Oxford Vaccine Group
University of Oxford
Centre for Clinical Vaccinology and Tropical Medicine,
Churchill Hospital, Headington, Oxford OX3 7LE
Telephone: 01865 611400 info@ovg.ox.ac.uk www.ovg.ox.ac.uk

PARTICIPANT INFORMATION SHEET
(Group C)

LEGACY04: Mechanism of early tissue responses in vaccination with mRNA vaccines (MechRNA)

You are invited to take part in a study to investigate how lymph nodes respond mRNA vaccines such as COVID-19 vaccine and how these changes with age and under anti-TNF therapy.

The study is being run by the Oxford Vaccine Group, which is part of the University of Oxford.

You are invited to participate in this study because you are 18 - 50 years old and currently on anti-TNF immunosuppressive therapy.

Before you decide on whether to participate in this study, it is important that you take the time to understand why the research is being done and what it would involve. Please read this information sheet carefully. If you have any further questions about the study, please do not hesitate to contact us (contact details are below and at the end of the leaflet).

If you are interested in taking part in this study, then please complete the online pre-screening questionnaire at: https://www.ovg.ox.ac.uk/studies/legacy04

If you have further questions about the study that you would like to discuss with our team, please contact us at:

Email: info@ovg.ox.ac.uk

Tel: 01865 611400

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Summary

Who can take part?	Adults in generally good health • Aged 18 to 45 years (Group A) • Aged 65 years or over (Group B) • Aged 18 to 50 years and on anti-tumour necrosis factor (TNF) therapy (Group C)
Study injections (vaccines) being used	Two different vaccines will be given at separate times: • COVID-19 booster vaccine (such as Moderna Spikevax vaccine or Pfizer Co-mirnaty vaccine) • Seasonal influenza (flu) vaccine
Procedure	Lymph node cell sampling using fine needle aspiration (FNA) of both armpits on two occasions • 2 weeks after study injection and then • 16 weeks after study injection In addition, an optional FNA visit will be offered at 2 weeks after the flu vaccine (6 weeks after the mRNA COVID-19 vaccine study injection) for those who choose to opt in.
Study Aims	To test immune responses to the vaccines using both blood and lymph node samples and compare responses in older people and people taking an immune medication to control inflammatory bowel disease (anti-tumour necrosis factor medication) with those in younger people not taking this drug.
Chief Investigator	Prof Katrina Pollock
Principal Investigator	Prof Katrina Pollock
Study Site	Oxford Vaccine Group, University of Oxford Centre for Clinical Vaccinology and Tropical Medicine Churchill Hospital, Headington, Oxford, OX3 7LE

What happens in the study?	Each in person study site visit (up to 7 in total) will include a blood test
	• **Screening visit**
	  ○ Volunteers will attend a screening visit, to decide their eligibility to take part, and to obtain their consent
	• **Study injection mRNA COVID-19 vaccination visit**
	  ○ One dose of COVID-19 vaccine booster will be given into the left arm
	• **At 2 weeks – 1st lymph node sampling visit**
	  ○ A Fine Needle Aspiration (FNA) will be performed to take cells and fluid from a lymph node from both armpits.
	• **At 4 weeks – Follow up and seasonal influenza vaccine visit**
	  ○ One dose of seasonal influenza vaccine will be given into the right arm
	• **At 6 weeks - Optional additional FNA sample Visit**
	  ○ An optional FNA will be used take cells and fluid from a lymph node only from the **right** armpit
	• **At 16 weeks – 2nd Lymph Node Sample visit**

	○ A FNA will be performed to take cells and fluid from a lymph node from both armpits • **At 42 weeks (6 months) – Follow up visit (end of study)** ○ Blood test and Safety review The safety of participants will be closely monitored throughout the study
Reimbursement	Screening visit: £110 Study Injections (vaccination with mRNA COVID-19) visit: £110 FNA visits: £150 per visit Follow up visit: £90 per visit Diary card: £30 per diary Total reimbursement (for all visits including optional FNA visit): £960
Risks of participation	After **FNA**, there may be some discomfort, bruising or bleeding. Very rarely infection may occur. These risks, along with potential rare complications, are detailed below (page 11). After **study injections (vaccination),** short-lived symptoms may occur, such as fatigue and discomfort of the arm. A full discussion of risks, including potential rare but serious reactions, can be found on page 10.
Benefits of participation	By participating in this study, you will receive COVID-19 and flu vaccines (at separate times). You will be helping research into understanding how immune responses to vaccination change with age. You will also be helping in the development of new vaccines that can be used in people of different ages.

Invitation

You have been invited to participate in this study because you are 18 - 50 years old and currently on anti-TNF immunosuppressive therapy.

What is the purpose of this study?

The main purpose of this study is to test the response of cells in lymph nodes before and after an mRNA vaccine in people taking an immunosuppressive medication (anti-TNF), and those of different ages not taking this medication. This way we can find out why mRNA vaccines like some COVID-19 vaccines don't work so well as we get older or for those on immunosuppressive treatments.

We are studying how lymph nodes respond to mRNA vaccines. Lymph nodes are small, bean-shaped organs found throughout the body. When a vaccine is given in the arm, the lymph nodes in the armpit swell as they react. Inside these lymph nodes are cells that make antibodies. These are special proteins that recognise viruses and protect us from infection once we have been vaccinated.

We can collect cells from lymph nodes using a small needle in a procedure called fine needle aspiration (FNA). This is a common test used for diagnosing in the clinic, and in research it lets us study immune cells directly. What we learn will help us design better vaccines and decide how to give them to different groups of people, such as older adults, to provide the best protection against disease.

As part of the study, we will also offer the seasonal flu vaccine separately, since many people would be getting it around the time of this study, and it will provide an additional health benefit.

Why is this study being done?

Messenger RNA (mRNA) vaccines, like those used for COVID-19, are an exciting new type of vaccine. However, they do not always work as well in older adults or in people taking certain medicines that affect the immune system. A protein in the body called tumour necrosis factor (TNF) helps control how our immune cells "talk" to each other. Anti-TNF therapy is one type of medication that changes how the immune system works. People on this therapy often have lower responses to vaccines. Similarly, as we age, our immune system can change, which can also lower how well vaccines protect us. This may also be linked to TNF in the body. By studying these changes, our goal is to create better vaccines that protect people of all ages, including those taking anti-TNF, from serious infections like COVID-19.

What is fine needle aspiration (FNA)?

Fine needle aspiration (FNA) involves taking cells and fluid from a lymph node (gland).

You will have an examination to feel for lymph nodes (glands) in your armpit. An ultrasound scan will look closely for your lymph glands. Once a suitable gland has been identified, the area will be cleaned and numbed using local anaesthetic. Using the ultrasound scan for guidance, a needle will be used to collect a small amount of fluid and cells from the gland. You should not feel any pain but may feel some pressure. This procedure will then be repeated on your other armpit. The whole visit can take up to 90 minutes, but the FNA procedure itself takes only a few minutes.

Ultrasound guided FNA is commonly performed in outpatient clinics to help diagnosis in patients with different health conditions, for example for lumps or swollen glands. It will be performed by a doctor or other skilled health professional such as a radiographer who is trained in the technique. This study is the fifth study conducted by the Chief Investigator using this technique for research.

Further details of FNA including risks are listed further on page 10, 'Are there any other potential risks from taking part in the study?'

Which vaccines are being used?

In this study you will receive two vaccines, an mRNA COVID-19 booster vaccine (such as Moderna Spikevax vaccine or Pfizer Comirnaty vaccine) and a seasonal flu vaccine. These will be given at separate times. Both vaccines chosen for the study are licensed for use in adults

Both vaccines are recommended and offered to many people in particular high-risk groups such as older adults and adults in at-risk groups. Both vaccines are also routinely offered to younger adults, such as the seasonal flu vaccine, but for some it will be additional to their usual care. Both vaccines used in this study have been very widely used in millions of people and they have a well understood safety profile.

We are however required to report any unusual side effects to the Medicines and Healthcare products Regulatory Agency (MHRA) using the Yellow Card scheme. Through the Yellow Card scheme, the MHRA collects and monitors information on suspected safety concerns involving healthcare products, like side effects caused by a medicine, or adverse incidents involving medical devices. Please let the study team know if you have any concerns.

What happens in the study?

1. Recruitment and eligibility screening

We wish to recruit up to 45 people to take part in this study at the Oxford Vaccine Group, University of Oxford. Participants should be aged either between 18 and 50 years and taking anti-TNF therapy. Volunteers will be asked to complete an initial online questionnaire, followed by a phone call from the study team, to assess whether they are eligible to take part. After this, volunteers will be invited to attend a screening visit which will include a medical assessment. Those who are eligible will then be invited to attend their COVID-19 mRNA vaccination (study injection) visit.

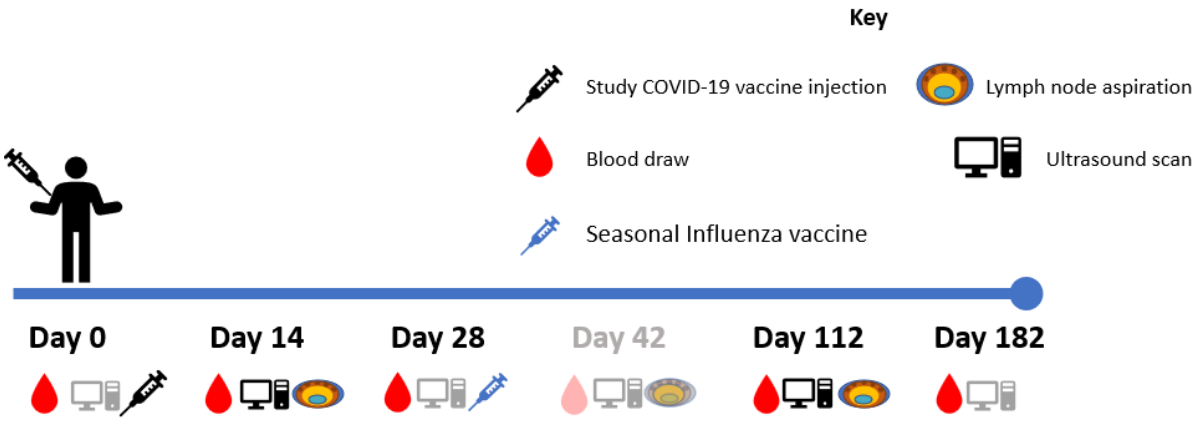
2. Allocation to a study group

Which study group you are in depend on whether you are taking anti-TNF therapy or not. There will be no randomisation in this study.

Group	Number of participants	Age
C	12 -15	18-50 years individuals on anti-TNF therapy

3. Study visits

Below is a timeline highlighting the timeline of the study:



Images in grey and all procedures listed at Day 42 represent **optional** interventions, and will be carried out depending on-site staff capacity and resources

How long would I be in the study?

If you are eligible to take part, we will enrol you into the study for 6 months starting from your COVID-19 mRNA study injections (vaccination) visit. You can, if you decide to (for whatever reason), withdraw from the study at any time (see What happens if I do not wish to carry on with the study? (Page 12).

Can I take part?

If you choose to take part in the study, all the following **must apply** to you**:**

You must

Be aged between **18 to 50 years** at the time of your screening visit
Be **in good health** without unstable ongoing medical conditions
Be able and willing to **comply with all study requirements** including attending all follow up visits
Be willing to **allow your past medical and vaccination history to be checked by the study team** (either by allowing us to discuss your medical history with your GP, or by giving us a medical history summary)
Be willing to **register with TOPS** (The Over-volunteering Protection System)
Agree to **refrain from blood or blood product donation** during the study
Tell us about any **vaccinations** you may have received recently or expect to receive soon including flu vaccine
Tell us about whether you have received a primary (two dose) schedule of any authorised or licensed COVID-19 vaccine
Receiving anti-TNF therapy (for example a medication called infliximab)
Contraception
(If applicable) For participants who could potentially become pregnant: Use **contraception** for the duration of the study **and** have a **negative pregnancy test** at the screening visit and study injection (vaccination) visit

You must NOT have

Current and Past Medical Problems
A **serious long-term illness** *e.g.*, a condition (other than inflammatory bowel disease) that requires hospital or specialist follow-up
A **body mass index (BMI) above 35**
A history of a **blood transfusion** or **immunoglobulin infusions** within 3 months of the study
Regular **anticoagulant** (blood-thinning) **medication** (*e.g.,* warfarin, edoxaban)
A history of **suppression of your immune system unrelated to anti-TNF therapy**
Regular **immunosuppressive therapy other than anti-TNF therapy**
A history of a **severe allergic reaction to a vaccine or local anaesthetic, including hypersensitivity**
A history of **cancer that is ongoing**
A **serious ongoing mental health condition** if this may affect your participation in the study
A history of **bleeding disorders** or history of **significant bleeding or bruising following injections or blood tests**
An intake of more than **42 units of alcohol per week** on average (The NHS recommends the following calculator: https://alcoholchange.org.uk/alcohol-facts/interactive-tools/unit-calculator)
Injected recreational drugs within the last 5 years
A history of **hepatitis B**, **hepatitis C** or **HIV infection**

A history of serious pericarditis, myocarditis or other **heart inflammation**
Other Clinical Trials
You must NOT receive a drug or vaccine in **another clinical trial** in 12 weeks before the study starts and for the duration of the study
(If applicable) Pregnancy/Breast Feeding During the Study
You must NOT be pregnant or breastfeeding during the study

If you are unclear whether you might be eligible to be involved in the study, you can contact the study team (details at the end of this information sheet).

Do I have to take part?

No. It is up to you to decide whether to take part. If you do decide to take part, you will be given this information sheet to keep (it will be sent electronically but you can request a paper copy) and you will be asked to sign a consent form.

What will happen if I decide to take part?

Below is a table to list in detail what to expect during study visits.

Visit	**What to expect**
Pre-screening phone call	There may be a phone discussion about your medical history and to answer your questions about the study. We will ask you to complete a consent form to retrieve a summary of your medical and vaccination records. This information will be kept confidential.
Screening visit	• Discussion of study • Sign consent form • Identity check • Review of medical history • Physical examination, including "vital signs" (temperature, pulse, blood pressure) • Blood test (and urine pregnancy test, if appropriate)
Study Vaccine injection (Vaccination) visit	• Vital signs (temperature, pulse, blood pressure) • Blood test (and urine pregnancy test, if appropriate) • Ultrasound scan of both armpits • Vaccination in **left** arm for COVID-19 vaccine and **right** arm for seasonal flu vaccine • COVID-19 vaccine will be given at Day 0 (at the start of the study) and season flu vaccine will be given at Day 28 of the study
FNAs	• Vital signs ((temperature, pulse, blood pressure) • Fine needle aspiration (FNA) and ultrasound scan of both armpits • Blood test
Follow up visits	• Blood test • Review for serious medical events related to FNA or vaccination

Online pre-screening questionnaire and medical records consent

If you decide that you would like to take part in this study, then you will need to complete a short set of online questions that cover some of the key criteria for participation in the study. In addition, we will ask you to provide consent for the study team to access your medical records via the electronic patient records or through your GP. This consent is only to allow access to your medical records, and not the consent for enrolment into the study. If you choose to participate in the study, a separate consent will be taken (see below). If the study is right for you at this point, we will contact you to invite you to an in-person screening visit.

Screening visit

This may take place up to four months before the mRNA COVID-19 vaccine study injection (vaccination) day. This, and all other study visits, will take place at the Oxford Vaccine Group, University of Oxford.

At the screening visit, you will meet with study staff, who will discuss this information sheet with you and would provide an opportunity for you to ask any questions you might have about the study and what's involved. The study staff will also ask you more questions about your medical history, any medications that you take, and lifestyle factors (including smoking and alcohol use). You may take as much time as you feel necessary before making any decision on whether to take part. If you then decide to take part, and the study team consider that you have understood the information, you will be asked to sign the study consent form.

This will be followed by a symptom directed physical examination, which will include the doctor listening to your heart and lungs with a stethoscope and examining your abdomen. Your vital signs (blood pressure, pulse, and temperature), weight and height will be measured. A blood sample will be taken (approximately 10 mL). If applicable, a urine sample may also be taken to perform a pregnancy test. **This visit will take about 90 minutes.**

mRNA COVID-19 vaccine study injection (Vaccination) visit

If you qualify to be in the study after the screening visit eligibility checks, we will arrange for you to attend the mRNA COVID-19 vaccine study injection (vaccination) visit. First, we will check there have been no new problems since your screening visit. Your blood pressure, pulse and temperature (vital signs) will be checked, and a blood sample taken (approximately 50ml). If appropriate, you will have a urinary pregnancy test before study vaccinations. You will have an ultrasound examination of both armpits.

You will then be given a single dose of the mRNA COVID-19 vaccine into the **left upper arm**. **Overall, the study injections (vaccination) visit will take about one hour.**

FNA visits (see page 3-4, 'What is fine needle aspiration?')

FNA visits will be performed, at 14 days AND 112 days after the COVID-19 study injection (vaccination visit). **These visits will take about 90 minutes**. We will ask about any recent serious medical problems. You will have a blood test (approximately 60mLs) and you will have an ultrasound examination and FNA of both armpits.

In addition, an optional FNA visit will be offered to participants at 2 weeks after the flu vaccination (42 days (6 weeks)) after the COVID-19 mRNA study injection for those who wish to take part. **This visit will also take about 90 minutes** and we will ask about any recent serious medical problems. You will have a blood test (approximately 60mLs), an ultrasound examination, and an FNA of the armpit on the same side as the flu vaccine injection.

Electronic symptom diary 'eDiary' (to be completed at home)

During the FNA visits you will be given access to an online symptom eDiary. This will be set up using your personal e-mail address. We will ask you to record if you have any symptoms of pain, swelling and/or tenderness you may experience in your armpits in the 7 days following the FNA procedures. If you forget to fill in the diary, you will receive automatic reminders; you may also be contacted by a member of the study team.

Follow up visits

After mRNA COVID-19 vaccine study injection, you will attend the clinic for several follow up visits, as shown in the diagram above. **These visits will take about 30-45 minutes**. The visits are for us to check if you are experiencing any problems after the study injections and review your injection and FNA sites. At each visit you will have a blood test (approximately 50 mL).

During the study, you may also be asked to attend for an extra visit, for example, if a blood test needs to be repeated.

Seasonal flu vaccine administration

During one of the follow up visits, around 28 days after your COVID-19 study injection (vaccination) visit, we will arrange for you to receive the seasonal flu vaccine. Similar to the COVID-19 study injection (vaccination) visit, we will check there have been no new problems since your follow up visits. Your blood pressure, pulse and temperature (vital signs) will be checked, and a blood sample taken (approximately 50ml). If appropriate, you will have a urinary pregnancy test before the vaccine. You will have an ultrasound examination of both armpits. You will then receive a single dose of the seasonal flu vaccine in the **right upper arm** (opposite the one used for the COVID-19 study Injection). **Overall, this visit will take about one hour.**

What other medical matters are relevant to the study?

Other vaccinations or medications during the study

If during the study you require any vaccinations for health, travel, or occupational reasons, you should inform the study team beforehand. We ask you not to receive any other vaccines within 30 days (before and after) of receiving the study injections. If you are prescribed any new medications during the study, please inform the study team.

Private insurance

If you have private medical insurance or travel insurance, participation in a study will often not affect your cover for any conditions unrelated to the study; however, to be certain, you should tell your insurer you are planning to participate.

Contraception

It is a requirement of participation that volunteers who could become pregnant are not planning pregnancy during participant in the study. If this applies to you, then you may wish to use contraception (exceptions to this are below).

Acceptable contraception methods include:

- Oral, injected or implanted hormonal contraceptives that prevent ovulation
- Intrauterine device (IUD)
- Intrauterine system (IUS)
- Sole sexual partner is a vasectomised male
- Barrier methods: e.g., Condoms.

Female participants where any of the following apply will not need to consider contraception:

- Post-menopausal
- Surgical sterilisation
- Complete abstinence from sex with a male partner

Pregnancy

If you were to become pregnant during the study, you should tell us immediately. There are no safety concerns but we should not take unnecessary blood from you during pregnancy and so would discontinue your involvement.

What should I avoid during the study?

Blood donation

Under current UK regulations, participants must refrain from blood donation during their involvement in the study. However, you will be able to restart blood donation once the last study visit has been completed.

Taking part in other clinical trials

You should not take part in other clinical trials in which drugs or vaccines are administered, or which involve repeated blood sampling, whilst participating in this study as this may affect the results of this study.

Are there any risks from seasonal flu and COVID-19 vaccines?

Potential risks are summarised below:

Vaccine site - 'local' reactions

As with any vaccine, you may experience some discomfort at the injection site. Usually this is mild, but some individuals experience more significant pain which might interfere with their usual activities. Post-vaccination arm pain usually resolves completely within a few days, although it may occasionally persist up to a week or even longer.

Other less common, but possible, symptoms around the injection site might include redness, swelling, itchiness or a feeling of warmth.

General reactions

During the first 24-48 hours after study injections (vaccination), you may experience flu-like symptoms such as muscle aches, joint aches, feverishness, chills, headache, nausea, tiredness and feeling generally unwell. We would expect these symptoms to resolve within a few days.

Are there any other potential risks from taking part in the study?

Fine needle aspiration (FNA) sampling

FNA is a safe and well-tolerated procedure but, as with any medical intervention, it carries some risks:

Pain: The FNA should not be any more uncomfortable than a blood test. Any tenderness afterwards will resolve. You can take a simple painkiller like paracetamol if you need it; avoid taking aspirin, as this may increase the risk of bruising.

Bleeding: The needle used is fine but bleeding under the skin may sometimes occur after the FNA. It usually stops quickly by itself. Any bruising will fade within 2 weeks.

The risk of bleeding is higher if you are taking any medications that make your blood thinner such as warfarin, aspirin or clopidogrel. If you regularly take any of these medications you will not be able to participate in the study. **If you take any aspirin or blood thinning medication in the 7 days before the FNA procedure please let us know.**

Infection after FNA is rare. If you get redness, pain and/or tenderness in the days afterwards you may need antibiotic treatment.

Damage to adjacent tissues and organs: It is possible for the needle used in a fine needle aspiration (FNA) procedure to damage underlying structures; however, such occurrences are extremely rare. Among these, a rare but potential complication of FNA of axillary (armpit) lymph nodes is a pneumothorax. This occurs when air leaks into the space between the lung and chest wall, which can cause pain and, in some cases, difficulty breathing. A small pneumothorax can heal by itself with rest. Fine needle aspiration procedures are conducted under ultrasound guidance to prevent this from happening.

If the doctor is not able to collect enough sample, he/she may decide to repeat the FNA with your permission.

Blood samples

Blood sampling may cause slight pain and occasionally bruising. Occasionally, people feel lightheaded, nauseous or faint. At most visits we will take about 50ml of blood, which should be well tolerated by healthy adults. The **total** amount of blood we will take from each participant over the whole study period is approximately 300 mL. For comparison, a **single** donation to the NHS blood bank would be approximately 470 mL.

What if we find something unexpected?

Since we carry out several medical tests throughout the study, we may possibly detect previously unknown health issues (e.g., high blood pressure, abnormal blood results). If abnormal results or undiagnosed conditions were to be found during the study, these would be discussed with you and, if you agreed, your GP would be informed. We would refer any newly diagnosed conditions to your GP.

Sometimes incidental medical findings require your GP to carry out further investigations, such as blood tests, scans or referral to specialists.

What are the advantages of taking part?

By participating in this study, you will receive flu and COVID-19 vaccines and may benefit from increased protection against flu and COVID-19.

Would my taking part in this study be kept confidential?

All information that is collected about you during the research will be kept strictly confidential. Any information about you that leaves the clinic would have your name and address removed so that you could not be recognised, except for your signed consent form and letters sent to your own GP. To enrol into this study, you are required to consent for us to contact your GP.

We will write to your GP to inform them when you enrol in the study and when you complete it, so they can update your medical records accordingly. Your GP may also be asked to share information about your medical history and give access to any other medical records as required to ensure there

are no medical reasons that would prevent you from taking part. We would only notify your GP of the results of any medical tests with your permission.

Responsible members of the University of Oxford and Oxford University Hospitals NHS Foundation Trust, may also be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations. No one else will be told that you are involved in the study.

Will I be paid for taking part in this study?

Study participants will be reimbursed for their time and inconvenience. The reimbursement provided are considered to be reasonable amounts to cover the costs of participating in this research. There should not be any consequences for tax or benefit purposes.

Reimbursement for all participants will be based on the following figures:

- Screening visit: £110
- Vaccination visit: £110 x2 = £220
- FNA visits: £150 x 2 = £300
- Optional FNA visit: £150
- Follow up visit: £90
- Full completion of the FNA diary card: £30 x 3 = 90

The sum reimbursed is based on the number of visits you attend. If you choose to withdraw partway through the study, we will calculate your reimbursement based on the visits you have attended. The reimbursement for a volunteer who completes all the study visits is £960.

Payments are made directly by bank transfer in instalments during the study. For this reason, we require participants to provide their bank details at the screening. Bank details are kept confidential.

Personal information such as your name, bank details and national insurance number may be shared with the University finance team to process or verify your reimbursement payments. Financial auditors may also audit the records where this information is held. All confidential data will be stored according to the UK General Data Protection Regulation (see below).

If we ask you to attend any additional (unscheduled) visit, you would be reimbursed for this at the rate appropriate for the type of visit.

What if new information becomes available?

Sometimes during a study, new information relevant to the study becomes available (such as results from this or other studies). If this were to happen, we would tell you about it and discuss whether you would want to, or should, continue in the study. If you decided to continue to take part, you would be asked to sign an updated consent form. On receiving new information, we may consider it to be in your best interests to withdraw you from the study.

What happens if I don't want to carry on with the study?

At any time during the study, you are entirely free to change your mind about taking part, and to withdraw from the study. This would not result in any penalty, nor will your legal rights be affected; however, you will only be reimbursed for the study visits you have attended. Unless you state otherwise, any blood taken whilst you have been in the study would continue to be stored and used for research, as detailed below. You may request that your blood samples are destroyed at any time

during or after the study. For safety, if you withdraw, we may still ask to follow up any medical problems you might have experienced whilst in the study.

Once you have given informed consent but lose capacity to consent during the course of the study, you will be withdrawn from the study. Any identifiable data or tissue already collected with consent will be retained and used in the study. However, if you or your guardian requests that the data already collected should not to be utilised, in this instance, we would withdraw all collected samples from analysis (except those that have already been utilised). No further data or tissue will be collected or any other research procedures carried out.

In exceptional circumstances, your participation in the study might also be stopped early by the study doctor or the sponsor of the study.

What will happen to any samples I give during the study?

Clinical safety blood samples are sent to local NHS laboratories and follow local sample labelling requirements (which may include personal identifiers). As part of processing the clinical safety blood samples, the laboratories may be required to add the results to your medical records.

Samples sent to research laboratories for processing will not have personal identifiers (they will be identified by study number and participant number only). However, as your DNA is unique, samples can never be completely anonymous.

The lymph node samples and blood samples collected during this study will be analysed in the Oxford Vaccine Group and University of Oxford research laboratories. We may also send de-identified samples to other researchers working with us on this research project. This may include researchers in other countries, including outside of the United Kingdom.

If you choose to take part in this study, we will also ask for your permission to store your samples that remain after the study is over (including cells and DNA). If you do not wish for your samples to be stored and used for future research, they will be destroyed 12 months after the end of the study.

The following tests will be performed on your blood samples:

- Blood tests for blood cell counts and liver and kidney function.
- Blood tests for Hepatitis B, Hepatitis C and HIV (at the screening visit). A reactive test may mean you are ineligible for this study as the vaccine is new and has not been tested in this setting.
- A blood test for glucose (at the screening visit).
- A blood test for HLA typing, a genetic test of components of the body's immune system.
- Tests of immune responses following study injections looking at your antibodies and immune cells.
- If you opt in, samples taken in this study may be used for research involving the creation of specific antibodies called 'monoclonal antibodies.'

Detailed immunological tests will be performed on your lymph node samples. These may include RNA and DNA sequencing analyses, which show which proteins the cells are making and indicate the activity of the cell's genes.

The medical practitioners in the study team are legally obliged to report a case of acute infectious hepatitis to the UK Health Security Agency. This may involve a referral to your GP or specialist for further testing if a blood test for hepatitis B or C is reactive.

Will any genetic tests be done?

We will do genetic tests on your blood and lymph node samples to look at the patterns of genes that regulate your own individual immune response. This will help us to work out which aspects of the immune response to vaccines are due to genetic differences between individuals. We will also try to identify and study the genes that appear to be important in your immune response to the study injections. Other genetic tests may be done if you consent to your samples being stored and used for future research. You will not receive the results of any genetic tests performed.

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 from your medical records, your GP, and/or your hospital records for this research project. We will share your information related to this research project with the following types of organisations:

- local NHS laboratories as part of processing the clinical safety blood samples (please see page 13)

This information will include your initials, NHS number, name, home address/contact details, email address. People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

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

- Data will be collected and held by the Oxford Vaccine Group. It will be accessible to staff at the Oxford Vaccine Group, responsible staff from the University of Oxford who may monitor/audit the data collection process, and inspectors from ethics.
- The University of Oxford Data management and IT Team will be able to view your email address, which is necessary for the eDiary to function.
- Storing in secure database servers held by the University of Oxford.

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

- For analysis by collaborating research groups

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:

- Academic institutions such as universities

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 rules visit the Information Commissioner's Office (ICO) website: https://ico.org.uk/for-organisations/report-a-breach
- 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 visit the Information Commissioner's Office (ICO) website: 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. We will keep your study data for the minimum period of time required by:

- We will store the research data and any research documents with personal information, such as consent forms, securely for up to 25 years after the end of the study, or as per national regulatory requirements.
- Research data (anonymised) will be stored for at least 99 years. If you only complete online screening (i.e., before you give informed consent) your data will only be kept to the end of the study.
- At the completion of the study, unless you consent otherwise (e.g., if you request to be informed of other studies), your personal details will be destroyed. If you agree to future contact (e.g., to be informed of other studies) your contact details will be held separately from the study data and you can request at any time to have your details removed.
- Your national insurance or passport number for "TOPS Database Registration" and payment processing will be taken at the screening visit. We will securely retain copies until the end of the study. Your bank details will be stored for 10 years after the project ends in line with the University of Oxford's financial policy.
- Some of the de-identified research data may be made available in open, online research databases. Sharing the results of the study in this way means it can continue to contribute to scientific progress in future.

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 choose to stop taking part in the study, we would like to continue collecting information about your health from [central NHS records / your hospital / your GP]. If you do not want this to happen, tell us and we will stop. (Also see page 12 - What happens if I don't want to carry on with the study?)

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 at info@ovg.ox.ac.uk.
- sending an email to info@ovg.ox.ac.uk.
- calling us on 01865 611400
- 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/

What if something goes wrong?

The investigators recognise the important contribution that volunteers make to medical research and make every effort to ensure your safety and well-being. The University of Oxford, as the 'research sponsor', has arrangements in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study.

In the event of harm being suffered, 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 action and refer you to a doctor within the NHS for treatment, if necessary. If you are referred to the NHS during the study, then NHS indemnity operates in respect of the clinical treatment which may be provided.

Complaints statement

If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you should contact the research investigators at info@ovg.ox.ac.uk or 01865 611400. Alternatively, you may contact the sponsor organisation of this study (University of Oxford) at the Research Governance, Ethics and Assurance (RGEA) team office on email rgea.complaints@admin.ox.ac.uk.

TOPS database registration

Volunteers participating in this study must not be enrolled in another study that involves receiving investigational medications or vaccines at the same time. To check this, you will be asked to provide your national insurance or passport number. This will be entered on to a national database which helps prevent volunteers from taking part in too many clinical trials. More information can be found at https://www.hra.nhs.uk/about-us/committees-and-services/the-over-volunteering-prevention-system/.

What will happen to the results of the research study?

The results of this research study may be presented at scientific meetings or conferences and published in a scientific medical journal. This can take approximately 2 years after the study is completed. Your individual results would not be identifiable, nor would you be identified in any report or publication. A reference to the publication(s) will be available on the Oxford Vaccine Group website and other study site websites as appropriate. If you contact the researchers in the future, you can obtain a copy of the results.

The de-identified research data from this study will be shared with the collaborating partners who are organising and funding this research work. Data from this study may be used to file patents or licence vaccines in the future or make profits in other ways. You would not be paid for any part of this. Data from this study may be used as part of a student post-graduate degree, for example a MD or PhD.

Who is sponsoring, organising and funding the research?

The study is organised and sponsored by the University of Oxford. The study is funded by the UK Research and Innovation, Medical Research Council.

Who has reviewed the study?

This research has been checked by an independent group, the Research Ethics Committee, who protect participants' interests. This study has been reviewed and approved by North West - Haydock Research Ethics Committee.

The Oxford Vaccine Centre Patient Public Involvement (PPI) group have reviewed the main participant-facing documents associated with this study (participant information sheet, informed consent form and advertising materials).

Further information and contact details

We hope this information sheet has given you enough information to decide whether to volunteer for this study. If you would like further information about participating in research, please visit the following website: https://www.nhs.uk/tests-and-treatments/clinical-trials/

For independent advice about participating in this study, you may wish to contact your GP.

If you are interested in taking part in this study, then please complete the online pre-screening questionnaire at: https://www.ovg.ox.ac.uk/studies/legacy04

If you have further questions about the study that you would like to discuss with our team, please contact us at:

Email: info@ovg.ox.ac.uk

Tel: 01865 611400

Thank you for your interest in taking part in this study.