# Participant Information Leaflet (PIL): Healthy Adults 60-69yrs

# Research: Experimental Human Pneumococcal Challenge (EHPC): establishing a model using SPN3

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 studying a bacteria (a type of germ) called pneumococcus. We think that small numbers of this bacteria living in the nose (“nasal colonisation”) may protect people against pneumococcal disease. Small numbers of pneumococcus are often found in the nose of healthy adults (at least once per year) and more often in children – these people are called “carriers”. Usually, the carrier does not know the bacteria are there but, in some people, it can cause illness. Mild infections with pneumococcus are very common, such as ear infections in children. Pneumococcus can also infect the lung (causing pneumonia); more severe infections of the brain (causing meningitis) or the blood (causing sepsis) 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.

For the purpose of this study we will put small number of pneumococci in the nose of participants, as described later in this information leaflet, using an Experimental Human Pneumococcal Challenge (EHPC) model. This will allow us to learn about the protective mechanisms that occur in the nasal lining and we may be able to use this information later in the development of new pneumonia vaccines.

More than 1200 participants have already been studied safely using this method of putting pneumococci in the nose called Experimental Human Pneumococcal Challenge (EHPC) using 3 different pneumococcal strains (SPN) 23F, 15B and 6B. We now want to test the model using a different strain of the bacteria that is commonly found in the community, SPN3.

## 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 participants that are fit and healthy and aged 60-69 years old. We will check for reasons which may put you at higher risk for taking part in 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 are eligible if you:**

* Are aged 60-69 years (inclusive)
* Speak English fluently - to ensure a comprehensive understanding of the research project and your proposed involvement
* Have access to your own mobile telephone - to ensure safety and timely communication
* Have the capacity to give informed consent

**You are not eligible if any of the following apply to you:**

**Research participant:**

* You are currently involved in another study unless observational or non-interventional except for the EHPC bronchoscopy study\*
* You are a participant in a previous EHPC trial within the last 3 years (at the discretion of the study team i.e. Not inoculated/exposed nasally with pneumococcus)

**Vaccination:** You received previous pneumococcal vaccination PPV23 or PCV13 (routine in UK babies born since 2005 or US 2001) or PCV10.

**Allergy:** to penicillin or amoxicillin

**Health history:**

* Chronic ill health including, immunosuppressive history, diabetes, asthma (on regular medication), recurrent otitis media or other respiratory disease
* Medication that may affect the immune system e.g. steroids, inflammation altering (e.g. nasal steroids, roacutane) or disease-modifying anti-rheumatoid drugs.
* Recent antibiotics (within the last 28 days or long term for known active chronic infection)
* Current illness, acute illness within 14 days prior to inoculation
* Major pneumococcal illness requiring hospitalisation
* Other conditions considered by the clinical team as a concern for participant safety or integrity of the study

**Direct caring role or close contact** with individuals at higher risk of infection

* Children under 5 years of age
* Chronic ill health or immunosuppressed adults

**Smoker:**

* You are a current or ex-smoker (regular cigarettes, regular e-cigarette/vaping and regular smoking of recreational drugs) in the last 6 months
* Previous significant smoking history - more than 20 cigarettes per day for 20 years or the equivalent (>20 pack years)

**Women of child-bearing potential (WOCBP**) who are:

* not deemed to have sufficient/effective birth control or confirmed abstinence
* pregnant

**History or current drug or alcohol abuse** (frequently drinking alcohol: men and women should not regularly drink >3 units/day and >2 units/day respectively) at discretion of the clinician

**Overseas travel planned** in follow upperiod of the study visits

**Natural pneumococcal colonisation at baseline** It is anticipated that 10-15% of screened participants will have natural pneumococcal colonisation at the time of recruitment as demonstrated by the initial nasal wash. These individuals will be excluded from the study after screening visits.

## What happens if I choose to take part?

If you choose to take part in this study and the research team agrees that you are suitable, you will be asked to sign the consent form. A copy of this information sheet and your signed consent form will be given to you to keep.

The study will involve 5 clinic visits over approximately of 3-4 weeks.

**What samples do you take?**

We collect nasal and blood samples to look at the immune response and bacteria in the nose.

**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 (s)**: We take a small cotton swab and wipe the back of your throat in a circular motion. This is used to detect bacteria and viruses in your throat.

**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) during this visit.

**Saliva:** We will ask you to spit into a tube to provide approx. 1ml.

**Urine sample:** We take a small amount of urine (10ml) to test for bacteria. Female participants will have a urine pregnancy test during the screen visit.

## What will happen at each visit?

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| **Screening Period** |
| **Consent Visit****Screening Visit** | A member of the research team will discuss the study involvement with you, this may be done as a group presentation. You will have the opportunity to ask questions and discuss the study directly with the researcher in private following the presentation. If you are happy to take part in the study, you will be asked to complete a questionnaire to demonstrate that you understand the study involvement before signing a consent form. We will inform your GP that you are taking part in the study and we may request a brief medical history from your GP.This will take approximately 30-45 minutes. We will ask some routine questions about your medical health and we will listen to your heart and lungs. This is done to make sure you are fit and well. We may perform a test to assess your breathing, this requires you to take a deep breath in and rapidly exhale with force into a machine. This is repeated to obtain 3 similar recordings. You may be given an inhaler via spacer device to check for any respiratory disease. The test may need to be repeated after 15minutes. We will take blood, throat swabs, nasal wash, saliva and a urine sample. A urine sample will be taken to check for pregnancy (pre-menopausal females only).  |
| **Inoculation** |
| **Inoculation Visit (Putting the bacteria into your nose)** | We will take a throat swab before the inoculation. We use a dropper (pipette) to put a small amount of water containing a small number of pneumococcus into each nostril. Usually participants have no symptoms afterwards. There will be a doctor or nurse available by telephone 24hours a day, 7 days a week to answer questions. We will give you a safety pack to keep with you throughout the study, this includes:* A course of antibiotics to keep with you in case you are unwell
* A thermometer to check your temperature at home
* A safety information sheet
* A study contact card

You will then be permitted to return home. We will ask that you inform us of your temperature and symptoms daily for the next 3-4 days using text or an App available on i-phones/android phones. |
| **Monitoring Period** |
| **Clinic appointments on day 2, 7 and 14 post inoculation** | At each visit, a number of samples will be taken which may include throat swab (s), nasal wash, saliva, urine and blood tests  |
| **End of the study** | Participants that are colonised with SPN3 at any time point will be asked to take the antibiotics from the safety pack to clear/reduce the amount of pneumococcusAmoxicillin 500mg three times per day for 3 days\*. |

\* Colonisation positive participants only

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

The risks that you should consider *before* participation in this study are the risks associated with venepuncture, nasal sampling and inoculation with live bacteria.

**Blood sampling:** The risks associated with blood sampling (venepuncture) and cannulation are minimal, but thismay cause temporary pain, bruising and/or bleeding to your arm. The blood sampling will be performed by trained medical professionals.

**Nasal sampling:** There are limited risks associated with these samples. During a nasal wash, you may swallow a small amount of salty water however this is harmless.

**Throat swab (s):** There are limited risks associated with these samples. This sample may make you gag a little.

**Saliva sampling:** There are no adverse effects of the saliva sampling.

**Urine sampling:** There are no adverse effects of the urine sampling.

**Inoculation with Pneumococcal 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 monitor them closely. We have experience of using this model safely in more than 1200 healthy participants with no serious side effects. We provide a safety pack as described above and access to the research team by phone 24/7. We give you a separate leaflet which explains the safety precautions and what to do if you feel unwell.

## What if there is a problem?

You can contact the research team 24 hours-a-day by phone. They will answer any questions, and this 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. You can also contact the sponsor by email on lstmgov@lstmed.ac.uk Complaining will not affect the medical care you receive now or in the future.

The study is sponsored by the Liverpool School of Tropical Medicine (LSTM) and is covered by Clinical Trial Insurance.

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

If you do start 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 do start 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 that have already been taken and information that we have already collected, no further samples or data will be collected. You will be paid for the visits completed up to that point.

The study team may stop your involvement in the study for the following safety reasons:

* If you develop a condition that is in the exclusion criteria
* If you start a new medication that is prohibited
* If you become pregnant
* If you are unable to follow study instructions or the team are unable to contact you.

## 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 that allows us to understand more about the samples, for example, your age or sex. However, people 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.

Data collected during the study and your research and medical notes may be looked at by independent monitors, auditors, regulatory authorities or the funding body (Pfizer). They will be assessing the quality of the trial to ensure that it is conducted correctly in accordance with Good Clinical Practice guidelines. They will not have access to confidential information.

We will ask your permission to inform your GP that you are taking part in the study 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 LSTM for a minimum period of 10 years. Your medical notes and research data may be looked at by those who monitor the research.

Data that is collected during the study will be anonymised and may be transferred outside of the UK where data protection laws may differ from the UK. All this data however will be anonymous. Published research will include data however this will be anonymous and cannot identify you in any way.

## What will happen to my samples?

The samples taken during this study will be processed and stored in the LSTM, Royal Liverpool University Hospital and Pfizer. These samples will be gifted for future use in ethically approved research.

Samples that are sent to external collaborators (namely Pfizer) will be gifted and analysed for the purpose of pneumococcal research and stored for up to 15 years after which, they will be destroyed. All these samples are anonymous.At the end of the study, remaining samples will be transferred to a research tissue bank held at LSTM. All samples will be anonymised at the point of sampling. The stored samples will be analysed as and when new technology becomes available, when new scientific questions arise relating to protection and susceptibility of respiratory disease. Samples may be sent to national and international collaborating laboratories for their expertise however all identifiable information will be removed.

DNA will be extracted from your samples and stored to determine if there are genetic factors that relate to protection or susceptibility to pneumonia.

## What are the benefits of taking part?

You will be a valuable part of a research study that we hope will eventually lead to the development of new methods to prevent respiratory infections through vaccination. You will not gain any direct benefit in this study.

## How much will I get paid?

The money you are paid is compensation for inconvenience, loss of income, and discomfort. 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.

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| **Procedure** | **Duration** | **Payment** |
| Initial visit (study information, eligibility questions, informed consent, consent quiz, GPQ a) | 60 mins | £0 |
| Screening appointment (clinical exam, medical history, vital signs, blood, nasal, throat and urine samples) \*For those in the 60-69-year-old group needing a spirometry an extra £5 payment will be made to compensate for time taken to do this test b | 30 mins45mins b | £ 30£35 b |
| Inoculation with pneumococcus and throat swab. Also includes participant making daily telephone contact for the first 3-4 days; contact payment may be withheld if the participant does not make daily contact | 45 mins | £ 40Includes the daily contact at £5/day |
| Clinic visit samples on day 2, 7 and 14 | 15 mins | £ 15 x3 |
| **Total Remuneration £115-£120** |

a Older adults only

b If spirometry required

## **Contact details**

General questions: please contact the research team on 07740 410 290 or 0151 702 9424 during normal working hours. Web site: <http://www.lstmed.ac.uk/research/topics/pneumonia>

**Emergency contact details at any time day or night:** Mobile: 07912 053 981

*The Chief Investigator for this study is* ***Dr Andrea Collins****. You may contact her at the Liverpool School of Tropical Medicine (LSTM), Liverpool Life Sciences Accelerator Building, 1 Daulby Street, Liverpool, L7 8XZ, UK. Telephone: 0151 702* *9439. This research is sponsored by the LSTM and the Royal Liverpool and Broadgreen University Hospitals. It is funded by Pfizer. The research has been reviewed for scientific content by an external panel. The National Research Ethics Service Committee Liverpool East has reviewed the study and given approval for it to take place.*

*Liverpool School of Tropical Medicine (LSTM) is the sponsor for this study based in the United Kingdom. We will be using information from you and your medical records in order to undertake 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 properly. LSTM will keep identifiable information about you 10 years after the study has finished.*

*Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.*

*You can find out more about how we use your information by contacting* *dataprotection@lstmed.ac.uk**.*

*LSTM will use your name, NHS number and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from LSTM and regulatory organisations may look at your medical and research records to check the accuracy of the research study. LSTM (research site) will pass these details to LSTM (sponsor) along with the information collected from you and your medical records. The only people in LSTM who will have access to information that identifies you will be people who need to contact you to regarding your participation in the research or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.*

*LSTM (research site) will keep identifiable information about you from this study for 10 years after the study has finished.*

*LSTM will collect information about you for this research study from you and/or your GP records. Your GP will not provide any identifying information about you to LSTM. We will use this information to confirm your eligibility This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.*

**Consent Form: Healthy Adults 60-69yrs**

**EHPC: establishing a model using SPN3**

Participant Study number

**Please initial the box if you agree with each statement. Then, print and sign and date below.**

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| I have read and understand the information sheet version **1.0** for the above study. I have been able to consider the information and to ask questions. I confirm that the study procedures and information have been explained to me. I have had the opportunity to ask questions and I am satisfied with the answers and explanations provided. | Initial |
| I understand that this study is voluntary and that I am free to withdraw without giving any reason without my medical care or legal rights being affected.  | Initial |
| I understand that the section of my medical notes relevant to my taking part in this research and data collected may be seen by the regulatory authorities or NHS Hospital. I give permission for these people to access my medical records. | Initial |
| I agree that anonymous data can be transferred outside of the UK for the purpose of the research. | Initial |
| I agree to my GP being informed of my participation and providing information or for the researcher to access my electronic GP summary record relevant to the study.  | Initial |
| I understand that the samples collected will be used and stored for the research described above, and that samples may be sent to national and international collaborating laboratories as part of the study.  | Initial |
| I will gift these samples so that they may be used for future ethically approved research in the UK and overseas. | Initial |
| I understand that these samples may be stored up to 15 years by the LSTM and Pfizer. | Initial |
| I understand that these samples will be transferred to a research tissue bank for future use in ethically approved research at the end of this study. | Initial |
| I give permission for the DNA to be extracted from these samples and gifted for use in future studies and may be sent to research collaborators (national/international).  | Initial |
| I confirm that I am not planning to conceive, and I will use effective contraception if required during the study.  | Initial |
| I agree to take part in this study.  | Initial |

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Name of patient (print) Signature Date

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Name of person taking consent Signature Date

Copies: 1 for participant, original for site file and one scanned or filed in hospital medical notes