to heal or cause scarring.

Skin punch biopsy

Skin punch biopsy is a commonly performed diagnostic procedure. The potential risks (1 in 10 people) include minor bruising, bleeding, and skin discomfort. A 4-6mm punch biopsy will be performed using local anaesthetic to reduce discomfort. The injection of anaesthetic can cause stinging during injection which fades quickly as the anaesthetic takes effect. It is common (in at least 1 in 10) for a small scar or persistent skin discoloration to be visible once the skin has healed—this usually fades over time but may be permanent. In rare cases (less than 1 in 1000), certain individuals can develop more prominent scars (called keloids). We will exclude people from the study who are known to have developed keloids previously, or have a family history of this, because we know this increases the risk of keloids. There is a small risk (1 in 50) of infection following skin biopsy—this is minimised by use of skin antiseptic at the time of biopsy, and careful technique of the doctor performing the biopsy.

11. Will my General Practitioner (GP) be informed of my participation?

If we incidentally find an issue during the study that may be important for your health (e.g. high blood pressure, blood test abnormalities), we will inform your GP, or ask you to contact them, to ensure appropriate follow-up can be arranged.

12. Will my taking part in the study be kept confidential?

Information about participants will be kept confidential and managed in accordance with applicable policies and regulations. Confidentiality will be maintained as far as it is possible unless you tell us something which implies that you or someone you mention might be in significant danger of harm. In this case, we would have to inform the relevant agencies but we would discuss it with you first.

Further information about how your personal data is used is provided in the section "What will happen to my data".

13. Will I be reimbursed for taking part?

You will be compensated by bank transfer for your travel costs, time and inconvenience related to taking part in this study. The total amount of compensation you receive will depend on your degree of involvement:

- £35 if you attend the screening visit, but do not enter the main study (either due to your choice or decision of the study team).
- £190 if you attend the screening visit, and take part in the visit 1 study procedures, but do not complete all study procedures and follow-up (e.g. If you withdraw from the study, either due to your choice or the decision of the study team).
- £760 for completing all study procedures and follow-up. This amount is calculated based on the estimated cost of travel to attend the visits, total number and type of study procedures performed, and the duration of each study visit.

To claim this reimbursement, at the completion of your involvement in the study we will send you an electronic claim form via email – once you complete this we will submit the information to the University finance team and the payment will be made directly into your bank account. This process can take up to 1-2 months.Your bank details will be stored securely for 7 years in accordance with University of Oxford Financial policy.

We will not pay tax or National Insurance from the money due to you. It is your responsibility to pay these and to check how any compensation received from taking part in the study affects any state benefits to which you are entitled. Contact HM Revenue & Customs for information (http://www.hmrc.gov.uk/ or telephone 0300 200 3300).

14. What will happen to the samples I give?

Blood and skin samples that you give will be primarily stored and analysed in facilities based at NDORMS, University of Oxford. Your samples will be used in a form that does not identify you, mainly by the Translational Pharmacology research team, but also ethically approved research projects which may take place in hospitals, universities, non-profit institutions or commercial laboratories worldwide.

We will ask for your consent for the use of your samples to be stored indefinitely, and used in future ethically approved studies. If you agree to this, your samples will be used mainly by local researchers (if applicable), but ethically approved research projects may take place in hospitals, universities, non-profit institutions or commercial laboratories worldwide. If you agree to your samples being used in future research, your consent form will be held until the samples have been depleted or destroyed. To help keep your information confidential, your sample and any information recorded about you in this study will be assigned a study code that is used instead of your name and other identifiers. However, your DNA is unique to you so it can never be completely anonymous. Raw and summary data generated

from this study, that does not contain any participant identifying information, will also be shared with the study funder, UCB Pharma.

15. What will happen to my data?

Data protection legislation requires that we, the University of Oxford (whose legal name is The Chancellor Masters and Scholars of the University of Oxford), state the legal basis for processing information about you. In the case of research, this is a 'task in the public interest'. The University of Oxford is the sponsor for this study and is responsible for looking after your information and using it properly.

We will need to use information from you for this research project. We will share your information related to this research project with the following types of organisations: the local NHS Trust, a national volunteering database (see above) and, only where necessary for context, research partners (both academic and commercial organisations).

We may use third party service providers or subcontractors to help with some of the research activities we carry out (e.g. IT provision, survey provision, transcription services etc.). We may therefore share your personal data with these providers when it is necessary to do so to allow them to carry out the services we require them to provide. However, we require all our third-party providers to have appropriate security measures in place to protect your data and we only allow them to process your data for the specific purposes we have stated in our instructions.

This information will include your:

- NHS number
- Name
- Contact details
- Demographic data (e.g. age and sex)

People will use this information to do the research or to check your records to make sure that the research is being done properly. Responsible members of the University of Oxford, regulatory authorities, and the relevant NHS Trust may be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations.

We will keep all information about you safe and secure by:

- limiting access to data to only those people who need it for the research
- using the minimum personally-identifiable information possible

- storing it as securely as possible, for instance in locked cabinets on University premises for written documents, or on password-protected University-controlled computers for electronic information

International Transfers

We may share data about you outside the UK for research related purposes to:

- Permit additional analysis
- Contextualise data arising from the study
- Gain the insight of academic partners

If this happens, we will only share the data that is needed. We will also make sure you can't be identified from the data that is shared where possible. This may not be possible under certain circumstances – for instance, if you have a rare illness, it may still be possible to identify you. If your data is shared outside the UK, it will be with the following sorts of organisations:

- Higher education institutions (i.e. Universities)
- Commercial organisations

We will make sure your data is protected. Anyone who accesses your data outside the UK must do what we tell them so that your data has a similar level of protection as it does under UK law. We will make sure your data is safe outside the UK by doing the following:

- (some of) the countries your data will be shared with have an adequacy decision in place. This means that we know their laws offer a similar level of protection to data protection laws in the UK
- we use specific contracts approved for use in the UK which give personal data the same level of protection it has in the UK. For further details https://ico.org.uk/for-organisations/uk-gdpr-guidance-and resources/international-transfers/
- we do not allow those who access your data outside the UK to use it for anything other than what our written contract with them says
- we need other organisations to have appropriate security measures to protect your data which are consistent with the data security and confidentiality obligations we have. This includes having appropriate measures to protect your data against accidental loss and unauthorised access, use, changes or sharing

- we have procedures in place to deal with any suspected personal data breach. We will tell you and applicable regulators when there has been a breach of your personal data when we legally have to. For further details about UK breach reporting rules https://ico.org.uk/for-organisations/report-a-breach

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

After the study ends, the retention period (this means the length of time we keep your data for) will begin and we will keep your data for a minimum of 3 years in line with the University Policy on Management of Data. Once the retention period has finished, the study data will be kept in a way that does not identify you.

What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have. You have the right to ask us to remove, change or delete data we hold about you for the purposes of the study. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this.

If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study. This will be stored locally by the Translational Pharmacology group.

You can find out more about how we use your information, including the specific mechanism used by us when transferring your personal data out of the UK, by:

- asking one of the research team: philip.drennan@ndorms.ox.ac.uk
- sending an email to translationalpharmacology@ndorms.ox.ac.uk
- calling us on 01865 613728
- contacting the University's Data Protection Officer data.protection@admin.ox.ac.uk
- looking at the University's privacy notice available at: https://compliance.admin.ox.ac.uk/research-data.

If you would like to find out more about the use of confidential data in research, the HRA has developed a general information leaflet which is available at: https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/data-protection-and-information-governance/gdpr-guidance/templates/template-wording-for-generic-information-document/.

16. What will happen if I don't want to carry on with the study?

Participation is entirely voluntary. If you change your mind you can withdraw at any time without giving a reason and without penalty. If you withdraw from the study, any samples and data collected before your withdrawal will be used for research as detailed in this participant information sheet, unless you specifically request otherwise. However, if any of your anonymised data has been incorporated into the study, it will not be withdrawn or erased in order to maintain the scientific integrity of the study.

17. What happens at the end of the study?

The results of this project will be disseminated via standard scientific channels: publication in scientific journals, poster and oral presentations at scientific conferences. The data will contribute to the fulfilment of doctoral research project and presented in the thesis. You will not be able to be identified in any of these. When you enter the study we will ask if you would like to be informed of the results when they become available, and how you would like to receive them (e.g. email, post, and/or link to a website).

18. What if we find something unexpected?

If we incidentally find an issue during the study that may be important (e.g. high blood pressure, blood test abnormalities), we will inform your GP, or ask you to contact them, to ensure appropriate follow-up can be arranged.

19. What if there is a problem?

If you wish to complain about any aspect of the way in which you have been approached or treated, or how your information is handled during the course of this study, you should contact the Chief Investigator, Dr Philip Drennan (contact details at the top of this form) or you may contact the University of Oxford Research Governance, Ethics & Assurance (RGEA) office at rgea.complaints@admin.ox.ac.uk.

The investigators recognise the important contribution that volunteers make to medical research, and will make every effort to ensure your safety and wellbeing. The University of Oxford, as the research sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your taking part in this study. If something does go wrong, you are harmed during the research, and this is due to someone's negligence, then you may have grounds for a legal action for compensation. While the Sponsor will cooperate with any claim, you may wish to seek independent legal advice to ensure that you are properly represented in pursuing any complaint. The study doctor can advise you of further clinical action and refer you to a doctor within the NHS for treatment, if necessary. NHS indemnity operates in respect of the clinical treatment provided.

20. Who is organising and funding the study?

- This study is sponsored by the University of Oxford. It is being funded by Union Chimique Belge (UCB).
- The funding agreement between the University of Oxford and UCB provides that the University of Oxford will give UCB a royalty-free licence to commercially exploit the results of the study.
- All researchers involved in this study are employees of the University of Oxford. No members of the study team will receive additional payments for enrolling you in this study.

21. Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect participants' interests. This study has been reviewed and given favourable opinion by the **East of England – Cambridgeshire and Hertfordshire Research Ethics Committee.**

22. Participation in future research:

At the end of the study, we will ask for your consent to be approached to be involved in future studies, or to provide additional blood samples for research related to this study. All contact will come from the research team of this study in the first instance. Agreeing to be contacted does not oblige you to take part in future research, and you can be removed from this register at any time you wish.

23. Further information and contact details:

Please contact Dr Philip Drennan (Chief Investigator and Clinical Pharmacologist) or Dr Loren Kell (Co-Investigator, Postdoctoral Researcher, NDORMS) using the details at the top of this form if you would like further information or to ask any questions.

Thank you for reading this information sheet and for considering taking part in this research study.