Participant information sheet

Study Title: An experimental medicine study of seasonal influenza vaccination responses in Lymph nodE single-cell Genomics in AnCestrY (LEGACY01)

Study code: LEGACY01 **IRAS ID: 314444**

Brief Summary:

- We are researching how our ancestry influences the way our lymph nodes respond to vaccination and developing an atlas of the single cell responses.
- An atlas is a reference database formed of the results of many studies. The data will not identify you. The atlas can be used by other researchers for their research.
- We are working with researchers at the University of Oxford and the Uganda Virus Research Institute and inviting healthy volunteers with African or Asian ancestry to take part.
- Participants must have been mostly resident in the UK for at least 5 years
- Please take time to read the following information carefully. It provides details about the study procedures and asks for your consent. Please ask us if there is anything that is not clear or if you would like more information.
- You are free to decide whether to take part. Your decision will not affect your usual healthcare. You can stop taking part at any time, without giving a reason.
- We will ask you to have a seasonal influenza (flu) vaccine and to have fine needle aspirations of lymph nodes in both armpits before and after vaccination.
- The procedures will be overseen by an experienced doctor.
- If you regularly take blood thinning medication, or have severe allergies, you will not be able to participate in the study.
- You will be paid a contribution towards travel for the screening visit and for attending study visits should you enrol.
- Thank you for reading this information. If you decide to take part, you will be given a copy of this information sheet and your written consent.

Contact:

If you have any questions about this study, please talk to the lead researcher:
Dr Katrina Pollock
Tel 020 3313 8070

If you are interested in participating, please contact the recruitment team:
imperial.recruitment.icrf@nhs.net
Tel 020 3313 1086

1. The purpose of the study

We are researching how our ancestry and ethnic diversity influences the way we respond to vaccination. To do this we are sampling the cells that respond to a vaccine. These cells are in lymph nodes throughout the body including in the armpit. The data that we get from these cells will be used to create a reference dataset, called a single-cell atlas that will be shared to answer many research questions about vaccines and about the human immune system. In this study we are investigating the response to influenza (flu) vaccine.

2. What do I have to do?

There are very few changes to your normal lifestyle – you can eat and drink as you would usually, drive a vehicle, play sport, continue any medication that you might be on, and donate blood if you wish.

However, if you are a woman, you must avoid getting pregnant during the study, and must use highly effective contraception until 12 weeks after the flu vaccine. We'll discuss with you which forms of contraception are acceptable.

All participants must avoid all other vaccines (except COVID-19 vaccine) within 4 weeks either side of the flu vaccine and the fine needle aspiration samples and must not be participating in a clinical trial with an investigational drug or device, or have recently received an investigational drug.

We advise you to avoid vigorous activity for 24 hours after donating a fine needle aspiration sample.

3. The screening visit

Before you can join the study, you will attend a screening visit at the NIHR (National Institute for Health Research) Imperial Clinical Research Facility (ICRF), at Hammersmith Hospital. The study team will discuss the study with you, and your suitability to take part. You will have the opportunity to ask questions about the research. After giving your consent, you will have a medical examination and have some blood tests, including a test for hepatitis and HIV infection, to check your general health. If you are a woman who can get pregnant, you will have a urine pregnancy test. The whole visit will take about 2 hours.

4. What happens during the study?

If the screening assessments show that you are eligible to participate, you will be asked to attend 4 more visits at the ICRF. At all these visits we will ask questions about your health, take blood samples, and do a medical examination. At the first visit you will have a lymph node fine needle aspiration (FNA) from both armpits. The study team will telephone you five days afterwards to check how you are. At the next visit you will have a seasonal flu vaccine, by injection into a muscle in your upper arm. If you are a woman who can get pregnant, you will have a urine pregnancy test. Five days later, you will have a second lymph node FNA from both armpits. The final visit in the study will happen 4 weeks after the vaccine and you

will be asked to complete a paper survey to collect feedback on your experience in participating in this study. Participation in this survey will be voluntary and confidential.

5. Optional FNA Visit

Participants in cohort 2 (2023-24 flu season), up to six in total, can attend an additional lymph node FNA visit 6 weeks after study vaccination if they wish. The study team will telephone you five days afterwards to check how you are. This additional visit is entirely optional and is not a requirement of the study participation. The number taking part in this optional visit is based on the short time-frame to complete the visit during the flu season.

All the visits will take about 90 minutes, except for the final one which will take about 30 minutes. The total amount of blood we will take is (220 millilitres (a little under ½ a pint or 270 millilitres if you have opted for the third FNA visit).

Please refer to the table below for a summary of study visits and what they involve.

Procedure/assessment	Visit					
	1 (Screening)	2	3	4	5	6
Fine needle aspiration of lymph nodes from both armpits		✓		✓		✓
Injection of flu vaccine			✓			
Medical questions and examination	✓	✓	✓	✓	✓	✓
Blood samples for health check and/or immune response	✓	✓	✓	✓	✓	✓
Urine sample for pregnancy test (women only)	✓		✓			
Participant feedback survey (paper)					✓	

6. Payment for participation

You will be reimbursed for your time, inconvenience, and travel, at the end of the study, as follows:

- Screening (Visit 1): £10
- Visits which include an FNA (Visits 2, 4 and optional 6): £120
- Vaccination visit (Visit 3): £80
- Final visit (Visit 5): £60.

7. What is a single cell atlas?

An atlas is a reference database formed of the results of many studies. The data will not identify you. The atlas can be used by other researchers for their research.

An atlas of single cells has data from the detailed study of individual human cells. In this study, the single cells are immune cells found in specialised organs called lymph nodes and in the blood. Immune cells are especially important in the response to vaccination.

The Human Cell Atlas is a worldwide project to create a map of all the cells in the human body. The Atlas is made up of lots of smaller atlases from studies like this one. You can find out more about the Human Cell Atlas at https://www.humancellatlas.org/

8. Why study volunteers with African or Asian ancestry?

To make the best use of single cell research it needs to be representative of our population. Currently, single cell genomic data is not as diverse as our population. That's why we are asking you to contribute to this project. If you want to find out more about this project and the others that are making genomic research more diverse you can read about it at Ancestry Networks for the Human Cell Atlas Projects - CZI (chanzuckerberg.com). Diversity in the Human Cell Atlas will enable new scientific discoveries for the benefit of all.

9. How are the different organisations working together?

This study brings together expertise from four institutions. Imperial College London is working with University of Oxford and the Uganda Virus Research Institute to design the study. The study visits will be conducted at the ICRF, which is part of Imperial College Healthcare NHS Trust. Samples will undergo analysis by researchers at Imperial College London and at University of Oxford. Staff from the Uganda Virus Research Institute will contribute to study visits and/or sample and data analysis.

10. About fine needle aspiration

A fine needle aspiration (FNA) involves taking cells and fluid from a lymph node (gland). It is a procedure 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.

The whole visit can take up to 90 minutes but the FNA procedure itself takes only a few minutes. You will have an examination to feel for lymph nodes (glands) under the arm. An ultrasound scan will look closely for your lymph glands under the arm. 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. The procedure will be repeated on the opposite side.

On the same day as the procedure, we'll take a blood sample so that we can compare the immune response in the blood with those in the lymph nodes.

11. What are the risks of a fine needle aspiration and flu vaccine?

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

- 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 but 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 should stop 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 blood thinning medication you will not be able to participate in the study. Please let us know before the procedure if you take any blood-thinning medications.
- Not enough sample: If the doctor is not able to collect enough sample, he/she may decide to repeat the FNA with your permission.
- Infection after the biopsy is rare. If you get redness, pain and/or tenderness in the days afterwards you may need antibiotic treatment.

The flu vaccine is called Adjuvanted Quadrivalent Influenza Vaccine (Surface Antigen, Inactivated) Seqirus (also marketed as Fluad Tetra) and is used in the UK in people aged 65 years or older. The short name for this flu vaccine is aQIV. For the purposes of this study, we will refer to the vaccine as aQIV.

This vaccine is not licensed for use in younger people. It has been tested in >4,000 adults aged 65 years and older, and in >5,000 children aged at least 6 months but younger than 6 years. In those studies, the side effects of aQIV were broadly similar to those of most licensed vaccines. We have chosen to use it in this study because we think it will cause your lymph nodes to swell slightly, and therefore make it possible to find the responding lymph node for FNA.

The following side effects have been reported during clinical trials of aQIV in adults 65 years of age and older.

Mild side effects

Very common (may affect more than 1 in 10 people):

- Pain at injection site
- Fatigue
- Headache

Common (may affect up to 1 in 10 people):

- Joint pain (arthralgia)
- Muscular pain (myalgia)
- Redness at injection site (erythema)
- Hardening of the skin at injection site (induration)
- Diarrhoea

- Shivering
- Nausea
- Loss of appetite
- Bruising at injection site (ecchymosis)
- Flu-like symptoms

Uncommon (may affect up to 1 in 100 people):

- Vomiting
- Fever (≥ 38°C)

Most side effects were mild or moderate and went away within 3 days of appearing.

Next to the above side effects, the following side effects occurred occasionally during routine use of another vaccine like aQIV.

- reduction in the number of certain types of particles in the blood called platelets; a low number of these can result in excessive bruising or bleeding (thrombocytopenia); swelling of the glands in the neck, armpit, or groin (lymphadenopathy)
- swelling, pain and redness at the injection site extending to more than 10 cm and lasting more than one week (injection site cellulitis-like reaction)
- extensive swelling of injected limb lasting more than one week.
- allergic reactions
- sudden fall in blood pressure due to severe allergic reactions that in rare cases can lead to failure of the circulatory system to maintain adequate blood flow to the different organs (shock)
- swelling most apparent in the head and neck, including the face, lips, tongue, throat, or any other part of the body (angioedema)
- muscular weakness
- pain on the nerve path (neuralgia), unusual feeling of touch, pain, heat and cold (paraesthesia), fits (convulsions), neurological disorders that may result in stiff neck, confusion, numbness, pain and weakness of the limbs, loss of balance, loss of reflexes, paralysis of part or all the body (encephalomyelitis, neuritis, Guillain-Barré Syndrome)
- skin reactions that may spread throughout the body including itchiness of the skin (pruritus, urticaria), rash
- severe skin rash (erythema multiforme)
- blood vessel swelling that may cause skin rashes (vasculitis) and temporary kidney problems

Like any vaccine after authorisation for use, the aQIV is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions via a national reporting scheme. This information is taken from the patient leaflet for Adjuvanted Quadrivalent Influenza Vaccine (Surface Antigen, Inactivated) Seqirus suspension for injection in pre-filled syringe Influenza vaccine, Adjuvanted with MF59C.1 suspension for injection in pre-filled syringe.

If you have any concerns following the procedure or vaccination, please do not hesitate to contact us on 02033131703 (0900-1700, Monday to Friday) or 07826903646 if outside of normal working hours.

12. What are the possible benefits of taking part in this study?

The study health check might be a benefit, and you should get some immunity from the influenza vaccine. The study results will help research of the human immune system. Many people feel that it is rewarding to make this very personal contribution to science.

13. What are the possible disadvantages of taking part in this study?

Although flu vaccine is given to pregnant women, the vaccine in this study (aQIV) is different from the one usually used in pregnancy. We don't yet know the effects of using aQIV in pregnancy. It is possible that if aQIV is given to a pregnant woman it could harm the unborn child. Pregnant women must not therefore take part in this study, and neither should women who plan to become pregnant during the study. Women who could potentially get pregnant will be asked to have pregnancy tests at screening and again before vaccination and must use highly effective contraception until 12 weeks after aQIV. We'll discuss with you which forms of contraction are acceptable. Any participant who finds that she has become pregnant while taking part in the study should immediately tell the research team.

14. How will the data from this study be used?

Research data may include images from the ultrasound scans, data from genes, data from processes that happen inside cells and immune system data. These data will be processed and analysed so that you are not identifiable. The findings from the study will be published in scientific journals and presented at conferences. Some of the research data will be made available in open, online databases – https://www.humancellatlas.org/ for example. You will not be identifiable from this online data. Sharing the results of the study in this way means it can continue to contribute to scientific progress in future.

15. More information about taking part

Can I stop taking part during the study?
You can stop taking part in all or any part of this study, at any time and without giving a reason, but you must talk to your study doctor or nurse first. They can advise you about any concerns you may have. If you decide not to have the flu vaccine or the FNA, we will ask to continue collecting information about you until the end of your participation in the study. This is important, because it helps us to ensure that your wellbeing is protected, and the results of the study are reliable. A decision to stop taking part will not affect the care you usually receive from your doctor.

Can I still have a COVID-19 vaccine, or another flu vaccine, if I take part in the study?
You can receive a COVID-19 vaccine if you take part in the study, **but please speak to us first so we can advise on the timing**.
If you have the flu vaccine as part of the study, you should not need another flu vaccine until the following year.

How will your samples be collected and stored?
The samples you donate will be stored and tested by researchers at Imperial College London and the University of Oxford. Remaining samples may be stored at Imperial College London and University of Oxford for future authorised research. Access to your samples will be restricted to authorised staff.

Future research
Data from this research or remaining samples may be provided to researchers running other studies at Imperial College London, at the University of Oxford, and in other research organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with relevant legislation, ethics and NHS research policy requirements. We won't share information with others that can identify you. It will not be used to make decisions about future services available to you, such as insurance.

Who is sponsoring and funding the study?
This study is sponsored by Imperial College London and funded by the Chan Zuckerberg Initiative.

Who has approved the study?
This study has been reviewed and approved by the London - Central Research Ethics Committee, by the research management team at the NIHR Imperial Clinical Research Facility, by the study scientists at Imperial College London and the University of Oxford, and by two independent lay members who represent participant involvement in study design.

Will my healthcare be affected?
We do not expect any effect on your usual healthcare. However, the health check-up for the study might reveal unexpected and important information about your health. We would discuss the information with you, and we could refer you to your GP. The check-up will include tests for hepatitis and HIV, and the results will enter your NHS healthcare record. We will report new cases of hepatitis and HIV infection to the national surveillance systems.

What if something goes wrong for me?
As Sponsor, Imperial College London holds insurance policies which apply to this study. If you experience harm or injury because of taking part in this study, you will be eligible to claim compensation without having to prove that Imperial College London is at fault. This does not affect your legal rights to seek compensation.
If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during this study then you should immediately inform the Investigator: Dr Katrina Pollock (k.pollock@imperial.ac.uk). The usual NHS mechanisms are also available to you. You may also contact the Imperial Research Governance and Integrity Office: 020 7594 1862, rgit@imperial.ac.uk

How will we use information about you?

Your GP will be notified if you participate in the study. We may request information from your GP, or access your GP record, if we need details about your past medical history.

Your details will be entered on The Over-volunteering Prevention System (TOPS), which aims to prevent participants from taking part too frequently in clinical research studies. This is not a public database and can only be accessed by various registered clinical sites.
Imperial College London is the sponsor for this study and will act as the data controller for this study. This means that it is responsible for looking after your information and using it properly. Imperial College London requires the NHS site hosting the study to keep your personal data for 10 years after the study has finished in relation to data subject consent forms and other readily identifiable data.

We will need to use information from you, from your medical records and from your GP for this research project. This information will include your NHS number, name, and contact details. People will use this information to do the research or to check your records to make sure that the research is being done properly. However, this information will not be released by the NHS site hosting the study. All of your information leaving the site will be identified with a code number instead. Therefore, people who do not need to know who you are will not be able to see your name or contact details.

The NHS site, Imperial College London and its collaborators will keep all information about you safe and secure. Some of your information will be made available in open, online databases – https://www.humancellatlas.org/ for example. The databases must follow Imperial College London's rules about keeping your information safe. Any reports will be written in a way such that no-one can work out that you took part in the study.

Legal basis

As a university Imperial College London uses personally identifiable information to conduct research to improve health, care and services. As a publicly funded organisation, Imperial College London has to ensure that it is in the public interest when it uses personally identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, Imperial College London will use your data in the ways needed to conduct and analyse the research study.
Health and care research should serve the public interest, which means that Imperial College London has to demonstrate that its research serves the interests of society as a whole. It does this by following the UK Policy Framework for Health and Social Care Research.

International transfers

There may be a requirement to transfer information to countries outside the European Economic Area (for example, to a research partner). Where this information contains your personal data, Imperial College London will ensure that it is transferred in accordance with data protection legislation. If the data is transferred to a country which is not subject to a European Commission (EC) adequacy decision in respect of its data protection standards, Imperial College London will enter into a data sharing agreement with the recipient organisation that incorporates EC approved standard contractual clauses that safeguard how your personal data is processed.

Sharing your information with others

For the purposes referred to in this privacy notice and relying on the bases for processing as set out above, Imperial College London will share your personal data with:

- The University of Oxford – data such as your age, ancestry and the dates you gave samples and were given the flu vaccine will be shared so that scientists at the university can categorise and interpret the results of the tests they do on your samples
- Open, online databases, https://www.humancellatlas.org/ for example – the same information above, along with test results, will be made available to other scientists in publicly-accessible global databases, for the advancement of science.

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.

- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.
- If you agree to take part in this study, that entails future research using your data saved from this study at https://www.humancellatlas.org/ for example.

Where can you find out more about how your information is used

You can find out more about how we use your information:

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team
- by sending an email to imperial.crf@nhs.net
- by ringing us on 020 3313 8070

Complaint

If you wish to raise a complaint on how we have handled your personal data, please contact Imperial College London's Data Protection Officer via email at dpo@imperial.ac.uk, via telephone on 020 7594 3502 and/or via post at Imperial College London, Data Protection Officer, Faculty Building Level 4, London SW7 2AZ.

If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO). The ICO does recommend that you seek to resolve matters with the data controller (Imperial College London) first before involving the regulator.

Thank you for taking the time to consider taking part in this study.

Consent Form **Subject ID: _____**

Study Title: An experimental medicine study of seasonal influenza vaccination responses in Lymph nodE single-cell Genomics in AnCestrY (LEGACY01)

Study code: LEGACY01 **IRAS ID: 314444**

Write initials in box

I confirm that I have read and understood the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving any reason, and without my participation in the main study, medical care or legal rights being affected.	
I understand that my medical records may be reviewed by responsible individuals from Imperial College London, University of Oxford or the Uganda Virus Research Institute and regulatory authorities. I understand that my data will be treated confidentially and give permission for these individuals to have access to my records.	
I understand that my GP will be informed of my participation in research and may give a summary of my relevant medical history, and that my personal data will be entered into the TOPS database.	
I understand that I may not benefit directly by participating and that the data is for current and future benefit to research.	
I consent to undergo all study procedures including vaccination and ultrasound guided fine needle aspiration of lymph nodes.	
I understand that my stored samples will be shipped to collaborating researchers in the study.	
I understand that my personal identifying data will be held securely in a database at the NIHR Imperial Clinical Research Facility.	
I understand that my research data will be analysed, reported, and shared in an online database in a way that I cannot be identified.	
I understand that my research data will include information about genetics. I consent to this information being used for research.	

I understand that my research data will include biological and clinical information about ancestry. I consent to this information being used for research.	
I understand that Imperial College London is the sponsor of the trial and is responsible for the processing of my personal data. I understand that, in accordance with the provisions of the General Data Protection Regulation, I have the right to access my personal data, to correct them, and to object to the collection and transmission of data that may be used in the context of this research.	
I understand that if I withdraw my consent to participate, collected data will be kept legally and confidentiality to avoid any bias in the study, and to ensure my security. I understand that my rights to access, change or move my data are limited.	
I give my consent for my de-personalised data (without personal identifying details) to be used for future research and training for which it will be processed in accordance with the data protection regulatory framework. I understand that some of these projects will be led by other scientists in this country and abroad. I understand that the results of these research projects are unlikely to have any implications for me personally. I understand that I will not be identifiable from this data.	
I agree to take part in the above study.	

Optional consent for future use of samples

Write initials in box

My stored samples may be used for future approved research, carried out by other researchers in this country and abroad. I understand that the results of these research projects are unlikely to have any implications for me personally.

I agree ☐

I decline ☐

Optional FNA Visit

Write initials in box

I agree to the optional FNA visit. I understand that consent for this is not a requirement to participate in the study. I understand that up to six participants will take part.

I agree ☐

I decline ☐

Name of participant	Date	Signature
Name of person taking consent	Date	Signature