# Participant information sheet

# Research: working towards a nasal vaccine for pneumonia

# *The effect of new strains of bacteria - Would you like to take part in our research?*

This information leaflet tells you how you could take part. A member of our team will also discuss it with you: please ask us if you have questions. You may want to talk to other people about the study: please do so. Take your time to decide if you want to be involved.

## What is the purpose of the study?

We are developing a new vaccine to protect against bacteria called **Pneumococcus.**

Small numbers of these bacteria are often found in the nose. Usually, the carrier does not know the bacteria are there. In most adults this is present at least once per year and more often in children. We think that small numbers of bacteria present in the nose (“nasal carriage”) can help to protect people against disease.

Mild infections with pneumococcus are very common, such as ear infections in children. But pneumococcus can also infect the lung (causing pneumonia) or the brain (causing meningitis) or the blood (causing sepsis). These severe infections are very uncommon in healthy adults: about 50 cases in Liverpool per year. Very young children and adults who are elderly or those who have other illnesses are more likely to become ill.

We may be able to protect people against severe disease from pneumococcus using a vaccine which could be sprayed into the nose. We don’t yet know if this will work.

To test the idea, our research team want to study what happens when small numbers of the bacteria are put up the nose of healthy volunteers. We have already studied this: more than 400 volunteers have been safely studied using another single strain (type) of these bacteria.

We now want to do the same with different strains. This will let us compare whether the presence of this bacteria provides protection from one strain with another.

## Do I have to take part?

No. Taking part in this study is voluntary.

## Why have I been asked to take part?

We are looking for volunteers who are fit and healthy.

We check for reasons which may put you at higher risk from the study. We also make sure that your participation will provide helpful information to us. If we find any reason you may be at higher risk of infection, then we will not invite you to take part.

**You will not be eligible if:**

* You are younger than 18 or older than 50
* you are a regular smoker or have a significant history of daily smoking
* you are vaccinated against pneumococcus
* you have taken part in similar research
* you are allergic to penicillin or amoxicillin
* you are in close contact with those who have lower immune levels (such as young children and the elderly)
* you are pregnant or trying to conceive
* the study doctor thinks that a health condition, or medication means that you are at increased risk of infection.

## What happens if I choose to take part?

1. **Health check** – for safety, we check that you are healthy. This includes a clinical assessment and check the list above.
2. **Consent** –We ask you to sign a consent form when you are sure you want to take part.
3. **Taking samples** – We take samples from the nose, throat and blood *(see below*).
4. **Being given drops of pneumococcus in the nose** - We put a few drops with a small numbers of bacteria up your nose
5. **Monitoring**– we will ask you to write down any symptoms and contact us daily to make sure you are well for a week.
6. **Monitoring visits** – We take samples from your nose to see whether the bacteria is present.

**Part one** takes less than four weeks then after three to six months we will invite some participants to repeat this for part two.

## What kind of samples do you take?

### **Nasosorption:** to collect fluid from your nose we place a small piece of blotting paper inside your nostril for a few minutes.

### Some participants may also be asked to collect two nasosorption’s and eight saliva samples (spit into a tube) over 48 hours at home (or workplace etc). This is an additional option. Home samples they must be collected within 15 minutes of a set time. Therefore, we will ask you to send a photograph of the sample to confirm the time taken.

### **Nasal Cells:** we also insert a curette (very small plastic spoon) that is withdrawn in a sweeping motion to collect small cells from the inner surface of the nose.This will be repeated up to 4 times (twice per nostril). In the event where no cells are visible on the spoon, the sample will be repeated immediately.

**Nasal Wash:** we gently squirt a little salty water into your nose. After a few seconds the water runs out into a sample bowl. This will tell us about the bacteria in your nose and your immunity.

### **Throat swab:** we wipe the back of your mouth with a sterile swab (like a cotton bud). The laboratory can use this to find out if there are any bacteria.

### **Blood samples:** We take blood samples from a vein in your arm (using a needle). We will take up to 50 mL (about the same as 10 teaspoons) on two occasions.

You may choose to allow the researchers to study the DNA from your blood sample. If you choose not to donate your DNA you may still take part in the study.

**PART 2 :**

**Hand swabs:** if you are carrying our bacteria in your nose on visit 3 (in part 2 of the study) we will take 2 hand swabs on visit 4. 1st swab we will wipe the back of your hands with a sterile swab (like a cotton bud) which has been moistened with sterile water. Then we will clean your hands with ethanol spray, following this we will ask you to rub your nose with the back of the right hand and then repeat the swab of the back of the hand. The laboratory can use this to find out if there are any bacteria on your hands.

## What will happen to my samples?

We will process your samples in laboratories at the Liverpool School of Tropical Medicine

(LSTM) and at the Royal Liverpool University Hospital. We will measure the levels of bacteria and viruses in your nose, and we will look in detail at how your immune system responds to the pneumococcus bacteria.

To make full use of your samples, we ask that you “gift” your samples to LSTM. We will *store them so that in the future, we can go* back to them with new tests to answer new questions. For some specialist tests, we may send samples to laboratories in the UK and abroad.

## What will happen at each visit of Stage 1?

|  |  |
| --- | --- |
| Visit 1:Screening check, consent, and taking samples | We make sure you are fit to take part in the study. We ask routine questions about your medical health, check your blood pressure, temperature and listen to your heart and lungs. We do the throat swab, nasal cells, the nasal wash and a blood test. For women, we check that you are not pregnant using a urine test.We book your next appointments. If you have problems and can’t come on a specific date, we can be flexible to accommodate you. |
|  | *between 1 to 7 days later*  |
| Visit 2:Being given pneumococcus up the nose | We collect a sample from your nose using a swab similar to blotting paper. We use a dropper to put a small amount of water containing a small number of bacteria into each nostril. Usually, volunteers have no symptoms afterwards. There will be a doctor or nurse available by telephone 24 hours a day to answer questions. We will give you a course of antibiotics to keep with you, in case you are unwell. Each day for the next week we will ask you to contact the research team by phone or text to ensure that all is well and to check your temperature reading (a thermometer is provided in the study) and record any symptoms each day in a diary (symptom log).  |
|  | *Daily phone call or text /SMS. Then 2 days later…* |
| Visit 3: Monitoring | Nasal wash, nasal cells and swab *(similar to blotting paper)* |
|  |  *Continue with a daily text /SMS. Then 5 days later:*  |
| Visit 4: Monitoring | Nasal wash, nasal cells and swab *(similar to blotting paper)* |
|  | *Then 7 days later*  |
| Visit 5: Monitoring | *Nasal wash, nasal cells and blood sample* |
|  | *Up to 2 days later* |
| End of Part 1of the study | If our laboratory test finds that the pneumococcus bacteria stays in your nose, at this stage we will ask you to take a course of antibiotics to clear it. When this is was present, we will ask you to be in part 2 of our study. |

## What about Part 2?

We think that having small number of bacteria in your nose might protect you against illness from this bacteria possibly for a long time. But we cannot be certain. To test this, we may ask you to have the pneumococcus put into your nose a second time, after 3 to 12 months We will only ask those who we know carried the bacteria in the first stage of the study. In total, part two visits will take about 2 to 3 weeks.

## What will happen at each visit of Part 2?

|  |  |
| --- | --- |
| Visit 1:Screening check, consent, and taking samples | We make sure you are still fit to take part in the study, by repeating the questions and examination done at Part 1.We do the throat swab, the nasal wash and a blood test.For women, we check that you are not pregnant using a urine test. |
|  | *between 1-7 days later* |
| Visit 2:Being given pneumococcus up the nose | We collect a sample from your nose using a swab similar to blotting paper. We use a dropper to put a small amount of water containing a small number of bacteria into each nostril.Each day for the next week we will ask you to contact the research team by phone or text to ensure that all is well and to check your temperature reading (a thermometer is provided in the study). **Home samples:** some participants may be asked to collect two nasal strips and eight saliva samples at home over a 48 hour period and send a picture of each sample.  |
|  | *Daily phone call or text SMS. Then 2 days later…* |
| Visit 3: Monitoring | Nasal wash and swab (similar to blotting paper) |
|  | *Continue with daily phone call or text SMS. Then 5 days later…* |
| Visit 4: Monitoring | *Nasal wash and blood sample**If you are carrying our bacteria in your nose at visit 3 we will also take 2 hand swabs on this visit.*  |
|  | *Up to 2 days later* |
| End of the study | At the end of Part 2, if our laboratory confirm that you have had pneumococcus in your nose, we will ask you to take the antibiotic course (amoxicillin for 3 days) to clear it. |

## What are the risks of being in the study?

### Risks of being given live bacteria

Because the bacteria are alive, there is a very small risk of infection to you or your close contacts. We do not expect anyone to develop an infection but this is why we choose participants carefully, and why we monitor them closely. We provide a thermometer and antibiotics that treat these bacteria. We give you a separate leaflet which explains the safety precautions, and what to do if you feel unwell. If you carry the pneumococcus bacteria in your nose at the end of the study, we will ask you to take the antibiotics to kill the bacteria.

As a precaution we advise participants not to become pregnant during the study and to advise the research team if they do become pregnant.

### Risks of nasal sampling

The only side effect is a little discomfort and some experience a runny nose.

### Risk of taking blood

There are very small risks associated with blood sampling. Some people can feel light-headed. Sometimes, may have a bruise.

## What if there is a problem?

You can contact the research team 24 hours-a-day by phone. They will answer any questions, and an emergency service will be available day and night. Any medical care you need will be provided by the NHS.

## What if I wish to complain?

If you wish to complain about any aspect of the study, you can contact the study doctor or nurse. The NHS complaints procedures are also available to you. Complaining will not affect the medical care you receive now or in the future.

## What if I change my mind, or want to stop?

Even if you do start in the study, you are free to stop at any time and without giving a reason. If you decide not to take part, or to withdraw from the study, this will have no effect on your future health care.

If you decide to stop, we will continue to use the samples and information that we have already collected unless you tell us not to. You will be paid for the visits completed up to that point.

## Will my details be kept confidential?

Yes. For safety, we collect information about your medical history and contact details before you take part. The clinical research team use this information to check you are healthy, and to contact you when needed.

We will also collect information which allows us to understand more about the samples, for example, you age or sex. However, those outside of the clinical team are never given information that can identify you. Your samples are given a unique number, and your name is not used.

We will ask your permission to inform your GP that you are taking part in the trial as this may be relevant to your medical care outside the study. We do not expect to find anything which would affect your health care. If we do, we will let you and your GP know about it.

All data will be collected and stored at the Royal Liverpool University Hospital and the Liverpool School of Tropical Medicine. It will be stored for a minimum period of 10 years. Your medical notes and research data are may be looked at by those who monitor the research.

## What are the benefits of taking part?

There are no direct benefits to you. You will be a part of what we believe is a valuable research study that may help us to improve medical care for others.

**Optional Bronchoscopy and Lavage**

We may ask some participants who have been invited back for part 2 of the study, to consider consenting for a bronchoscopy and lavage at the end of the study.

A bronchoscopy is a camera test to look inside the lungs. A lavage is washing of a small segment of the lung.

## What does bronchoscopy and lavage involve?

The test is carried out in the hospital. You must not eat for 4 hours before the procedure but a few sips of water may be taken 2 hours before the procedure.

For comfort we use a spray or gel to numb the inside of your nose and mouth. We offer sedation using a medicine called Midazolam if you choose (this procedure does not require a general anaesthetic).

We take a throat swab (see above for procedure) and nasal swab before the bronchoscopy to look for any bacteria in the nose and throat at the time of the procedure. For the nasal swab, we wipe the back of your nostrils with 2 sterile swabs (like a cotton bud). Taking a nose swab takes only a few seconds but may be a little uncomfortable and may make the eyes water.

We will also take a blood sample (4mls about a teaspoon) to compare markers in lung fluid with blood taken at the same time. We will take the blood while inserting a cannula which is a needle with an inner plastic tube which be left in your vein during the procedure so that we may give sedation or other medicine if required. We monitor the blood pressure and heart rate throughout the procedure and administer oxygen as required.

We pass a bronchoscope (a flexible tube the same diameter as a small pen) either through the nose or mouth to the back of the throat. Using a channel in the bronchoscope we can put some local anaesthetic in to numb the upper and main airways. This may make you cough at first then as it takes effect in most cases you will not feel the bronchoscope inside your lungs.

The doctor will check the bronchoscope is in the correct position. Then 200ml of sterile saline (about the same amount as in a cup) is introduced and withdrawn immediately using gentle hand suction.

This procedure collects lung secretions and cells and is known as bronchoalveolar lavage. It takes about 20 – 30 minutes including the preparation

After the procedure, we observe you for approximately 2 hours so that any medication can wear off before you leave. You will be offered something to eat and drink. You will be asked to contact us the next day to say whether you have any side effects of the procedure. If so you may be asked to come to the hospital for a follow up assessment.

## What are the risks of bronchoscopy and lavage?

The British Lung Foundation describe bronchoscopy as a safe procedure. Your nose and throat may be a little sore for a day or so afterwards. You may experience a minor nose bleed.

You may feel tired or sleepy for several hours, caused by the sedative and may forget some of the procedure. There is a slightly increased risk of developing a throat or chest infection following a bronchoscopy. Some people get a mild pain under their right arm which can last for up to 24 hours due to inflammation from the lavage. We would advise you to take paracetamol and may ask you to attend clinic for an assessment.

Serious complications from a bronchoscopy are extremely rare. We monitor participants during the procedure and there are medical and nursing staff available. It is possible that you will experience a drop-in oxygen during the procedure or breathlessness if these occur we will stop the procedure immediately. If you choose to have sedation we advise you to ask someone to collect you and that you do not drive on the day following sedation.

## How much will I get paid?

The money you are paid is compensation for inconvenience, loss of income, and possible risks of taking part. The first payment will be made at the end of part one. If you are eligible and choose to take part in the second study you will receive a second payment at the end of part two. Our payments are below.

|  |  |  |
| --- | --- | --- |
| **Part 1**  |  |  |
| Visit 1: Screening and samples  | 30 min | £30 |
| Visit 2: Having pneumococcus put up your nose. This includes you making daily email/SMS/telephone contact for the first 7 days. (We will withhold £5 per day if you do not contact us) | 30 min | £50 |
| Visit 3: Nasal samples  | 20 min | £10 |
| Visit 4: Nasal samples  | 20 min | £10  |
| Visit 5: Nasal samples and blood sample | 30 min | £15 |
| **Part 2**  |  |  |
| Visit 1: Screening and samples from the nose and blood | 30 min | £30 |
| Visit 2: Having pneumococcus put up your nose, and follow-up, as above | 30 min | £50 |
| Visit 3: Nasal samples | 20 min | £10  |
| Visit 4: Nasal samples and blood sample | 30 min | £15  |
| Total for Part 2 |  | £105  |
|

|  |  |
| --- | --- |
| Optional a proportion of participants may be invited to take home samples- Home samples of saliva and nasal strips £6 for each episode of samples taken at home on time.  |  |

 |  | £48 |
|

|  |  |
| --- | --- |
| Bronchoscopy/lavage/blood sample optional after further consent  |  |
|  |  |

 |  | £100 |
| Maximal possible payment for Part 2 |  | £253 |

**Contact details**

General questions: please contact the research team on 0151 706 3381 during normal working hours. Web site: \*\*\*\*\*

**Emergency contact details at any time day or night:**

Mobile:

Royal Liverpool Hospital Switchboard: 0151 706 2000.

Please ask for the study team for the “Flu Study or EHPC team”

*The Chief Investigator for this study is Dr Jamie Rylance. You may contact him at the Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, L3 5QA, UK. Telephone: 0151 705 3775.*

*This research is sponsored by the Liverpool School of Tropical Medicine and the Royal Liverpool and Broadgreen University Hospitals. It is funded by the Medical Research Council. The research has been reviewed for scientific content by an external panel.*

*The National Research Ethics Service Committee (XXXX) has reviewed the study and given approval for it to take place.*