GERMINATE Participant Information Sheet

GERMINATE is a study to compare how immunity forms in the nose and lung following flu infection or vaccination by nasal spray. In this study, healthy volunteers aged 18-55 years will be given one or the other and we will take samples to understand how to better prevent infection with flu.

Study Title:	**GERMINATE: GEneRating Mucosal immunity after INfluenzA infection and vaccination in lung and lymphoid TissuE**
PIS Version:	Version 5.0 16-JAN-2026
Sponsor and Sponsor Ref:	Imperial College London 172251
Chief Investigator:	Professor Christopher Chiu Department of Infectious Disease, Imperial College London
Study Location:	Imperial College Healthcare NHS Trust
Study Team Contact Details	Email: imperial.humanchallenge@nhs.net Phone: 07872 850212

- We would like to invite you to take part in this research study.
- Before you decide it is important for you to understand why the research is being done and what it will involve.
- Please take time to read the following information carefully and discuss it with others if you wish, after which one of our team will go through this information with you.
- Please ask us if there is anything that is not clear or if you would like more details.
- You do not have to take part in this study and can change your mind at any time.

IMPORTANT

There are two arms in this study.

- General information on the study that is applicable to **all participants** taking part in either study arm will be in **blue/black**.
- Information specific to the **Vaccine Arm** of the study will be in a **green box.**
- Information specific to the **Challenge Arm** of the study will be in an **orange box.**

Participants in this study will either be enrolled into either the Vaccine Arm OR the Challenge Arm. You will know which arm you are taking part in and you will **not** be randomly assigned to the study arm. We will do our best to take your study arm preference into account, but we cannot guarantee you enrolment into a specific arm. We therefore ask that you keep an open mind about taking part in either arm and read the information for both study arms.

Key points you should know before making your choice:

- If you take part in this study, you will either receive a live-attenuated influenza vaccine by nasal spray and be followed up through clinic visits OR you will be given an Influenza virus (the cause of flu) by either nasal spray or drops in the nose and required to stay in the hospital for a minimum of 9 days after receiving it.
- You may be given a choice on which arm you can take part in (the Vaccine Arm or the Challenge Arm) but this will depend on the ongoing recruitment process.

- If you take part in the Vaccine Arm, you may develop mild symptoms experienced after nasal influenza vaccination, most commonly blocked or runny nose, cough, raised temperature and muscle aches.
    - There is a very small risk that you could experience more serious side effects such as an allergic reaction to the vaccine but this is very rare and the clinical research team are trained in how to deal with and treat allergic reactions. We will go through these risks with you in detail.
- If you take part in the Challenge Arm, you may develop flu-like symptoms, including runny/blocked nose, cough, muscle aches, tiredness and fever. These will get better by the time you leave quarantine.
    - There is a very small risk that you could become more unexpectedly unwell if you develop flu, but this is extremely rare in healthy people aged 18-55 years and you will be cared for in the hospital during the time you have the most symptoms. We will go through these risks with you in detail.

Who is eligible to take part on this study?

Before reading this Participant Information Sheet (PIS) further, please read the study's key eligibility criteria to see whether you might be suitable to take part.

Eligibility Criteria:

- ✓ You must be 18-55 years old (inclusive) at the time of enrolment.
- ✓ You must be willing and able to commit to the study procedures and visits.
- ✓ You must be in good health with no clinically significant medical conditions.
- × You must NOT have a history of, or currently active, clinically significant illness. Examples include:
    - Cancer.
    - Cardiovascular, thromboembolic or cerebrovascular diseases such as high blood.. pressure, stroke, heart failure and bleeding or clotting disorders.
    - Respiratory diseases such as asthma, COPD and cystic fibrosis.
    - Diabetes (Type 1 or 2).
    - Any immunodeficiency or autoimmune disease.
- × You must NOT have used inhalers or inhaled steroids in the last 12 months.
- × You must NOT have had a cold or sinusitis in the past 6 weeks.
- × You must NOT have received blood or blood products, or lost most than 550mL of blood in the last 3 months, including through blood donation.
- × You must NOT have a significant history of using recreational drugs or excessive amounts of alcohol.
- × You must NOT currently take drugs through the nose or by inhalation.
- × You must NOT be a current regular smoker (including the use of e-cigarettes)
    - If you are an ex-smoker, you must have quit more than 3 months ago and not smoked more than 5 pack years in your lifetime (use the Smoking Pack Years Calculator: https://www.smokingpackyears.com/).
- × You must NOT have severe allergies or intolerances, for example, to foods or medications, that cause severe allergic reactions such as anaphylaxis.
- × You must NOT be in close domestic contact (e.g. live with) anyone under 3 years old, or anyone over the age of 65 years or anyone who has a problem with their immune system or has a chronic lung condition.
- × You must NOT have taken part in another human viral challenge study in the last 6 months
- × You must have a Body Mass Index (BMI) between 18kg/m2 and 28kg/m2

If you are a person of child-bearing potential:

- × You must NOT be currently pregnant.
- × You must NOT be breastfeeding or have been breastfeeding within the last 6 months.
- × You must NOT have been pregnant in the last 6 months.
- ✓ You must be willing to use effective contraception, such as the pill, an IUD (the coil), the implant or injection, or you must use condoms, until 6 months after enrolment.

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1. What is the purpose of the study?

Influenza ('flu') is one of the most common causes of lung infection. Seasonal influenza affects between 10 and 46% of the population each year and causes around 12 deaths in every 100,000 people infected, mostly in frail elderly and people with pre-existing heart and lung problems. There are three main types of flu virus: Influenza A, B and C. Influenza A causes most seasonal influenza cases. The virus can also be found in many different animals, such as birds and pigs, and can spread between them and into humans, potentially causing pandemics.

Flu is transmitted by droplets, as well as aerosols and secretions from the mouth or nose of an infected person. It can also be spread by hand to mouth contamination from surfaces. Up to half of flu infections can show no symptoms, so it's possible to spread it without knowing you're infected. The incubation period, when someone is infected but yet to show symptoms, can be 1-5 days (average 2-3 days).

Common symptoms of flu include fever, chills, headache, muscle and joint pain and fatigue, as well as a cough, sore throat or stuffy nose. Most healthy people recover within 2-7 days. Complications are rare but more common in children under 6 months, older people, those with underlying health problems such as lung or heart disease or who are immunosuppressed, as well as pregnant women.

The best way to protect against flu is through vaccination. Although influenza vaccines are available, these currently need to change every year to overcome rapid changes in the virus and are not completely protective. We urgently need better vaccines that can:

1. Protect against many different flu strains
2. Provide longer-lasting protection
3. Stop the spread of flu between people

The flu vaccine routinely used in the UK for adults over the age of 18 is given by a jab in the arm. How well this vaccine protects against flu infection depends on several factors, such as the circulating strain of the flu virus, and differences in how each individual responds to it. Because the vaccine given this way doesn't completely protect against flu infection, there is a need to better understand how the body's immune system fights flu in the nose, throat, and lungs. As the flu virus gets into the body through the airways, focusing on the immune system in the airway can help design better vaccines that could block the spread of flu outbreaks.

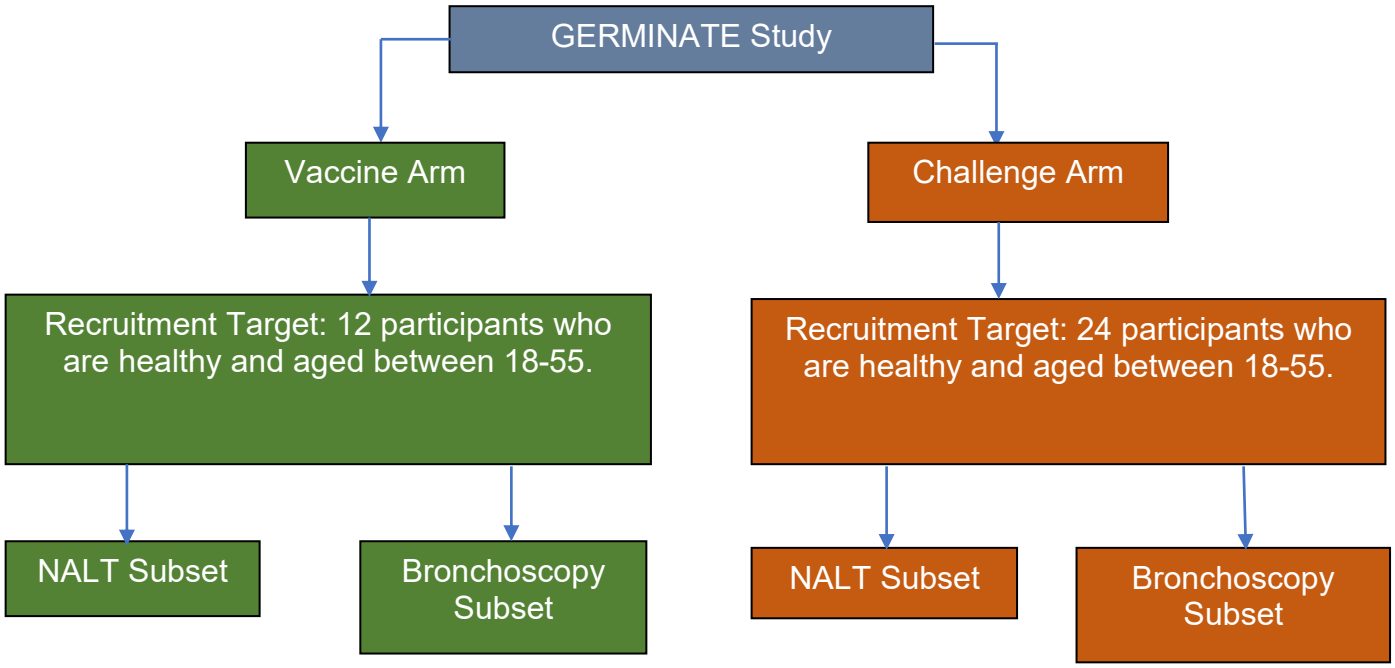
In this study, we'll compare the immune response when people get infected with flu versus when they receive a nasal spray flu vaccine. We will do this by taking blood, swabs and upper airway samples. This includes taking washes from the nose (nasal lavage), using a soft paper strip to collect fluid from the lining of your nose, and taking some cells from the lining of the nose called a nasal scrape. In addition, we will take samples from the lower airway using a procedure called bronchoscopy in some participants. In another group of participants, we will take samples of their lymphoid tissue from the back of the nose. Lymphoid tissue in the upper airway (nose and throat) - which is similar to the tonsils - has been shown to play an important role in the immune response to a flu vaccine given via the nose in children. This tissue is thought to play a role in helping create longer term and stronger immunity to flu but this is not well understood. The details of all the sampling procedures are explained further in Section 7. Similar studies to this have been done many times in the past (at Imperial and elsewhere), including in volunteers with asthma and other lung diseases, with no serious side effects.

2. Why have I been chosen?

We are inviting you to take part in this study because you have expressed an interest in taking part. Before participating in this study, we need to make sure that you fully understand and agree to what is going to happen and that you are healthy and unlikely to experience any side severe side effects from the vaccination or get severely ill from the virus.

Please make sure you read and understand this PIS before you make the decision to take part. If you have any questions or concerns, please ask a member of the study staff and, if you want to, discuss any of this information with your family, friends, and your General Practitioner (GP) before you decide to take part. If you do not want to, you do not have to take part in this study as it is voluntary. Even if you do consent to take part, you can withdraw at any time without giving a reason. This will not affect your healthcare now or in the future.

3. What are the two arms of the study?



For this study, we aim to recruit up to 12 participants in the Vaccine arm and 24 participants in the Challenge arm (36 in total), who are healthy and aged between 18 – 55 years.

Vaccine Arm

Participants in the Vaccine Arm of the study will be given a Live-attenuated influenza vaccine (LAIV). The vaccine is called Fluenz and contains live but weakened flu viruses. It is commonly available and has been widely used for many years, has been tested extensively for safety, and is licensed for use in children in the UK by the Medicines and Healthcare Products Regulatory Agency (MHRA). The vaccine is grown in eggs and contains highly purified porcine gelatine which acts as a stabiliser to keep the vaccine safe and effective during storage.

Short-term risks and symptoms of live-attenuated influenza vaccination:
If you take part in the Vaccine Arm, you may develop mild symptoms commonly experienced after nasal influenza vaccination including runny nose, cough, headache, decreased appetite and feeling "under the weather" (malaise). Less commonly, you may experience slightly raised body temperature, and muscle aches. These symptoms typically last no more than 1-2 days after vaccination.

As with any vaccination, there is a risk of rare, but serious side effects, such as an allergic reaction (hypersensitivity). These may be related to an over-reaction of the immune system. Severe allergic reactions to vaccines, called anaphylaxis are very rare (less than 1 in 10,000), but can be cause serious problems with breathing and very low blood pressure. Medication for treating allergic reactions is always kept in the clinic room in the case of this unlikely event, and the study doctors and nurses are appropriately trained in the emergency treatment of anaphylaxis.

Other rare risks of live-attenuated influenza vaccination:

- There have been very rare (less than 1 in 10,000) reports of Guillian-Bare syndrome.
    - This is a condition that mainly affects the nerves of the feet, hands and limbs, causing problems such as numbness, weakness and pain. It can be treated, and most people eventually make a full recovery, but it can occasionally be life-threatening and some people are left with long-term problems. It can be caused by infections including the flu and stomach bugs (gastroenteritis), and sometimes the immune system mistakenly attacks and damages nerves.
- No data exists regarding the possible effects of Fluenz on male or female fertility.

Challenge Arm

Participants in the Challenge Arm will be given an Influenza virus. This influenza virus has been used in many studies previously, where it has been shown to be safe. It has been made specifically for human studies under the strictest conditions. It has been carefully tested to ensure it is free from other bacteria or viruses. Unlike medicines, there are no special rules for preparing viruses in this country, but the conditions for producing it complied fully with the US Food and Drug Administration (FDA – the US organisation that approves foods and medicines) approved methods. The virus is grown in eggs so you will not be able to enrol if you are allergic to eggs or egg products.

Short-term risks of influenza challenge:
The most common side symptoms you might experience are typical of a common cold or flu and include mild fever, tiredness, headache, feeling under the weather (malaise), blocked or runny nose, sore throat, cough and sneezing. These symptoms usually last for 3-4 days. Symptoms may last for up to two weeks, but this is unusual. Very rarely, healthy people can develop complications from flu, such as pneumonia, which can sometimes be life-threatening but there are antiviral medicines available to treat this.

You will be carefully monitored during the quarantine period and if you become more unwell, you care will be transferred to the clinical team within the main hospital, who will provide full treatment.

Long-term risks of influenza challenge:
Sometimes, symptoms related to flu drag on for longer than 2 weeks. How often this happens is not clear but it is less frequent than "long COVID" and generally improves steadily. The risk of longer term symptoms from deliberate infection with Influenza are low and have not been observed in participants who have previously taken part in influenza challenge studies.

Transmission to others:
We ask participants to remain in quarantine for 10 days if they become infected from the influenza virus to prevent the spread of the virus in the community where vulnerable people may become infected and experience more serious complications of flu.

The study team will wear personal protective equipment (PPE) after you have been inoculated to prevent them for getting influenza virus or spreading it to others.

4. Are there other risks of taking part?

Pregnancy
For this study, for both the vaccine and challenge arm, you cannot take part if you are pregnant. If you are likely to become pregnant during the study (including the follow-up period after quarantine), you should not take part. You must notify the study doctor if you or your partner become(s) pregnant during the study. If you do become pregnant, your study participation will be stopped, your pregnancy will be monitored, and we will follow up on your health to ensure there are no long-term complications.

If you are female:
You must not donate eggs within 6 months of being given the study virus/receiving the vaccine.
You must agree to use an effective method of contraception from 2 weeks before to 6 months after viral challenge/vaccination.
Acceptable methods of contraception include:

- the coil
- female sterilisation
- oral, injected or implanted hormonal methods of contraception
- barrier methods such as condoms
- true abstinence from heterosexual sex
- Female participants with a vasectomised male partner, where the vasectomised male is her sole partner.

If you are male:
You must not donate sperm within 6 months of being given the study virus/vaccination.
You must agree to use an effective method of contraception from the date of viral challenge/vaccination to 6 months after viral challenge/vaccination including:

- barrier methods such as condoms
- true abstinence from heterosexual sex

The study doctor will discuss the birth control methods allowed during the study and for the period of time they will be needed after viral challenge. Please share this information with your partner and talk to your GP or the study staff to decide the best method of birth control.

Ionising Radiation from Chest X-Ray
If you take part in this study you will have a chest X-ray. This will be extra to those that you would have if you did not take part. This procedure uses ionising radiation to form images of your body and provide your doctor with other clinical information. Ionising radiation may cause cancer many years or decades after the exposure. We are all at risk of developing cancer during our lifetime. 50% of the population is likely to develop

one of the many forms of cancer at some stage during our lifetime. Taking part in this study will add only a very small chance of this happening to you.

5. Do I have to take part?

No, taking part in research is entirely voluntary. It is up to you to decide whether or not to take part.

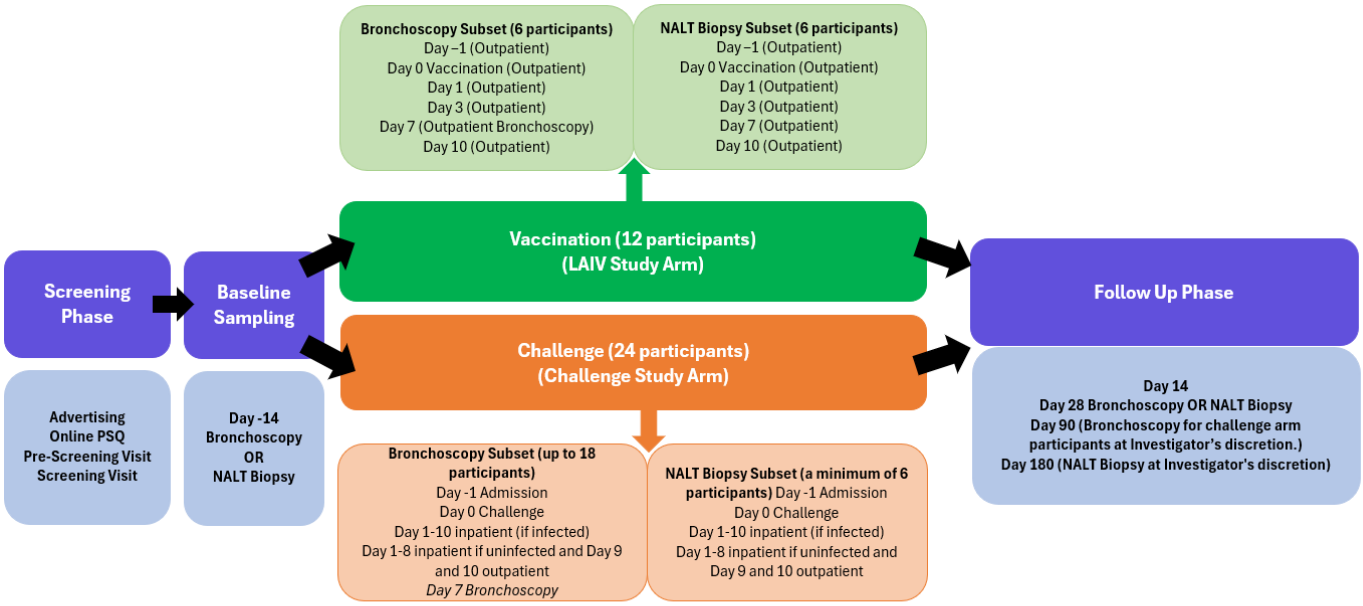
If you are not eligible to take part, you will be contacted by post, email or phone, thanking you for your time and explaining that you were not eligible.

If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive. You will be paid for the time you have spent in the study.

6. What does the study involve?

The study comprises 4 phases: Screening Phase, Baseline Sampling, Vaccination OR Challenge Phase and the Follow Up Phase.

Study design



Pre-Screening

Once you have registered your interest in taking part with the study team, either by completing the online pre-screening questionnaire, or by contacting the study team directly, your details will be added to a database along with your health information. The study team will then contact you by phone to ask further questions pertaining to the full study inclusion/exclusion criteria. If inclusion/exclusion criteria are provisionally met based on answers to these questions, they will then invite you for a pre-screening visit and send a confirmation email with the visit details.

Pre-Screening visits will be conducted at Imperial Clinical Research Facility (ICRF). The study team will discuss the pre-screening process with you and answer any questions you may have. If all your questions

have been answered and you would like to go ahead with the pre-screening visit, the study doctor or nurse will ask you to read, sign and date the pre-screening consent form. They will then also sign this consent form and provide you with a copy.

Following informed consent, the following assessments will take place at the pre-screening visit:

- Confirmation of your name, age, gender, and contact details
- Brief eligibility check
- Blood sampling for influenza antibodies

Once the results of the antibody tests have come back, if you are still eligible to take part, you will then be invited for a full screening visit. If you are not eligible the study team will contact you by phone, email or letter to explain the outcome of the antibody test results and thank you for your interest in taking part in the study. If you are not eligible to take part, any leftover samples will be destroyed.

You will be paid £30 for attending this initial pre-screening visit.

Screening

Screening visits will be conducted at Imperial Clinical Research Facility (ICRF). These visits can happen up to 90 days in advance of Day 0 (vaccination or viral challenge). First, the study team will discuss the full screening visit process and the main study with you and answer any questions you may have. If all your questions have been answered and you would like to go ahead, the study doctor or nurse will ask you to read, sign and date the relevant consent form. They will then also sign this consent form and provide you with a copy.

Following informed consent, the following assessments will be completed at screening:

- Confirmation of name, demographics and contact details
- Review of the eligibility criteria to make initial eligibility assessment
- Review full medical and medication history including questions about past and present health including clinically significant family history
- Examination for signs of illness or disease (a physical examination).
- Height and weight measurements to calculate BMI
- Pulse rate, blood pressure, temperature and breathing rate checked (Vital Signs).
- Quality of life questionnaires including the GAD-7 Anxiety Test questionnaire and PHQ-9 Depression Test questionnaire.
- Electrocardiogram (12-Lead ECG)
- Lung function test (spirometry)
- Optional: Peak Inspiratory Flow measurement
- Nasal sample: Mid-turbinate swabs
- Urine samples to test for:
    - Pregnancy (for females of childbearing potential)
    - Drugs of abuse & nicotine
- Blood samples obtained for:
    - Safety blood tests, including full blood count, renal and liver function tests.
    - Hepatitis B and C and/or HIV (the virus that causes AIDS)
    - Human leukocyte antigen (HLA) typing (genetic analysis)
        - The HLA typing sample will be collected at screening from all participants, but will be reserved and tested at a later date once your eligibility has been confirmed. If you are not eligible to take part, this sample will be destroyed.
- Chest X-Ray

You will be asked to bring proof of your National Insurance Number and ID with you to this visit. If you do not have a National Insurance Number, you will need to bring your passport. This is so we can check and register you on The Over-Volunteering Prevention System (TOPS).

We will also need to review your medical history records. We may be able to view some of your medical history during screening (after informed consent) using the hospital's electronic patient record system (such

as Cerner) but we will also send a letter and enclose your consent form to your GP practice so they can send us a summary. If your GP practice is signed up to ACCURX, we can use this system to view your medical records. The study nurse or doctor will request access to view your record and it will send an authorisation code to your mobile phone. You will then share the authorisation code with the study team so that they can get access to the summary. Again, this will only be looked at once you have signed the informed consent form for the study. Once all the test results and the GP summary has come back, the study team will review everything to determine if you are eligible to take part in the study. After deciding to take part in this initial screening, you can still change your mind at any time and withdraw from further assessments and study participation.

If, based on the screening results, you are eligible for the study, you will be invited to take part in either the Vaccine Arm or Challenge Arm of the study.

If you are not eligible, because the test results have identified something that makes you ineligible for the study, the study team will discuss this with you. If any abnormal results are found and deemed clinically significant, we will ask for your permission to inform your GP so they can arrange to follow up with you. Future mortgages, travel insurance, private healthcare or life insurance may be affected if a previously unrecognised problem is found during screening.

You will be paid £75 for your time for attending a screening visit regardless of whether you are found to be eligible for the study or not

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Day -14 Baseline Visit

There will be a baseline visit conducted around 14 days prior to Day 0 for each study arm.

- For the Vaccine Arm (up to 12 participants), 6 participants will undergo a bronchoscopy and 6 participants will undergo a NALT biopsy.
- For the Challenge Arm (up to 24 participants), a minimum of 6 participants will undergo a NALT biopsy and the remainder of the participants will undergo a bronchoscopy.

You will only undergo either the bronchoscopies or the NALT biopsies, not both. While we will try to take preferences into account, the study doctor will assign you to one or the other. All participants will also have the specified the blood and nose/throat sampling.

During this baseline visit, the following assessments and procedures will be conducted:

- Examination for signs of illness or disease (a physical examination).
- Pulse rate, blood pressure, temperature and breathing rate checked (Vital Signs).
- Bronchoscopy OR NALT Biopsy - more details can be found in Section 7.
    - Females of child-bearing potential will have a urine pregnancy test prior to the procedure
- Blood samples
- Upper airway samples including:
    - Nasosorption
    - Mid-turbinate swab
    - Nasal wash
    - Saliva

Vaccine Arm Visits (Day -1, Day 0, Day 1, Day 3, Day 7, Day 10)

Participants taking part in the vaccine arm will be invited to the vaccination visit after they have been deemed fully eligible to take part and have undergone the Day -14 baseline visit.

The vaccination visit will take place at the Imperial Clinical Research Facility (ICRF).

Day -1 (day before vaccination)

You will be asked to attend the day before your vaccination. We will ask you a few questions to check there have been no new problems since your previous visit. We will check your vital signs, take blood samples, a saliva sample and collect as a nasal sample that we will test to make sure you are not currently infected with any other respiratory viruses. If you are a woman of childbearing potential, you will be required to provide a urine sample for a pregnancy test, which needs to be negative to be able to continue in the study.

Day 0 Vaccination (approximately 3 hours)

If your test confirms that you do not have currently have any other respiratory viruses, your eligibility will be reviewed with a study doctor to confirm you are eligible to receive the vaccination. We will check your vital signs, do a physical examination and conduct an ECG and spirometry test.

After all pre-vaccination assessments and health checks are complete, you will receive the Fluenz vaccine by nasal spray.

Fluenz Vaccine

The vaccine being used in the Vaccine Arm of this study is Fluenz which is a nasal spray vaccine manufactured by AstraZeneca. Fluenz vaccine viruses are grown in chicken eggs. Each year the vaccine targets strains of influenza, following the annual recommendations by the World Health Organisation.

This study does **not** involve any placebo so if you are enrolled in the Vaccine Arm, you will receive the Fluenz vaccine by nasal spray.

You will not be given Fluenz:

- if you are allergic to gentamicin, gelatin or any of the other ingredients of this vaccine. The study doctor will check this with you.
- if you have ever had a severe allergic reaction to eggs or egg proteins. The study doctor will check this with you.
- if you have a blood disorder or a cancer that affects the immune system. The study doctor will check this with you.
- if you have been told by your doctor that you have a weakened immune system as a result of a disease, medicine or other treatment. The study doctor will check this with you.
- if you are already taking acetylsalicylic acid (a substance present in many medicines used to relieve pain and lower fever). This is because of the risk of a very rare but serious disease (Reye's syndrome).

The study doctor will check all the above with you before prescribing you the vaccine.

The vaccine will then be administered by a member of the study team. After receiving the vaccine, you will be observed for at least 30-60 minutes to ensure you do not experience any immediate reactions to the vaccine before being allowed to go home. You will be asked to complete a symptom diary for 14 days.

Day 1, 3, 7 and 10 (Outpatient Follow Up Visits)

You will attend on Day 1 (the day after receiving the vaccine), Day 3, Day 7 and Day 10 for safety review and for the study team to collect samples to assess the early immune responses to vaccination. This is summarised below for each visit:

Assessments and procedures	Day 1	Day 3	Day 7	Day 10
Review of any vaccine related symptoms	✓	✓	✓	✓
Vital signs	✓	✓	✓	✓
Physical exam				✓
ECG, Spirometry +/- peak inspiratory flow		✓		✓
Blood samples	✓	✓	✓	✓

Nasal, throat and oral swabs/samples	✓	✓	✓	✓
Bronchoscopy (for those in the bronchoscopy subset)			✓	

These visits should take around 1 hour, except for the Day 7 visit if you are undergoing a bronchoscopy procedure.

The study visits will take place between 09:00am-11:30am, Monday – Friday, excluding the bronchoscopy or NALT visits, which may start at 07:00am. The study team are unable to accommodate visits outside of these times due to the laboratory processing time that is required on the samples collected from you.

Challenge Arm Quarantine Stay (Day -1 to Day 10)

Participants taking part in the challenge arm will be invited to the quarantine stay after they have been deemed fully eligible to take part and have undergone the Day -14 baseline visit. The quarantine will take place at the Imperial Clinical Research Facility (ICRF).

Day -1 Admission Day

You will be admitted for the quarantine stay on the morning of Day -1 (the day before we plan to give you the study virus). The study team will orientate you to your room or shared bay. After this the study doctor will examine you to make sure you remain in good health. This will be followed by measuring vital signs, completing some mental health questionnaires, a lung function test (spirometry), 12-lead ECG, and then we will collect bloods, swabs and nasal samples.

We may also collect baseline samples from the environment around your bedspace, a mask which you'll wear and an exhaled breath collection known as PExA breath sample.

We will also test you for other cold viruses, including SARS-CoV-2, and in the case of a positive result, you will be excluded from the study. You might then be invited back once it has been 6 weeks since your positive result if the study is ongoing and should you still wish to continue.

Day 0 Inoculation Day

On Day 0, you will be inoculated with the influenza study virus. Before this, the study doctor will examine you to make sure you remain in good health. This will be followed by measuring vital signs, 12-lead ECG, spirometry taking bloods, swabs and nasal samples. Females of child-bearing potential will need to provide a urine sample for a pregnancy test prior to the procedure. The influenza study virus will be given as drops or by nasal spray into both nostrils. You will be asked to lie flat for the next 30 minutes and not to blow your nose for the rest of the day. The staff will observe you for the next hour to make sure you do not experience any early side effects, including local discomfort or reactions that might indicate an allergic response.

Day 1 to Day 8/10

You will stay for the next 8-10 days. Blood, swabs and nasal samples will be taken, and the symptom diaries completed daily.Other samples such as breath collection and samples from the environment around you may be collected during your quarantine stay. Staff from the study will visit every day and will be contactable by the ward's nursing staff 24 hours a day for any queries.

The reason we have this inpatient stay is to reduce the risk of spreading infection to vulnerable members of the community. Whilst at the facility, you will need to remain within your designated bay or room so that staff and other people are not exposed to influenza. Wherever you have the inpatient stay, there is free Wi-Fi, and you are free to bring laptops, mobile phones and other items with you for work or entertainment.

Food, drinks and snacks are provided, and you may bring as many additional snacks with you as you wish. Towels, and linen are provided during your stay. You are welcome to visit the inpatient facility in advance; please let us know if you wish to do so.

If at Day 8 you are symptom free and have no indication of influenza infection, you may be discharged. This will be a decision made by the study doctor.

If you continue to have symptoms or the study doctor feels it is necessary, you may remain an inpatient up to Day 9 or Day 10. You will be reviewed each day prior to this decision. If you are discharged before Day

10, you will need to attend a daily outpatient appointment for samples to be taken and your symptom diary reviewed.

If you are discharged against medical advice (i.e. you leave the study early), we advise that you confine yourself to your home and to strictly avoid any close contact with young children, the elderly or other high-risk individuals until after Day 10 and ask that you sign a self-discharge form.

Both Study Arms:

Follow Up Visits (Day 14, Day 28, Day 90 and Day 180)

All participants will have follow up visits on Day 14, Day 28, Day 90 and Day 180.

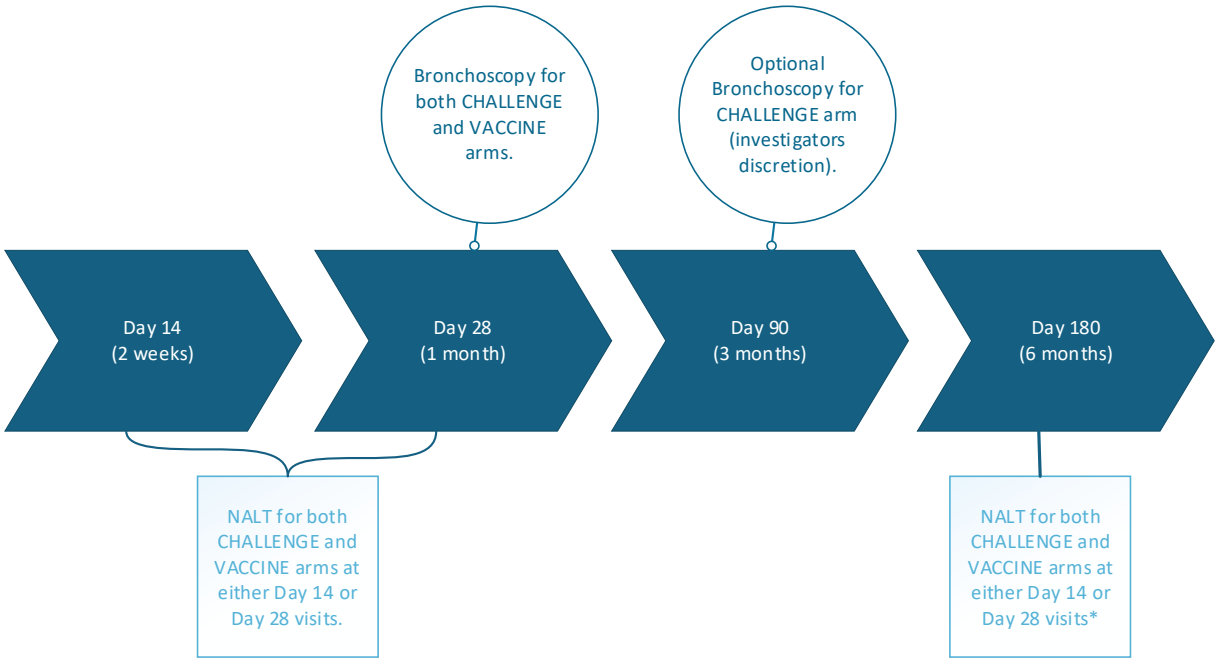
Study Visit Information

- Regular visits: **09:00–11:30, Monday–Friday**
- Bronchoscopy/NALT visits: **may start at 07:00**
- Visits outside these times **cannot be accommodated** due to sample processing requirements.

Follow-up Visit Windows

- Each visit has a flexible window (e.g., Day 14 ± 2 days).
- The study team will contact you to schedule; please attend within the timeframe and offered slots.

At these appointments you will be asked about any changes in your health. After this, samples will be taken. The last visit will be approximately 6 months after the start of the study.



The follow up visits will include blood and urine samples, nose and/or throat swabs, vital signs, physical exam, and other assessments and procedures as detailed in the Schedule of Events in the Appendix.

For the bronchoscopy subset of participants, there will be a bronchoscopy on Day 28 and there may be an optional bronchoscopy procedure on Day 90 for challenge arm participants only, at the investigator's discretion.

For the NALT biopsy subset, there will be a biopsy procedure on either Day 14 OR Day 28, and there may be an optional NALT biopsy procedure on Day 180 at the investigator's discretion. This will be the first time that NALT biopsy samples have been looked at following controlled influenza infection or vaccination and as

such, we have currently only definitely included a baseline sample and one sample collection on Day 28. If there are no meaningful changes detected between the baseline sample and the Day 28 sample for the purposes of our research, then we will not perform another biopsy on the Day 180 as it would not be acceptable to perform this invasive procedure if no changes are expected. If there are meaningful changes detected, then we would like to additionally collect a biopsy sample at Day 180 to understand how long these changes last for and differences between infection and vaccination.

Every visit is crucial to the study.
Please only agree to take part in the study if you expect to be able to attend all visits.

7. What tests and procedures will I have during the study?

During the study, we will look after you at all times and monitor your health as necessary. If the doctor wants to confirm a test result, they may ask you to have an extra test.

Tests/Procedures	
Documents	
Informed Consent Form	You will be given an informed consent form to read and sign before any study procedures are performed.
Symptom Diary Card	You will be asked to complete a symptom diary twice a day which asks you questions about how you are feeling and any cold-like symptoms you may have.
Mental Health Questionnaires	You may be given two short questionnaires. The Patient Health Questionnaire (PHQ-9) and the Generalised Anxiety Disorder Questionnaire (GAD-7).
Measurements/Scans	
Height and weight	You will be asked to remove your shoes and then stand against a height stick to record your height. You will also be asked to stand on scales to record your weight.
Vital Signs	We will measure your heart rate, breathing rate, blood pressure, oxygen saturation and temperature). Using an observation machine, we will place a cuff around your arm that will inflate and then deflate to measure your blood pressure, a small device will be clipped onto your finger to check the amount of oxygen in your blood, and it will also tell us your heart rate. A study doctor/nurse will measure your breathing rate by watching your chest expand as you inhale. A temperature probe will be given to you to place under your tongue to measure your temperature.
Physical Examination	A study doctor will look at your skin, listen to your chest, feel your abdomen, look in your mouth and feel the lymph nodes in your upper body (around your neck and in your armpits).
Chest X-Ray	This is performed once at the screening visit and is a safe and painless test that uses a small amount of ionising radiation to take a picture of your chest and lungs. You will be provided with a hospital gown to change into and asked to lie down or sit up for a short while during the scan.
Electrocardiogram (ECG)	This looks at your heart's activity. It is a painless procedure where small pads will be stuck to your arms, legs and chest (which may need to be shaved) while you lie still for a few minutes. You will be required to undress to the waist. The pads can sometimes cause minor skin irritation.
Spirometry	Spirometry is a type of lung function test. It is either a small machine attached by cable to a mouthpiece or a handheld device with a mouthpiece. You will take the deepest breath you can, then exhale long and hard into a tube. This can make you cough or feel short of breath for a short time.
Peak Inspiratory Flow	 A small handheld device attached to a mask is given to you and you will be asked to breathe deeply in through your nose to assess how blocked or stuffy your nose is.
Samples/Procedures	
Urine sample	You will be asked to provide a urine sample to test for infection, ill health, drugs of abuse, nicotine (from smoking), and pregnancy (for females of child-bearing potential only). These

	tests will be performed at the time of collection, and then the urine sample will be stored for later testing for markers of viral infection.
Nasosorption	Nasal fluid will be obtained by placing a nasosorption strip inside your nostril for 2 minutes. This strip is flexible and absorptive like filter paper.
Nasal swabs (Anterior, Mid-turbinate and Nasopharyngeal)	Nasal swabs will be obtained by placing a swab into your nostrils. Swabs may be taken from just inside (anterior) or the middle (mid-turbinate) or at the back of the nose (nasopharyngeal)
Nasal Wash	5ml of sterile liquid will be gently flushed in and out of each nostril to collect cells and mucous from the inside of your nose. This will happen daily during the quarantine and at all of your follow up visits, it helps us to understand whether you are infected with the virus and is not considered painful.
Throat swabs	We will ask you to tilt your head back and open your mouth while a swab is rubbed along the back of your throat. You will need to resist gagging and closing your mouth.
Oral swab	You will be given a swab with a sponge on the end to run across your gums and inside of your cheek for 1-2 minutes to collect saliva.
Saliva Sample	You will be asked to provide a saliva sample in a container of around 2mls.
Stool sample	This is an optional sample and will require you to collect a sample of stool if you open your bowels on the day of the study visit or collection time point. You will either be asked to collect stool into a tube or via a swab. Instructions will be provided.
Lateral flow tests (Challenge Arm only)	During the inpatient stay, participants in the challenge arm will be provided with a lateral flow test and asked to the test themselves following the manufacturer's instructions. Once performed, the lateral flow test will be immediately removed by study staff so the result cannot be read.
Blood Samples	We will take blood to test for: • Anaemia (low red blood cells) or problems with your immune system • Blood clotting problems • Liver, kidney, thyroid and heart function • HIV, Hepatitis B and Hepatitis C infection • Diabetes or impaired blood sugar control • HLA type (this tells us the types of proteins or "markers" on your cells) • Influenza antibodies (to check for evidence of infection and vaccination). We will take between one teaspoon and 5 tablespoons each time. The total amount of blood we collect will not exceed 550ml over 8 weeks (the same amount taken at a blood donation session), unless for safety reasons when additional samples may be required. So that you don't give too much blood, you should not donate blood from the time of the Screening visit until 3 months after the last study visit. You may feel dizzy when you have blood taken. Sitting or lying down when blood is taken should stop you feeling lightheaded or fainting.
Mask-wearing samples	You may be asked to wear a single use face mask for 30-60mins once or twice a day for us to take samples and study the levels of the virus that are present in your breath.
PexA Breath Sample	You may be asked to provide a breath sample into a PExA device. This is a small machine with a mouthpiece which can collect lower airway samples from your exhaled breath. The device can collect microscopic droplets and allows the team to understand biological processes in your small airways throughout the potential infection period.
Breath Collection	You may be asked to provide an exhaled breath or cough via a facemask connected to a chamber. This aims to detect any virus that you breathe out, which might be infectious to others, which helps us to understand how or why the virus can spread between people.
Muscosalivary fluid collection	You may be asked to provide a saliva sample via a small suction device that is placed into your mouth, aiming to collect between 5-10ml of saliva. This sample is non-invasive and should not cause discomfort. This sample aims to understand the properties of your saliva during infection and helps us to understand if some people are more infectious than others.
Bronchoscopy (more details below)	Some participants will undergo a bronchoscopy to obtain lower airway samples: this procedure uses a thin fibre-optic telescope (a bronchoscope) to look at the inside of your lung and air passages and take samples from your lower airways. This is a routine procedure done in the NHS and will be carried out by specialist respiratory doctors. You will

	only have this done if you are eligible for th study after the screening visit. This procedure is explained in more detail under this table.
NALT Biopsy (more details below)	Some participants will undergo nasal biopsies to collect a small amount of tissue. You will have topical local anaesthetic applied using a spray to numb the area. An ENT specialist doctor will then use a thin fibre-optic telescope (a nasendoscope) to look at the area at the back of your nose and use some small forceps to collect 1-3 biopsies. This procedure is explained in more detail below.

Table 1 Tests and procedures performed during the study

Bronchoscopy
Up to 6 participants in the Vaccine Arm and up to 18 participants in the Challenge Arm will undergo bronchoscopies during the study.

This will be performed by a doctor who specialises in lung disorders at the Imperial College Healthcare NHS Trust. Bronchoscopies are a commonly performed procedure in the hospital and are generally well tolerated even in patients with lung problems. In healthy people having bronchoscopies for research, the risks of complications are very low and any potential risks will be discussed with you by the bronchoscopist. . During the procedure, a thin tube, called a bronchoscope is passed through your nose or mouth down your throat into your lower airway. During the procedure, special devices will be passed down the bronchoscope to allow the doctor to look at your airways and obtain samples from your lungs for the purposes of this research study.

Prior to the bronchoscopy procedure, you will be required to fast for four hours**.** We use a mild sedative to make you relaxed – there is no need for you to be put to sleep completely. We will also use some spray to numb your nose and throat. You will be able to breathe normally around the tube. You may cough during the procedure – this is normal. The procedure will include obtaining several samples from your lungs, including a sample of the fluid lining the airway using a synthetic absorptive matrix fibre strip; brushings from the inside of the airway; small snips of the lining of the airway; and a wash of the lung with saline solution, all of which are collected by passing instruments or fluid into your lung via the bronchoscope. During the procedure, your oxygen levels (oxygen saturation), blood pressure and heart rate will be continuously monitored and access to your veins by the insertion of an intravenous cannula will be required.

The bronchoscopy will be explained to you in detail before the procedure begins, and you will be asked to sign a separate consent form for each of the bronchoscopies which will take place during the study. On the screening visit, you will undergo a single chest x-ray which allows the doctor to rule out any abnormalities in your lungs in advance of bronchoscopy. Please refer to the 'Bronchoscopy information leaflet for patients, relatives and carers' (written by Imperial College Healthcare NHS Trust) for more information, which details what will happen during the bronchoscopy procedure. You will be given a copy of this leaflet prior to your bronchoscopy appointment.

The entire bronchoscopy visit including preparation and recovery (to ensure the sedation wears off), will take around 6 hours. The bronchoscopy procedure itself will take approximately half an hour. After the procedure is complete, you will be observed for at least 2 hours before being allowed to go home. During this observation period, a study nurse or doctor will keep a close eye on you and perform regular observation checks. Before discharge, we will provide you with something to eat and drink and the study doctor will assess that you have recovered from the sedation and are ready for discharge.

<u>Risks and side-effects:</u>
After bronchoscopy, you may feel drowsy for the rest of the day due to the sedation. You may have a sore throat and/or a mild cough. Occasionally, you may cough up some small amounts of blood. These symptoms should all resolve by the next day. Additionally, the fluid used to wash the airways, can cause some irritation, which can result in a brief fever in a small number of cases. This is however, self-limiting and can be treated with paracetamol. Following the procedure, it is possible that you may experience some chest discomfort, minor bleeding caused by irritation of the airways (caused by the bronchoscope and/or sampling procedure), shortness of breath and a temporary drop in oxygen levels (hypoxia).

Minor bleeding occurs in less than 1 in 100 people, and if this does occur, this will not require treatment. Serious bleeding requiring treatment is very rare (less than 1 in 1000). On rare occasions, the airways can narrow – if this occurs, medication can be given to open up your airways. Very rarely (less than 1 in 1000), the lung can collapse (pneumothorax) after bronchial biopsy. If this occurs, we will arrange for all necessary treatment in the unlikely event should this occur.

You will be given a telephone number on discharge to ring in case of any problems after you are discharged from the unit. The study team will call you later in the day to follow up how you are feeling after the procedure.

FOR OUTPATIENT BRONCHOSCOPIES, YOU NEED SOMEONE TO STAY WITH YOU FOR THE REST OF THE DAY AND YOU SHOULD NOT DRIVE A CAR OR OPERATE MACHINERY FOR AT LEAST 24 HOURS AFTER SEDATION.

Nasal-associated Lymphoid Tissue (NALT) Biopsy
Up to 6 participants in the Vaccine Arm and a minimum of 6 participants in the Challenge Arm will undergo NALT biopsies during the study. It will be performed at the baseline Day -14 visit, on Day 14 OR Day 28 and at the investigator's discretion on Day 180.

This will be performed by an ENT (Ear, Nose and Throat) doctor at Imperial College Healthcare NHS Trust. This is a commonly performed procedure in the hospital and is generally well tolerated.

You will have a local anaesthetic applied using a spray to numb the area in the front and back of your nose. After this, an ENT specialist doctor will then use a thin fibre-optic telescope (a nasendoscope) to look at the area at the back of each nostril. After they assess which side is best, they will then thread some small forceps down the nasendoscope to the back of the nasal cavity and collect 1-3 biopsies. After the biopsies have been taken, the doctor will reinspect the nose to ensure any bleeding has stopped.

The NALT biopsy procedure will be explained to you in detail before the procedure begins, and you will be asked to sign a separate consent form for each of the biopsy procedures which will take place during the study.

The entire biopsy visit including preparation and recovery (to ensure no nosebleeds) will take maximum 2 hours and the biopsy procedure itself will take no more than 5-10minutes.

Participants will be given contact telephone details for the study team and appropriate 'safety-net' advice on complications and management, especially the risk of bleeding. Participants will be followed-up two weeks post procedure via a phone-call.

<u>Risks and side-effects:</u>

- Bleeding from the nose either immediately after the procedure or, more rarely, a couple of days or weeks after
- Infection at collection site
- Pain (headache/earache/nose/throat)
- Runny nose
- Ear fullness
- Reaction to the local anaesthetic

8. What do I have to do?

If you take part in this study, you will need to follow the schedule for visits, assessments and procedures as detailed in the Schedule of Events in Appendix 1 and 2. **You should consider how these tests and visits would affect your work and family life and decide if you are able to commit to the required visits, tests and daily record keeping.** We will monitor you closely during the study for any symptoms or side effects,

but it is very important that you also tell the study doctor about **any** changes in your health, or symptoms, even if you do not think they are related to taking part in the study.

Sample Collection
On the study visits, you will be required to provide blood, urine, oral, throat, and nasal samples periodically.

Medications
You must inform your study doctor of any medications you are currently taking; in case they interact with the study vaccine/challenge agent. Please also inform the doctor of any new medications you start taking whilst participating in the study. Whilst you are on the study you must not take any of the following:

- Any investigational (unlicensed) drugs or vaccines as part of another clinical trial
- Any vaccines (licenced or as part of another clinical trial) within 30 days prior to study enrolment until 30 days after receiving the study vaccine.
- Any blood products containing immunoglobulins 3 months prior to receiving the study vaccine/challenge agent.
- Inhaled bronchodilators or immunosuppressant medications, including steroids. Topical steroids are permitted.
- Medication (prescription or over the counter) to treat symptoms of rhinitis or nasal congestion.

Other Restrictions while taking part in this study:

- Smoking **(includes any inhaled products, such as cigarettes and vaping)** is not permitted 6 months prior to or during study participation.
- You must agree to refrain from blood donation during the course of the study.
- If you are a mother, you must not breastfeed whilst taking part in the study.
- If you are female of child-bearing age, you must agree to use effective contraception as previously described.

9. What are the possible disadvantages and risks of taking part?

The risks of the chest x-ray, vaccine, challenge virus, bronchoscopy and nasal biopsy procedures have been explained above. Additional risks of taking part may include:

Blood samples
Drawing blood may cause slight pain, with the possibility of some slight redness, and/or bruising developing at the site where the needle is placed into your arm. Rarely, people may also feel lightheaded or even faint. We will minimise this risk by asking you to recline or lie down during blood draw.

Nose, throat and oral swabs
We will take a number of samples from the nostrils, throat and mouth using either a sterile cotton swab or special sampling apparatus. This is to obtain cells and fluid lining your nasal cavity, throat and mouth (including your gums and inside of your cheek), for research purposes. This type of sample collection is usually painless; however, you may experience slight discomfort during the sampling process. During the collection of the throat sample, a tongue depressor may be used if required, and some subjects may experience a gag reflex.

Private Insurance
You should be aware that certain insurance cover, such as medical or travel insurance may be affected by participation in a clinical study. If this is applicable to you, please contact your insurance company to see if participating in the study will affect your insurance.

10. What are the possible benefits of taking part?

Taking part will not improve your health, although you may benefit from a general health check from the screening tests.

There is a chance you could develop some “immunity” against Influenza through vaccination or infection, but we don’t know if you will or for how long protection might last.

If any information or results arise from the tests you undergo as part of this study that are deemed abnormal, the study doctor will discuss this with you, and if necessary, ask your permission to inform your GP and may request you undergo further testing or treatment.

11. What if new information becomes available?

Sometimes during a research project, new information becomes available about the treatment/drug that is being studied. If new information arises about the seasonal influenza vaccine being administered in this study, your research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw, your research doctor will make arrangements for your care to continue. If you decide to continue in the study, you will be asked to sign an updated consent form.

We do not anticipate there being any relevant new information arising for the Influenza virus challenge agent being used in the study but if there were to be, your research doctor will tell you about it and discuss with you whether you want to continue in the study.

12. What expenses and compensation will I receive for being in the study?

You will be paid for your participation in the study as follows:

Vaccine Arm

	Bronchoscopy Subset	Biopsy Subset	Biopsy Subset + Day 180 Biopsy	Payment
Pre-screening	£30.00			Cash or Bank Transfer at visit (£30)
Screening	£75.00			Cash or Bank Transfer at visit (£75)
Day -14	£190.00			Bank Transfer Paid after visit (£190)
Day -1	£50.00			Bank Transfer Paid after Day 28 (£710/£810)
Day 0	£190.00			
Day 1	£50.00			
Day 3	£50.00			
Day 7	£150.00	£50.00		
Day 10	£50.00			
Day 14	£50.00			
Day 28	£150.00			
Symptom Diaries	£70.00			
Day 90	£50.00			Bank Transfer Paid after Day 180 (£100/£200)
Day 180	£50.00		£150.00	
TOTAL	**£1,205.00**	**£1,105.00**	**£1,205.00**	

Challenge Arm

<table>
<tr><th></th><th>Bronchoscopy Subset</th><th>Bronchoscopy Subset + Day 90 Bronchoscopy</th><th>Biopsy Subset</th><th>Biopsy Subset + Day 180 Biopsy</th><th>Payment</th></tr>
<tr><td>Pre-screening</td><td colspan="4">£30.00</td><td>Cash or Bank Transfer at visit (£30)</td></tr>
<tr><td>Screening</td><td colspan="4">£75.00</td><td>Cash or Bank Transfer at visit (£75)</td></tr>
<tr><td>Day -14</td><td colspan="4">£190.00</td><td>Bank Transfer
Paid after visit (£190)</td></tr>
<tr><td>Day -1</td><td colspan="4">£160.00</td><td rowspan="15">Bank Transfer
Paid after Day 28
(£2,240/£2,340)</td></tr>
<tr><td>Day 0</td><td colspan="4">£300.00</td></tr>
<tr><td>Day 1</td><td colspan="4">£150.00</td></tr>
<tr><td>Day 2</td><td colspan="4">£150.00</td></tr>
<tr><td>Day 3</td><td colspan="4">£150.00</td></tr>
<tr><td>Day 4</td><td colspan="4">£150.00</td></tr>
<tr><td>Day 5</td><td colspan="4">£150.00</td></tr>
<tr><td>Day 6</td><td colspan="4">£150.00</td></tr>
<tr><td>Day 7</td><td colspan="2">£250.00</td><td colspan="2">£150.00</td></tr>
<tr><td>Day 8</td><td colspan="4">£150.00</td></tr>
<tr><td>Day 9</td><td colspan="4">£150.00</td></tr>
<tr><td>Day 10</td><td colspan="4">£160.00</td></tr>
<tr><td>Day 14</td><td colspan="4">£50.00</td></tr>
<tr><td>Day 28</td><td colspan="4">£150.00</td></tr>
<tr><td>Symptom Diaries</td><td colspan="4">£70.00</td></tr>
<tr><td>Day 90</td><td>£50.00</td><td colspan="2">£150</td><td>£50</td><td rowspan="2">Bank Transfer
Paid after Day 180
(£100/£200)</td></tr>
<tr><td>Day 180</td><td colspan="3">£50.00</td><td>£150.00</td></tr>
<tr><td>TOTAL</td><td>£2,735.00</td><td>£2,835.00</td><td>£2,635.00</td><td>£2,735.00</td><td></td></tr>
</table>

Additional visits or expenses:

- If you are asked to return for a repeat visit, for instance to undergo some repeat screening tests, the study team will let you know in advance how much money you will get for attending any extra visits at their request.
- You will not be additionally reimbursed for travel or subsistence expenses to and from any study visits.
- At the study team's discretion, reimbursement of any additional cost incurred by the participants (for example private medical appointments, etc.) must be agreed with the study team prior to the cost being incurred by the participant. If it is agreed by the study team to be reimbursed, receipts must be provided.

Payment in the event of withdrawal, exclusion or missed study visits:
If you do not complete the study (for example if you withdraw your consent, are excluded, or are considered as a reserve participant) you will receive payment in line with the visits you attend (and the time you spend in the quarantine unit if applicable). You will not receive payment for missed visits.

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). Please note that there are some situations where we are required to tell the authorities about your payments if we are asked to.

13. What happens when the research study stops?

Your time in the study will end once you have completed your final follow up visit. You will not need to do anything further. You will be thanked for your participation and your final study payment will be made to you.

If you require any extra follow up with the study team after your final study visit for the purpose of the study, this will be discussed with you. If you require any extra follow up with your GP or specialist after the study, we will write to them to let them know you have completed the study, and they need to arrange a follow up with you.

14. Could my participation end early?

Yes, your participation in the study could end early. At no point can we guarantee that you will complete the study. The Sponsor (Imperial College London) or the regulatory authorities can stop the study at any time. Additionally, the study doctors could decide to take you out of the study at any point if they think it is necessary, as outlined below.

Throughout the Screening process, up to the point of administering the vaccination or study virus, we will be collecting information about your health, including from your GP and the screening tests. Sometimes, we identify reasons that may make us decide that it is not in your best interest to take part in the study. This decision would be made by the study doctors and is made to protect your well-being.

Sometimes we invite more participants to a study than are required as reserve participants, in case some are no longer suitable for the study. We will ask if you are happy to be a reserve participant and inform you when this may be the case so you can plan accordingly. If you are not required to participate further, you will be paid for your time up to that point.

If you do not cooperate, or, in our reasonable opinion, comply with the study procedures, you may be taken out of the study by the study team, which could lessen the amount of compensation you receive.

If you withdraw from the study, you will be asked to sign a form telling us how you would like us to use your study samples and information. You may also ask the study team to remove your personal details (e.g., address and date of birth) from its participant database. However please note, that any of your data which has been recorded in the clinical trial would not be withdrawn or erased from the study so that we can still meet our legal obligations and to maintain the scientific integrity of the study. A record of your decision would be kept. If you lose capacity to consent during the study, you will be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study, but no further data or tissue would be collected and no other research procedures will be carried out. We will continue to monitor you for safety reasons relating to the vaccination or viral challenge should it be deemed necessary by the Principal Investigator.

15. What if something goes wrong?

You must tell the study staff immediately if you have any health problems during the study. You will be given an emergency contact card, which provides a 24-hour telephone service in case you need to contact us outside of office hours. If you need to attend another doctor for health problems relating to the study, we will ask that doctor to provide details that will help us follow up your care and investigate the possible reasons for these health problems.

Imperial College London holds insurance policies which apply to this study. If you experience harm or injury as a result of taking part in this study, you will be eligible to claim compensation without having to prove that Imperial College 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 the course of this study then you should immediately inform the Investigator, Professor Chris Chiu (c.chiu@imperial.ac.uk). The normal National Health Service mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Imperial College, Research Governance and Integrity Team Research governance and integrity | Research and Innovation | Imperial College London.

16. How will we use information about you?

Research Study Title: GERMINATE: GEneRating Mucosal immunity after INfluenzA infection and vaccination in lung and lymphoid TissuE - A two-arm, non-randomised, open-label experimental medicine study to compare immune responses between healthy volunteers aged 18-55years receiving either an intranasal live-attenuated influenza vaccine or viral challenge with GMP influenza A/Belgium/4217/2015 (H3N2)
IRAS ID: 347523

Imperial College London is the sponsor for this study and will act as the Data Controller for this study. This means that we are responsible for looking after your information and using it appropriately. Imperial College London will keep your personal data for:

- 10 years after the study has finished in relation to data subject consent forms.
- 10 years after the study has completed in relation to primary research data.

The study is expected to finish in July 2026.

For more information / confirmation regarding the end date please contact the study team, see **'WHERE CAN YOU FIND OUT MORE ABOUT HOW YOUR INFORMATION IS USED'** for contact information.

We will need to use information from you, your medical records and your GP for this research project. This information will include your:

- Name, date of birth and contact details (phone, email and home address)
- NHS Number and National Insurance Number or Passport Number
- Ethnicity
- Bank details (so that we can pay you)

People within the College and study team (see section sharing your information with others) will use this information to do the research or to check your records to make sure that research is being done properly and the information held (such as contact) details is accurate.

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.

The Sponsor and/or Imperial College Healthcare NHS Trust will keep all the biological samples and related data collected from you during the study to allow us to fully study and understand the disease. The Sponsor and/or Imperial College Healthcare NHS Trust will send your biological samples for testing in laboratories where they will be stored securely until the end of the study.

Your biological samples will be kept for a maximum of 25 years from the end of the entire study. After this time, the samples will be destroyed.

Your biological samples will be labelled with your study participant number but we will not use your name or information that could identify you. There are some samples, such as bloods and swabs which are analysed by the NHS labs and ordered via the local hospitals electronic patient record (EPR) system. As these are ordered and processed within the Hospital system, they will be linked to your personal hospital record and

so can be linked to you. Your hospital record and the NHS Lab bloods and swabs, will not have your participant I.D number on. Only the study team will hold both elements of information.

At the end of the study, some of your leftover biological samples and data from this study could be useful for other health research and laboratory testing. You will be invited to consent to storage of your samples for future use in other ethically approved studies. Any movement and storage of biological samples will be in accordance with the Human Tissue Act 2004 and other relevant laws in the countries they are sent to. You would not be told the results of such other research. You can still take part in the study if you do not want your leftover samples and information to be stored for future research.

One of the important ways we will look at how your immune system responds is by measuring the genes that get turned on and off in your cells over the course of infection or vaccination. This is done by measuring the genetic sequence of your DNA (your genetic code that is present in every cell and acts as a blueprint) and RNA (which are short copies of parts of the DNA that act as messages, telling the cell what proteins to make). As your DNA sequence is unique to you, it could theoretically be tracked back to you, although in reality this would be highly unlikely unless your other personal details were linked in some way. To protect against this, the data from genetic testing is only labelled with your identification number and will be stored in an encrypted system with access restricted only to those with specific permission.

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.

As a university we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use 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, we will use your data in the ways needed to conduct and analyse the research study. Our legal basis for using your information under the General Data Protection Regulation (GDPR) and the Data Protection Act 2018, is as follows:

- Imperial College London - “performance of a task carried out in the public interest”); Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research

Where special category personal information is involved (most commonly health data, biometric data and genetic data, racial and ethnic data etc.), Imperial College London relies on “scientific or historical research purposes or statistical purposes

17. International transfers

There may be a requirement to transfer information to countries outside the United Kingdom (for example, to a research partner, either within the European Economic Area (EEA) or to other countries outside the EEA. 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 UK adequacy decision in respect of its data protection standards, Imperial College London will enter into a data sharing agreement with the recipient research partner that incorporates UK approved standard contractual clauses or utilise another transfer mechanism that safeguards how your personal data is processed.

Some of the data we collect from you will be shared with our collaborators at Copenhagen Respiratory Research, Herlev and Gentofte Hospital in Denmark but you will not be identifiable through this data. All data will be shared with your unique participant identifier and they will not be able to link this to you. These collaborators are also funded by the same funder (Novo Nordisk Foundation) as part of the CLAIM consortium to expand clinical vaccine research capacity and harmonise processes to maximise the value of data and samples across European sites.

18. Sharing your information with others

We will only share your personal data with certain third parties for the purposes referred to in this participant information sheet and by relying on the legal basis for processing your data as set out above.

- Other Imperial College London employees (including staff involved directly with the research study or as part of certain secondary activities which may include support functions, internal audits, ensuring accuracy of contact details etc.), Imperial College London agents, contractors and service providers (for example, suppliers of printing and mailing services, email communication services or web services, or suppliers who help us carry out any of the activities described above). Our third party service providers are required to enter into data processing agreements with us. We only permit them to process your personal data for specified purposes and in accordance with our policies.

19. Potential use of study date for future research

When you agree to take part in a research study, the information collected either as part of the study or in preparation for the study (such as contact details) may, if you consent, be provided to researchers running other research studies at Imperial College London and in other organisations which may be universities or organisations involved in research in this country or abroad. Your information will only be used to conduct research in accordance with legislation including the GDPR and the UK Policy Framework for Health and Social Care Research.

This information will not identify you and will not be combined with other information in a way that could identify you, used against you or used to make decisions about you.

20. Commercialisation

Samples / data from the study may also be provided to organisations not named in this participant information sheet, e.g. commercial organisations or non-commercial organisations for the purposes of undertaking the current study, future research studies or commercial purposes such as development by a company of a new test, product or treatment. We will ensure your name and any identifying details will NOT be given to these third parties, instead you will be identified by a unique study number with any sample / data analysis having the potential to generate 'personal data'.

Aggregated (combined) or anonymised data sets (all identifying information is removed) may also be created using your data (in a way which does not identify you individually) and be used for such research or commercial purposes where the purposes align to relevant legislation (including the GDPR) and wider aims of the study. Your data will not be shared with a commercial organisation for marketing purposes.

21. 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 because some research using your data may have already taken place and this cannot be undone.

- If you choose to stop taking part in the study, we would like to continue collecting information about your health from you, your NHS records and/or your GP. If you do not want this to happen, tell us and we will stop. This will not affect any healthcare or support you may be receiving separately.
- 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 this could affect the wider study or the accuracy of data collected.
- 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.

22. 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 study team
- by sending an email to imperial.humanchallenge@nhs.net
- by ringing us on 07872 850212
- by going to our website pages www.imperial.ac.uk/infectious-disease/research/human-challenge/germinate/

23. Complaint

If you wish to raise a complaint about how we have handled your personal data, please contact the research team first by sending an email to imperial.humanchallenge@nhs.net or by ringing us on 07566950862.

Following our response, if you are not satisfied 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 remain unsatisfied 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)- via www.ico.org.uk. Please note the ICO does recommend that you seek to resolve matters with the data controller (us) first before involving them.

24. What will happen to the results of the research study?

If any results or publications are made publicly available during your participation in the trial, the study team will inform you where you can read these or provide you with a copy. If any results or publications are made publicly available after you have completed the trial, information about these can be found on the www.imperial.ac.uk/infectious-disease/research/human-challenge/germinate/. You will not be identified in any report/publication/presentation.

There is also an optional statement on the consent form for you to agree to the study team contacting you after you have completed the study to send you relevant publications that arise from this study.

25. Who is organising and funding the research?

Imperial College London is the sponsor of this study. Novo Nordisk Foundation, a Danish philanthropic organisation, is the funder of this study. The funder will pay the sponsor who will, in turn, pay the study site (Imperial College Healthcare NHS Trust) for including you in this study. The researchers involved in the study will not receive any payment over and above their normal salary or any other benefits or incentives for their involvement in this study.

26. Who has reviewed the study?

This study was given a favourable ethical opinion for conduct in the by the London Fulham REC.

27. Media

We may ask to take photos and/or videos of you during the study. This media could be used in press releases, news articles, to promote the study on our website and social media platforms, and also for training purposes. You may be identifiable in these images and videos.

Agreeing to this is completely optional and if you do not consent, you will still be able to continue in the study. Your decision will not affect the care that you will get from the study doctor. If you do consent to this, any photos or videos that are taken will be securely stored.

If you do consent to this, you can change your mind at any time and withdraw your consent. If you wish to withdraw your consent, please notify the study doctor.

If you withdraw your consent, we may not be able to remove images of you that are already public but we can ensure they are not used going forward and we will not take any new images or videos of you.

28. Contact for Further Information

If you have any questions about taking part in this research study, please contact the study team:

Principal Investigator: Professor Christopher Chiu
Email: imperial.humanchallenge@nhs.net
Phone: 07566950862

If it is an emergency, please use the telephone number provided to you on the Emergency Contact Card to contact the study doctor as soon as you can.

Now that you have read this participant information sheet and a study team member has gone through it with you in detail, there will be a break. Please take the opportunity to make sure everything is clear to you and ask as many questions as you want.

Thank you for considering taking part in this study!

You will be given a copy of this information sheet and a copy of your signed Informed Consent Form to keep.

VACCINE ARM – SCHEDULE OF EVENTS

Study Day	Pre-screening	Screening	D -14	D -1	D0	D1	D3	D7	D10	D14	D28	D90	D180
Informed Consent	X	X											
Eligibility assessment	X	X			X								
Medical & medication history	X	X		(X)	(X)								
Demographics	X												
Physical Examination		X	X		X				X	X	X		
Vital Signs	X	X	X	X	X	X	X	X	X	X	X	X	X
Height, weight and BMI	X												
Mental Health Questionnaires		X								(X)	(X)		
Chest X-Ray		X											
12-lead ECG		X			X		X		X				
Spirometry +/- Peak Inspiratory Flow		X			X		X		X		X		
Urine test for drugs of abuse & nicotine		X											
Urine pregnancy test for females of child-bearing potential		X	X	X				X			X		
Vaccination					X								
Symptom diary				BD									
Blood sample collection	X	X	X	X		X	X	X	X	X	X	X	X
Nasal, throat and/or oral samples		X	X	X		X	X	X	X	X	X	X	X
Stool swab +/- stool sample			X	X		X	X	X	X	X	(X)	(X)	(X)
Urine sample collection				X		X	X	X	X	X	X		
NALT biopsy			X							X			(X)
Bronchoscopy			X					X			X		

Key: X means once on this day, (X) means optional on this day or at investigator's discretion, BD means twice a day

CHALLENGE ARM – SCHEDULE OF EVENTS

Study Day	Pre screening	Screening	D -14	D -1	D0	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D14	D28	D90	D180
Informed Consent	X	X																	
Eligibility assessment	X	X		X															
Medical & medication history	X	X		(X)	(X)														
Demographics	X																		
Physical Examination		X	X	X							X			X		X	X		
Vital Signs	X	X	X	TDS	TDS	TDS	TDS	TDS	TDS	TDS	TDS	TDS	TDS	TDS	TDS	X	X	X	X
Height, weight and BMI	X																		
Mental Health Questionnaires		X		X									X			(X)	(X)		
Chest X-Ray		X																	
12-lead ECG		X		X				X							X				
Spirometry +/- Peak Inspiratory Flow		X		X				X							X		X		
Urine test for drugs of abuse & nicotine		X																	
Urine pregnancy test for females of child-bearing potential		X	X		X							X				X			
Challenge virus administration					X														
Symptom diary				BD															
Blood sample collection	X	X	X	X	X	X	X	X	X	X	(X)	X	(X)	(X)	X	X	X	X	X
Nasal, throat and/or oral samples		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Self-performed lateral flow test						X	X	X	X	X	X	X	X	X	X	(X)			
Stool swab +/- stool sample			X	X	X	X	X	X	X	X	X	X	X	X	X	X	(X)	(X)	(X)
Urine sample collection				X		X	X	X	X	X	X	X	X	X	X	X	X		
Exhaled breath and mask samples				(X)		(X)	(X)	(X)	(X)	(X)	X	(X)	(X)	(X)	(X)	(X)	(X)		
Environmental sampling (air and surfaces)				X		X	(X)	X	(X)	(X)	(X)	X	(X)	(X)	(X)				
NALT biopsy			X													X			(X)
Bronchoscopy			X								X						X	(X)	

Key: X means once on this day, (X) means optional on this day or at investigator's discretion, BD means twice a day, TDS means three times a day