The Newcastle upon Tyne Hospitals NHS Foundation Trust

Newcastle University

PARTICIPANT INFORMATION SHEET

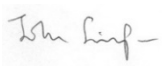
Immune response to Pneumococcal vaccination in older people (ImmuneVac)

Invitation and background

You are being invited to take part in a research study that aims to discover how the immune system responds to vaccines in older people. Our future aim is to find ways to make vaccines more effective in older people, to reduce cases of pneumonia. You have been sent this document because you are a healthy individual aged 60 years and above. The document will provide you with more detail about the nature of the study and what your participation would involve. If anything remains unclear after reading this document or you would like further information, please feel free to ask.

To help you navigate the rest of this document, the page numbers of the key sections are shown below.

Thank you very much for reading this document and considering our research



John Simpson, Professor of Respiratory Medicine, Newcastle University

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Why are we doing the study and what is involved?

Lung infections remain a major cause of illness and death across the world. The impact of lung infection is significantly greater in people aged 60years and older. In this age group, infections with germs like bacteria and viruses are more likely to lead to death. The germ causing most pneumonia in the UK is called *Streptococcus pneumoniae*, and many people over 65 are offered a vaccination against this germ, called Pneumovax 23. However, vaccines are not as effective in older people, which may partly explain the fact that unacceptably high numbers of older people who have been vaccinated still die from lung infections each year. We therefore want to find ways to boost the effectiveness of vaccines in older people.

We all produce a protein called granulocyte-macrophage colony stimulating factor (GM-CSF). This protein helps to produce cells in our lungs that fight infection. Some studies have shown that an injection of GM-CSF can boost vaccines, but this has not been tested in older people receiving respiratory vaccinations.

Our aim is eventually to run a clinical trial in which people aged 60 years and older receive Pneumovax 23 with or without GM-CSF, to determine if this approach is safe and if GM-CSF boosts the effectiveness of the Pneumovax 23 vaccine. However, we cannot design such a trial until we know, in fine detail, the size of the response to Pneumovax 23 in people aged 60 years and older. The purpose of the study described in this document is to provide such information so that we can go on to design the strongest possible clinical trial in the future.

In this study healthy volunteers aged 60 and above who have never received Pneumovax 23 will be recruited. Two groups of volunteers will be recruited – you can only be part of one group, and you can choose which group to be part of, unless one group has already been filled up.

If you take part in **Group 1**, you will come to the hospital three times – on the first visit, you will be asked for your written consent, and then be examined by a doctor, give a blood sample and then receive the Pneumovax 23 vaccine. You will return twice to give blood at around 7 and 28 days later. Further details are in the next section on the next page.

If you take part in **Group 2**, you will come to hospital four times – on the first visit you will be asked for your written consent and then be examined by a doctor to check you are well and to provide a blood sample. On the second visit you will have a blood test, and a camera test of your lungs called a bronchoscopy. This allows us to wash a small segment of your lung with saline (salty water) to retrieve cells from the lung. You will then receive the Pneumovax 23 vaccine. The day after we shall phone you to check that you are well. At the third visit (about a week later) you will have another blood test taken. At the fourth and final visit (about a month later) you will have the camera test and blood test again. The day after we shall phone you to check that you are well. Further details are in the next section on the next page.

The blood and lung wash samples will allow us to test a variety of immune responses to Pneumovax 23 in our labs. We shall test how well older people make antibodies to the vaccine, and how well cells designed to fight infection are boosted by the vaccine. We shall run some of these tests in the lab in the presence or absence of GM-CSF to see if GM-CSF boosts the immune response. We shall perform these laboratory tests in Newcastle, but also in collaboration with world experts in the University of Oxford and University College London.

The information we receive in this study will allow us to pick the best test(s) to take forward to our future clinical trial.

What will happen to you if you take part?

If you are invited to take part in group 1, or only wish to take part in group 1, read on but skip the section on group 2 further down this page, and go instead to page 9.

If you are invited to take part in group 2, or only wish to take part in group 2, skip the following section, and go to the section on group 2 on page 6.

If you would be willing to take part in either group 1 or group 2, read on and make your decision.

GROUP 1

You will come to the Clinical Research Facility (CRF) in the Royal Victoria Infirmary (RVI) on three separate days.

Your **first visit** would involve the following - Informed, written consent will be taken before any study procedures take place (including blood tests, medical history, and examinations). A doctor will first explain to you about the details of the study and then with your consent, ask you a few questions about your medical history, then take your pulse and listen to your heart and lungs.

A doctor or nurse will also check your temperature (using an ear probe) and your oxygen levels (by placing a small probe on your finger). They would then take a blood sample of around 40 millilitres (this is about a tenth the size of an NHS blood donation, or 3 tablespoonfuls). Blood will immediately be sent to NHS labs.

You will then wait about an hour for the results of the blood tests to come back (you can leave and come back in that time if you wish). If the medical history, examination, and blood tests all show that you fulfil criteria for the study, and you have had time to ask any questions about this document and the study, you will be invited to consider giving your written consent to take part.

A doctor or nurse will give you the Pneumovax 23 injection. This is usually given into a muscle at the top of your arm. You can then leave.

The first visit should take 2 hours in total (this includes the wait for blood results to return).

Your **second visit** will be approximately 7 days after your first visit and would involve coming to the CRF at RVI, where a doctor or nurse will take a blood sample of around 30 millilitres. You can leave after this. The second visit should take approximately 10 minutes.

Your **third visit** would be identical to the second visit but would be approximately 28 days after your first visit. This would be your final involvement in the study.

GROUP 2

You would attend the Clinical Research Facility (CRF) in the Royal Victoria Infirmary (RVI) on four separate days.

Your **first visit** would involve a screening visit as follows –Informed, written consent will be taken at the beginning of the first visit before any study procedures take place (including blood tests, medical history, and examinations). A doctor will first explain to you about the details of the study and then with your consent, ask you a few questions about your medical history, then take your pulse and listen to your heart and lungs. A doctor or nurse will also check your temperature (using an ear probe), your oxygen levels (by placing a small probe on your finger), your blood pressure (using a blood pressure machine), and a breathing test called spirometry (where you blow hard into a small machine). They would then take a blood sample of around 10 millilitres (this is about 2% of the size of an NHS blood donation, or the equivalent of 1 tablespoonful).

The first visit is expected to last about 30 minutes.

Your **second visit will occur** within a week of the first visit, and will take place in the Endoscopy suite of the RVI.

We shall check that you continue to give consent to the tests. Your temperature, oxygen levels, blood pressure and spirometry will be measured, as on your first study visit day. A 30-millilitre blood sample will be taken by a doctor or nurse. You will then have your bronchoscopy and bronchoalveolar lavage (BAL).

A bronchoscopy is a routine NHS medical procedure typically done to diagnose and investigate lung disorders. It involves a thin, flexible plastic tube (the scope) being passed via the mouth or nose into the lungs. The tube has a light and a fibre-optic camera to allow us to see inside your lungs, and a small port through which we can insert fluid into your lungs, or suck fluid back from the lungs.

To ensure your safety during the procedure we ask that you do not consume solid food for 4 hours before the test. You can continue to drink clear fluids until 2 hours before the test, and you can take any medications that you normally take. This is to make sure that your stomach is empty and there is no risk of food entering your lungs while your throat is numb.

The preparation for the procedure takes longer than the actual test itself. You will have the test in a dedicated room in the Endoscopy Suite. Your blood oxygen levels will be monitored throughout using a probe placed on your finger, and we will give you some oxygen through your nose if the blood oxygen levels are unexpectedly low at any point.

A local anaesthetic spray is given to your mouth to numb the back of your throat to prevent any discomfort. This sometimes makes your eyes water and can have a bitter taste. The local anaesthetic wears off after 2-3 hours. A small plastic tube called a cannula will be inserted into one of the veins in your arm or hand, using a needle. We can take your blood tests at the same time. After this, we will give you a sedative injection through the cannula if this is your wish. The goal of the sedative is to make you relaxed and sleepy during the test. We will put a mouth guard in to protect your teeth and the bronchoscope, and the test will begin when you are comfortable.

The actual procedure (see diagram below in Figure 1) is typically brief, lasting only around 10-15 minutes. The scope is passed through your mouth (or nose if you prefer, but the mouth tends to be more comfortable) to your voice box. At this point, we spray local anaesthetic down

the scope to numb your vocal cords and airways. This will initially trigger a cough, and you may briefly feel as if you have swallowed a small amount of liquid down the wrong way. Once your cough has eased, we pass the scope into the lungs and perform the bronchoalveolar lavage. This involves squirting sterile saline (a medical solution of salty water) into a single segment of your lung. There are 19 segments in your lungs in total, and only one of these should receive the saline. We gently suck the saline back up through the scope into specimen pots. This fluid now contains cells from deep inside your lungs that can be analysed in our labs. We remove the scope as soon as we have collected the fluid samples.

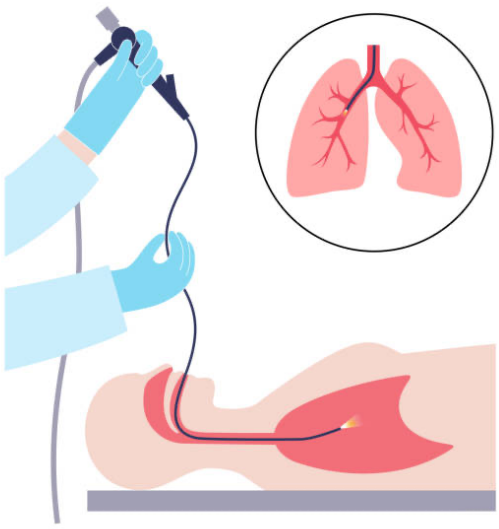

Figure 1: Diagram of bronchoscopy procedure

Bronchoscopy is considered a very safe procedure, even more so in healthy volunteers. The monitoring of your oxygen levels is routine practice during bronchoscopy in the NHS and enables us to give you more oxygen in the unlikely event that your oxygen levels are low.

The biggest drawback of the procedure is that some people find it temporarily unpleasant. We will outline some of the elements that people sometimes find difficult:

- We numb the mouth with a throat spray that has a bitter taste. It may make your eyes water briefly and can leave the sensation that your mouth is ‘swollen’ and that it is hard to swallow. In reality, there is no swelling, this is merely the sensation of having a numb throat (you may have had a similar sensation after having dental work before). We ask you not to eat or drink until your sensation has returned. This can vary from individual to individual but usually takes around 2-3 hours.
- Some people have a very strong gag reflex that triggers before we reach the vocal cords (voice box). This eases once we have applied more local anaesthetic to the vocal cords. In the rare situation that you find the test intolerable; we will simply stop the procedure.
- Most people have a bout of coughing when we first numb the vocal cords, or when we pass the scope into the lungs for the first time. Some people can experience a choking sensation. This almost invariably lasts less than 10 seconds in duration and does not affect your breathing or oxygen levels. We may ask you to do simple things like count slowly to 10, as this has proven to be an effective means of reassurance through a very brief discomfort.
- People rarely cough much when the saline goes into the lungs, though it can occur.

A note on sedation:

- While people generally find bronchoscopy tolerable with just local anaesthetic as described above, some prefer to have a sedative (midazolam) before the procedure. This is more common in clinical practice when we are performing longer and more complicated bronchoscopies in the presence of lung disease.
- If you would like to have sedation this is perfectly acceptable, however there are added precautions to consider following the test. A sedative drug can make you feel sleepier than normal, and even if you feel fully alert following sedation it can still affect your memory and judgement for several hours afterwards.
- If you have sedation**, <u>you must be accompanied home by a friend or relative.</u>**
- If you have sedation, **<u>you must not return to work duties, drive, cycle, operate moving machinery, or sign any legal document for the remainder of that day</u>**.

Following the procedure:

- You will rest and be observed in the recovery room of the Endoscopy Suite. The staff will monitor your pulse, blood pressure, temperature, and oxygen levels.
- After 2-3 hours you should be allowed to eat, once the effects of the local anaesthetic throat spray have worn off. Your throat may feel a little sore at first, but this is typically mild and eases quickly.
- A doctor will see you and confirm you are safe to return home, unless any unexpected findings arise.
- Following a bronchoscopy and BAL some people experience a rise in temperature later in the day or night. This is not a cause for alarm and is usually brief. Paracetamol is a simple and effective treatment for this.
- Occasionally people find themselves coughing more frequently for approximately 24 hours after a bronchoscopy, and very occasionally they can find specks of blood in their phlegm. This is also entirely normal and not a cause for concern.
- People are typically able to resume full normal activities the day after a bronchoscopy with no limitations.
- We will contact you by telephone the day after each bronchoscopy to ensure you are well, and to answer any questions you may have.

On your second visit, after the bronchoscopy and before going home, you will receive the Pneumovax 23 injection into a muscle at the top of your arm.

The second and visit is expected to last up to 5 hours (depending on how sleepy you are after sedation).

Your **<u>third visit</u>** will be approximately 7 days after your second visit and will involve coming to the CRF at the RVI, where a doctor or nurse will take a blood sample of around 30 millilitres. You can leave after this. The third visit should take approximately 10 minutes.

Your **<u>fourth visit</u>** will be identical to the second visit (the bronchoscopy) but will be approximately 28 days later. You will not receive the Pneumovax 23 vaccine during the fourth visit. You will have another 30 millilitre blood sample taken as well as having another bronchoscopy. You should follow the same advice as given for the second visit and we ask that you do not consume solid food for 4 hours before the test. You can continue to drink clear fluids until 2 hours before the test, and you can take any medications that you normally take. The fourth visit will be expected to last the sample length of time as the second visit, up to 5 hours. This would be your final involvement in the study.

Are there any benefits to taking part?

The only recognised benefit is that you will have some extra protection against future infections with *Streptococcus pneumoniae*.

What are the potential risks and disadvantages of taking part?

There are small risks associated with the various components of the study.

Blood samples

Blood samples can leave a small bruise in the skin for a few days. A small proportion of people feel faint, or may even pass out, when giving blood. We reduce the risk from these issues by performing blood samples in a clinical area, and with you in a self-reclining chair (so we can lie you flat if you feel faint).

Pneumovax 23

Pneumovax causes some redness, pain and swelling around the injection site, some stiffness in the arm, and often a high temperature in at least 10% of people. This usually lasts less than 24 hours and responds to paracetamol. However, some people have these symptoms for up to 3 days.

Bronchoscopy and BAL

Bronchoscopy is considered a safe, routine clinical procedure. As described earlier, the bronchoscopy can lead to a painful throat, a sensation of a numb throat, and a taste of salty water. When the scope approaches or enters the voice box and lungs you may cough or gag, and you may have a very brief sensation of choking. Some people can be wheezy or become breathless during bronchoscopy.

We reduce these risks by performing the procedure in a fully equipped medical department, by giving you local anaesthetic to your mouth/nose/throat, by offering you sedation if you wish, and by providing oxygen if you require it. Should you become wheezy we will give you inhaled treatment to reverse this.

The cannula placed in your vein can produce discomfort and bruising as with a blood test.

Payment/reimbursement

Because of the inconvenience and time involved, your time is reimbursed using gift vouchers.

If you are in Group 1 the reimbursement is £100 if you complete all the tests. If you give consent then at least the first blood sample and vaccination for Group 1, but do not complete the study, the reimbursement is £25.

If you are in Group 2 the reimbursement is £500, because the procedures are more involved and take longer. If you give consent then have at least the first bronchoscopy and BAL, but do not complete the study, the reimbursement is £100.

Regardless of which group you are in, travel costs will be reimbursed upon production of travel receipts.

What happens if we find a medical abnormality during the study?

If we come across a medically unexpected finding, we shall let you know. We shall ask your permission to let your GP know the result so that they can decide whether to act upon the findings according to usual clinical pathways and guidelines

What happens if you want to stop taking part in the study?

It is important to note that your participation is entirely voluntary. You are free to withdraw from the study at any time, and without giving a reason. Any procedure, that we would do (including taking of blood samples, administering vaccine, or performing bronchoscopy can be terminated if you express a desire to stop.

A decision not to take part, or to withdraw, will in no way affect the health care you receive now or in the future. While we obviously prefer participants to complete all the tests, including the return visits, you are under no obligation to do so.

If you do decide to withdraw from the study you will be asked if our findings up that point can be kept for the study, or if you would like all study data pertaining to you to be destroyed.

What if something goes wrong during your participation in the study?

We do not expect anything to go wrong as a result of you taking part in this research study. If something goes wrong and you are harmed during the research due to someone's negligence, then you may have grounds for a legal action for compensation against the Newcastle upon Tyne Hospitals NHS Foundation Trust, but you may have to pay your legal costs.

If you have a concern about any aspect of this study, you can speak to a member of the study team who will do their best to answer your questions. Further contact details are included at the end of this information leaflet.

If you are unhappy or have any concerns about any aspect of the study and wish to complain formally and confidentially, you can do so through the NHS complaints procedure. To discuss your concerns or make a complaint you can contact a member of the PALS (Patient Advice and Liaison Service) on 0800 0320 202, or Text/SMS: 0781 5500015 or by visiting northoftynepals@nhct.nhs.uk

Will we inform your general practitioner about your participation in the study?

We will ask you if you give consent for us to send your GP information about your participation in the study, and the results of any abnormal clinical findings. We will only forward this information with your consent.

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What will happen to the samples that you provide?

Blood samples taken during the study are for two purposes.

Some of the samples will be taken and processed at the NHS laboratories at the hospital to ensure there are no issues that prevent you from participating.

The remainder of the samples taken will be transferred to the laboratories at Newcastle University for further processing. Some of the samples processed will be sent to our collaborators in the University of Oxford and University College London, who have world-leading expertise in assessing the immune response to vaccines. All University laboratory samples will only be labelled with a study number, and no personal identifiable information. If we have any excess blood or cells that are not required for the study, then with your permission it will remain anonymously in our lab to assist future research by the team or our collaborators.

The samples of lung fluid from your bronchoscopy will be transported immediately to the laboratories at Newcastle University for analysis. Some of the samples processed will be sent to Oxford and University College London, as for blood samples described above. These will be labelled only with a study number, and no identifiable information.

With your permission, both the blood and lung fluid samples may be frozen and stored in an anonymised form after the completion of the study, for use in future research. As new information becomes available there may be good reasons to perform further tests on the samples in another medical research. If this situation should arise, testing will only proceed with your permission, and the resulting information will remain anonymous.

There are no plans to do any diagnostic genetic testing on the samples we obtain.

What will happen if I lose capacity to consent at any time during the study?

If you lose capacity to consent at any point during the study, you will be withdrawn from the study. Identifiable data and samples already collected up to this point will be kept.

Can you see the results of the study?

We cannot send you research results relating to your individual samples, but we would be happy to send you a summary of the study's overall results after the study is complete. If you would like for us to do this, please contact us on one of the contact addresses below or inform us during one of your study visits. We will add you to a mailing list and contact you when results are available.

We intend for the results of this study to be published in medical and scientific journals and presented at national and international meetings. All information within the public domain will be entirely anonymised. We hope that our findings will stimulate further research, and in particular a clinical trial assessing whether GM-CSF improves the way that Pneumovax 23 (and eventually other vaccines) work.

Who has reviewed the study and who is funding it?

We successfully applied to the Medical Research Council's Impact Accelerator Award scheme. This involved a panel of experts from Newcastle independently assessing the scientific quality of the application over a three-staged process.

The study is sponsored by the Newcastle upon Tyne Hospitals NHS Foundation Trust.
The study has been reviewed by South Central – Hampshire B Research and Ethics Committee.

Has there been patient and public involvement in the design of this study?

While there has not been direct public involvement in the design of this study, as it was devised to answer a scientific hypothesis, we have taken suggestions from members of the public who have kindly acted as lay committee members in previous work undertaken by our study group. This includes how to describe the bronchoscopy procedure, what remuneration is appropriate, and how to ensure potential volunteers are as well informed about the study as possible.

How will we use information about you?

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

- Initials
- NHS number
- Name
- Contact details

People will use this information to do the research or to check your records to make sure that the research is being done properly. 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.
The Newcastle upon Tyne Hospitals NHS Foundation Trust is the sponsor of this research.

The Newcastle upon Tyne Hospitals NHS Foundation Trust is responsible for looking after your information. We will share your information related to this research project with the following types of organisations:

- University of Oxford
- University College London

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

- Storing samples in temperature-controlled storage facilities in our laboratory before being transferred to the Newcastle University Biobank after the study concludes.
- Sending some of the samples in batches to University of Oxford and University College London with code numbers/sample numbers that will not include any identifying information, ideally within a year.

International transfers

Your data will not be shared outside the UK.

How will we use information about you after the study ends?

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

We will keep your study data for a maximum of 15 years. The study data will then be fully anonymised and securely archived or destroyed.

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.
- If you choose to stop taking part in the study, we would like to continue collecting information about your health from central NHS records / your hospital / your GP. If you do not want this to happen, tell us and we will stop.
- You have the right to ask us to access, remove, change or delete data we hold about you for the purposes of the study. You can also object to our processing of your data. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this.
- If you 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. We will store your samples in dedicated temperature-controlled facilities in our lab and the biobank at Newcastle University. The data will be stored securely via an appropriate central portfolio management system.

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

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

- From the HRA via **www.hra.nhs.uk/patientdataandresearch**
- By asking one of the research team
- By sending an email to nuth.dpo@nhs.net, or
- By ringing us on 0191 2825789.
- By contacting our Research Governance Manager Aaron Jackson, at The Newcastle upon Tyne Hospitals NHS Foundation Trust, Level 1 Regent Point, Regent Farm Road, Newcastle upon Tyne, NE3 3HD.

If you have any questions or concerns about taking part, please contact:

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