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A human controlled infection study to establish a safe, reproducible and practical human *Bordetella pertussis* colonisation model for the identification of correlates of protection against colonisation.

Volunteer information sheet – Phase B (Challenge Volunteers)

We would like to invite you to take part in a research study. Before making a decision about whether or not to take part, please take the time to read this information sheet and discuss it with friends, relatives and your General Practitioner (GP) if you wish. Please contact the study team if you have any questions about the details provided in this information sheet.

The following pages contain detailed information about what this study involves including study procedures, time commitments, risks, benefits and compensation, which you should read and understand before making a decision about whether or not to take part.

In this study, we are trying to find out how we can best protect people against the disease **whooping cough**. To do this, we will be performing a deliberate controlled infection of the nose, so that the body is transiently infected with the agent that causes this disease.

You do NOT have to take part.

Before you join we will explain in the following pages exactly what it entails but **first we want to highlight key points** that we think you should know before making a decision. If you are still interested in joining our study, we'll then go into more detail.

The key points are:

- You will be given a small dose of live bacteria into your nose once at Day 0 and again at week 14 (optional) over a period of (up to) 4 months
- We will then take swabs and other samples from your nose and throat, and blood tests to monitor the infection
- You will be treated with the antibiotic Azithromycin after 2 weeks after each time you are given the bacteria, to eradicate possible infection
- There is a possibility that these bacteria will spread to your bedroom contact
- We will need to know if this occurs, so we would like to monitor whether these bacteria have spread to your bedroom contact by taking nasal wash samples
- You and your bedroom contact will be required to follow infection control rules throughout the study including abstaining from intimate contact with any other individual for the duration of the study
- You and your bedroom contact will be given a dose of antibiotic treatment during the study
- There is a small chance you and your bedroom contact will get the symptoms of whooping cough but we will closely monitor you and treat early
- You mustn't have had any past problems with your immune system
- We must receive your medical history and have your GP confirm eligibility prior to enrolling onto the study

What is *Bordetella pertussis*?

Whooping cough, also called pertussis, is a bacterial infection of the lungs and airways. It is caused by a bacterium called *Bordetella pertussis* (*B. pertussis*). Whooping cough can cause repeated coughing bouts that can last for three months or more. Young babies under six months of age are typically affected and are in the age group that is most vulnerable to serious complications. In older children and adults it tends to be less serious, although it can still be unpleasant and frustrating. In some adults who are infected there may be no symptoms at all, so that the infection passes unnoticed. *B. pertussis* is spread in the droplets produced when someone with the infection coughs or sneezes. Therefore you can catch whooping cough if you come into close contact with someone with the infection. The first symptoms are similar to those of a cold, such as a runny nose, red and watery eyes, a sore throat, and a slightly raised temperature. Intense coughing bouts typically start about a week later. Antibiotics will help stop the infection spreading to others, and usually (*but do not always*) reduce the symptoms. If antibiotics are given during the early phase of the infection, it is believed that the cough can be prevented, but there are exceptions to this rule and it is possible that people who are given antibiotics even during the early phase of illness may go on to develop the cough. Although a pertussis vaccine is offered to all babies in the UK, the vaccine does not offer lifelong

protection. In fact, protection by the vaccine seems to be less nowadays in comparison to 15 years ago.

What is the purpose of this study?

This study is part of a project that aims to develop a better vaccine against whooping cough. To do this we need to know more about the immune response generated against carriage of *B. pertussis* and what kind of immune response protects against whooping cough. This study is designed to look at those particular questions by inoculating healthy volunteers with nose drops containing *B. pertussis*, trying to cause nasal colonisation without causing disease and then monitoring their immune response before giving them antibiotics to clear *B. pertussis*.

In Phase A of our study we investigated the effect of *B. pertussis* and optimised the dose of bacteria so volunteers get colonised without getting ill. In phase B, this phase, we will give the optimised dose in the form of nose drops to approximately 60 healthy volunteers and include persons who have close contact with them to see if they become a carrier as well.

Volunteers in Phase B who have been inoculated with *B. pertussis* will be required to attend several visits to the National Institute for Health Research (NIHR) Southampton Clinical Research Facility (CRF). 14 weeks after the initial inoculation you will be exposed to the same dose of *B. pertussis* and receive antibiotics again 14 days later (optional). We would like to re-challenge as many volunteers as possible at week 14 to show if volunteers will have consistent protection against colonisation or that initial inoculation has caused protection against colonisation.

Will the bacteria be transmitted from me to my friends and family?

B. pertussis is spread in the droplets produced when coughing or sneezing so can be transmitted from individuals to their close contacts, in particular to household members and those sharing a bedroom (bedroom contact).

We are asking for your bedroom contacts' consent to be involved in this study as there is a possibility that *B. pertussis* will be transmitted to them and that they will become infected with it. We would like to monitor this. We need to ensure that you and your bedroom contact have no underlying vulnerability which might make this unsafe.

We will issue you and your bedroom contact with antibiotics on day 14 and week 16 of the study or when you get a cold or a runny nose regardless of whether you have been a carrier or not.

In order to minimise the risk of transmission to other close contacts, we will not include volunteers who have household members who are have any problems with their immune system, pregnant women, frail individuals or children under 12 years old living in the same household. Both you, as a challenge volunteer, and your bedroom contact, as a contact volunteer, will be required to agree to infection control measures (detailed on page 8 of this information sheet) to minimise the risk of transmission of *B. pertussis* to any other individuals. You will need to agree not to share a bedroom or have intimate or sexual contact with any other individual(s) during the study period (From Day 0 to Day 16 and should you decide to take part in the optional re-challenge, from week 14 to week 16+ 2 days).

Am I eligible to take part?

In order to be involved in this study as a contact volunteer you must be:

- A healthy adult aged between 18 – 55 years on the day of enrolment
- Fully conversant in the English language
- Able to communicate easily by both mobile telephone and text messaging
- Able and willing (in the investigator's opinion) to comply with all study requirements
- Willing and able to provide informed consent to participate in the trial
- Able to correctly answer all questions in the infection control questionnaire
- Willing and able to give written agreement to abide by infection control guidelines (see page 8)
- Willingness to attend the NIHR Southampton CRF immediately if you become symptomatic
- Agreement to have no other bedroom contact(s) than your declared partner during the days between being exposed to the bacteria and two days after starting antibiotic treatment.
- For females only, willing to practice continuous effective contraception during the study and a negative pregnancy test on the day of screening
- Willing to take antibiotic eradication treatment when instructed to by the study team

Acceptable forms of contraception include:

- Established use of oral, injected or implanted hormonal methods of contraception
- Placement of an intrauterine device or intrauterine system
- Total abdominal hysterectomy
- Barrier methods of contraception (condom or occlusive cap with spermicide)
- Male sterilisation if the vasectomised partner is your only partner

- True abstinence when this is in line with your preferred and usual lifestyle

You would be unable to participate if:

- You have inviolable commitments during the study (from day 0 to day 16, if opting into the re-challenge week 14 to week 16 + 2 days) and/or make contact with:
    - unimmunised or partially immunised children and infants aged < 1 year
    - pregnant women >32 weeks who have not received pertussis vaccination at least a week prior to contact
- You have household contacts working with
    - unimmunised or partially immunised children and infants aged < 1 year
    - pregnant women >32 weeks who have not received pertussis vaccination at least a week prior to contact
- You are living in the same household as:
    - Children under the age of 12 years
    - pregnant women
    - immunosupressed individuals
    - frail individuals
- You live in a boarding school or dormitory during the study
- *B. pertussis* detected on nasal wash sample taken before the challenge
- You have signs of a current infection at the time of inoculation with *B. pertussis*
- You have been involved in other clinical trials over the last 12 weeks
- You have a confirmed or suspected problem with your immune system or have taken medication that affects your immune system for 14 days or more within the past 6 months (topical steroids are allowed)
- You have had a previous allergic reaction or serious side effect following the use of certain antibiotics.
- You have used systemic antibiotics within 30 days of or during the challenge
- You have a history of receiving *B. pertussis* vaccination in the last 5 years
- You have a history of never being vaccinated against *B. pertussis*
- You are a current smoker defined as having had a cigarette/cigar in the last week.
- You have any confirmed or suspected immunosuppressive or immune-deficient state
- You have used immunoglobulins or blood products within 3 months prior to enrolment

- You have a history of allergic disease or reactions likely to be exacerbated by any component of the inoculum
- You have a contraindication to the use of Azithromycin or macrolides
- You are pregnant, lactating or intend to become pregnant during the study
- You have any clinically significant abnormal finding on biochemistry, haematology, toxicology or serological blood tests, urinalysis or clinical examination during screening.
- You have any other significant disease, disorder, or finding which may significantly increase the risk to the volunteer because of participation in the study, affect the ability of the volunteer to participate in the study or impair interpretation of the study data, for example recent surgery to the nasopharynx

If you have private medical or travel insurance you are advised to contact your insurance company before participating in this trial, because involvement in this study may affect the cover provided by private insurance.

What makes someone immunosuppressed?

Immunosuppressed individuals are people who have a reduced ability to fight off infections, which may be due to medication or to an underlying medical condition. Examples are given below but specific situations can be discussed further at your screening visit:

- Cancer
- Recurrent severe infections
- Asplenia – a person who does not have a working spleen
- HIV infection / AIDS (dependant on blood results)
- Use of immunosuppressant medication e.g. after an organ transplant or using long term steroid tablets used for asthma

Do I have to take part?

No, it is up to you to decide whether or not to agree to be involved as a challenge volunteer. However, if you have a bedroom contact, in order to participate in this trial, he/she will need to agree to participate as a contact volunteer and both of you have to follow infection control guidelines. One of these guidelines is to not share a bedroom with any individual other than a declared volunteer during the days between being exposed to the bacteria and two days after starting antibiotic treatment. Therefore, if your bedroom contact decides not to give their consent then you – the challenge volunteer - will be ineligible to take part in this study if you continue to share a bedroom or have intimate contact with your bedroom contact during the study period.

You are free to withdraw from the study at any time without giving a reason, but you may be asked to take antibiotic treatment and come to a follow up visit for safety reasons.

What will happen if I take part?

If you do decide to take part there are specific visits and rules we require you to adhere to.

Screening visit

If you are interested in taking part in this study as a challenge volunteer, you will be invited to attend a screening appointment at the NIHR Southampton CRF at University Hospital Southampton, which will last up to two hours. This visit can be at the same time as your bedroom contact screening visit or at another mutually convenient time. The purpose of this visit is for us to discuss the study with you, answer any questions you might have, and for you to decide if you wish to participate. If you decide to participate you will be asked to sign a consent form.

We will then check that you do not have any health conditions that affect your eligibility for the study or make the study unsafe for you. A doctor will ask you some medical questions and examine you. We will do an ECG (heart rhythm tracing), take a throat swab and nasal wash sample, take some bloods and perform a urine test (including a pregnancy test for females). We will send a letter to your GP asking to confirm your medical history to make sure this study is safe for you and we will provide them with information about what the study involves.

Pre-inoculation visit (Day -7 and optional week 13)

If you are eligible for the study, we will ask you to come for a pre-inoculation visit 7 days before inoculation to check that you are still not carrying natural *B. pertussis* and take some baseline samples (throat swab, nasosorption sample, breath sample and saliva sample). Once this is confirmed you will be asked to return for your next visit and be inoculated.

Inoculation day (day 0 and optional week 14)

We aim to give you the bacteria nose drops twice; on day 0 and on (optional) week 14.

We will ask you not to eat or drink anything other than water for the hour prior to your inoculation. We will check that you are still happy to continue in the study and that nothing has changed with your medical history. Prior to the inoculation we will take some blood tests. Females will also have another pregnancy test.

You will then be given the inoculation of *B. pertussis*. You will be asked to lie on your back with your neck extended back and 0.5ml of fluid containing a carefully measured amount of bacteria will be dripped slowly into each nostril over approximately 1 minute for each nostril. You will be able to breathe through your mouth during this procedure. Following the inoculation you will be asked to remain lying down for 15 minutes.

Follow up (visits: day 3, day 7, day 14,day 28, and optional visits week 13, week 15, week 16 and telephone contact week 18)

After your day 0 visit you will be asked to return to the NIHR Southampton CRF for 8 follow up visits. At each of these visits we check you are well and we will take a throat swab, a nasal swab, a nasal wash, a nasal fluid sample and a breath sample to look for colonisation of *B. pertussis*. We will also take some bloods to look at your immune response.

		Initial challenge						*Re-challenge (week 14 -2/+6 weeks) (Optional additional visits)*				
Time-point	*Screening*	*D-7*	*D0*	*D3*	*D7*	*D14*	*D28*	*W13*	*W14*	*W15*	*W16*	*W18 (Phone call)*
Challenge volunteers												
Visit to CRF	x	x	x	x	x	x	x	x	x	x	x	
Screening examinations	x											
Challenge with bacteria			x						x			
Bloods	x		x	x	x	x	x		x	x	x	
Nasal and oral samples	x	x	x	x	x	x	x	x	x	x	x	
Breath sample		x	x	x	x	x	x					
Antibiotics						x					x	
Must adhere to Infection control measures			Yes	Yes	Yes	Yes (Plus an additional 2 days)		Yes	Yes	Yes	Yes (plus an additional 2 days)	
Contact volunteers												
Visit to CRF	x				x	x						
Screening examinations	x											
Nasal wash	x				x	x						
Antibiotics						x					x	
Must adhere to Infection control measures			Yes	Yes	Yes	Yes (Plus an additional 2 days)		Yes	Yes	Yes	Yes (plus an additional 2 days)	

Table 1. Summary of visits and procedures.

Daily nasal fluid samples

From Day 0 to Day 14 we would like to take a nasal fluid sample every day. If you have a follow up visit, the nurse will take the sample. The other days we would like you to take the sample yourself, store it in your fridge and bring it to the next follow up visit. We will teach you how to do this, and we encourage you to ask questions at any point if you are unsure.

You may be asked to attend extra visits if medically required, for example if you develop any symptoms that could be caused by *B. pertussis.*

Breath sample

A breath sample will be taken on visits Day-7, Day 0, Day 3, Day 7, Day 14 and Day 28. This involves wearing a mask which is attached to a small piece of equipment (similar to a large plastic test tube attached via plastic tubing). The mask will cover your nose and mouth. You will be asked to breathe normally for 10 minutes before removing the mask. You will be able complete the test whilst sitting comfortably.

Antibiotic eradication therapy

You will be given a course of an antibiotic called Azithromycin on Day 14 and week 16. Azithromycin is a licensed drug in the UK for the treatment of whooping cough, and the treatment consists of a 500 mg tablet once a day for 3 days. We will need to watch you take the first dose.

If you start to cough or have a runny nose between Day 0 and Day 14, or between week 14 and 16, we will give you antibiotic eradication therapy immediately. Following this we would like you to continue with the study visits and procedures as normal. We may also ask you to take the antibiotic eradication early if you or your spouse/partner need to withdraw or be withdrawn from the study early for any other reason. We will give you a second course of antibiotics for your bedroom contact for them to start at home on week 16 if they are taking part in the study. They will need to take the antibiotics even if they feel well and have no symptoms.

Infection control rules

In order to minimise unwanted infection with *B. pertussis* you and your bedroom contact will be required to follow infection control measures for the duration of your involvement in the study (from Day 0 to Day 16 and should you decide to take part in the optional re-challenge, week 14 to week 16 + 2 days). These measures will be explained at the screening visit and again after inoculation. You will be asked to complete a questionnaire to confirm your understanding and sign an agreement to adhere to these rules throughout the study.

During your involvement in the study:

- Volunteers must avoid heavily crowded social environments such as music festivals, crowded pubs and nightclubs
- Volunteers stay overnight in their own household only
- Volunteers refrain from bedroom sharing with any individual other than their contact partner

- Volunteers must not have any contact with high risk of transmission with any individuals other than their declared and consented bedroom contact/corresponding contact volunteer – such contact includes:
    - Bed sharing
    - Intimate/sexual contact
    - Contact that may involve transfer of respiratory secretions e.g. kissing
    - Sharing cutlery or drinking vessels
- Volunteers need to wash their hands before leaving their home and are not allowed to have direct face-to-face contact (< 2 metre distance) for greater than a cumulative period of 1 hour with other people
- Volunteers must be able to be return to the NIHR-Southampton CRF within 120 minutes

During the study:

- Volunteers must avoid contact with immunosuppressed individuals, pregnant women, frail individuals, children under the age of 1 year and unvaccinated children
- Volunteers must be contactable by mobile phone, which has the study emergency phone number programmed in, and contact the clinical study team if they have any symptoms early pertussis disease.

What are the risks of taking part?

Clinical samples

Throat swabs can be a little uncomfortable or cause gagging but this will resolve quickly and should not be painful or pose any risk to you.

We collect nasal fluid by performing a nasal wash. This process involves placing warm salty water into each nostril via a small syringe. We will only use 10 ml (2 teaspoons) of fluid at a time. We will then ask you to tip your head forward to let the fluid back out and collect it for analysis. It feels a little unusual but you can breathe normally through your mouth throughout the entire process.

Taking nasal fluid samples, breath samples and saliva samples does not cause any discomfort.

The inoculation with fluid containing *B. pertussis* may cause some irritation of the nose that will disappear within a few seconds.

The maximum total volume of blood taken during the study is approximately 529 ml over the study. The amount taken on one day will be a maximum of 90 ml (18

teaspoons). The volume of blood being taken over the course of the trial should not cause any problems in healthy people. There may be some temporary mild discomfort, such as bruising and tenderness at the site where the blood tests are taken. You may experience faintness as a result of the blood test. We will give you a copy of your blood test results if you request them, and will only send the results to your GP if you wish us to and will not report them to anyone else without your permission.

Whooping cough

The aim of the challenge model is to establish colonisation of *B. pertussis*, but not to cause whooping cough disease, **although there is a possibility that whooping cough may occur as a result of the inoculation.**

Initial symptoms of whooping cough in adults include a runny nose, sneezing and 'flu like' symptoms, hoarseness, sinus pain, headaches and a persistent cough. If you have one or more of these symptoms we will review you immediately. If you develop a cough or a runny nose we will give you antibiotic treatment immediately after taking blood, nasal and throat samples. We expect such early treatment to reduce the illness in comparison to natural infection where treatment is often delayed due to the typically mild and non-specific presentation. Of the first 34 volunteers who participated in phase A no one developed a lengthy cough. However there are always exceptions to every rule and we cannot exclude the possibility that you may be left with a lengthy cough as a result of taking part in the project. During Phase A no serious events were reported, none of the volunteers received emergency antibiotics and none withdrew from the study due to study-related activity. Complaints of a cough or runny nose occurred equally between those volunteers who were colonised and those who remained uncolonised.

In adults who develop whooping cough, coughing episodes may disturb sleep or result in vomiting, and occasionally cause whooping. Adults can develop complications from pertussis, but they occur less frequently and are usually less severe than in children. Reported complications of pertussis disease include urinary incontinence (during the coughing bouts), rib fractures, collapsed lungs, inguinal hernias, aspiration, pneumonia, seizures and ear infections. These complications have only been reported in children, or in debilitated adults who suffer from other diseases or who are older than 65 years.

Antibiotic treatment

To eradicate carriage or treat possible whooping cough you will be given a course of Azithromycin (once at Day 14 and again at Week 16) .

Azithromycin is generally well tolerated, but may cause some side effects. The side effects include:
Common: Abdominal discomfort; diarrhoea; nausea; vomiting
Uncommon: Jaundice; liver dysfunction; rash
Rare: Antibiotic-associated colitis; heart rhythm problems; pancreatitis; Stevens-Johnson syndrome; toxic epidermal necrolysis (serious skin conditions)
Frequency not known: Reversible hearing loss (sometimes with tinnitus) can occur after large doses.

If you experience any of these symptoms you should contact a doctor immediately, and then inform us.

Are there any benefits to taking part?

It is unlikely that you will benefit directly from this study; however there is the possibility that taking part will result in you having a degree of immunity to whooping cough. We hope that the information gained from this study will help inform the development of vaccines to prevent pertussis and the associated serious complications in the future. You may gain some general information about your health as part of this study. If abnormal results or undiagnosed conditions are found in the course of the study these will be discussed with you and your GP will be informed. For example, a new diagnosis of anaemia or psychological disorder might be made. Any newly diagnosed conditions will be looked after by your GP within the NHS.

Will my taking part in this study be kept confidential?

Yes, all information that we collect about you will be coded with a study number and kept confidential. The information will be available to the study team, safety monitors, sponsor, government regulatory agencies and external monitors who can ask to audit or monitor the study. All study information will be held in paper form in a locked room in the NIHR Clinical Research Facility or in electronic form on a secure server. Any information that leaves the hospital will have your name removed so that you cannot be identified.

What will happen to my personal data after the study has finished?

All essential research data including personal data will be stored securely within University Hospital Southampton or the University of Southampton. It will be anonymised and identifiable by a unique participant ID. This study is likely to be linked to future research studies which may take place over several years. Access to this research data by authorised persons may be required in the future and so this data will be archived for a maximum of 15 years.

Who is organising and funding this study?

This research is being organised by the University of Southampton and funded by The Periscope project, which has received funding from the European Union Innovative Medicines Initiative. It is being sponsored by University of Southampton. There are no conflicts of interest for any of the research team working on this study.

Who has reviewed this study?

All research in the NHS is reviewed by an independent Research Ethics Committee to protect your interests. The study has been reviewed and approved by the Health Research Authority. Samples taken during the study may be used in future research only after this future research is ethically approved.

Data Protection Privacy Notice

The University of Southampton conducts research to the highest standards of research integrity. As a publicly-funded organisation, the University has to ensure that it is in the public interest when we use personally-identifiable information about 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 information about you in the ways needed, and for the purposes specified, to conduct and complete the research project. Under data protection law, 'Personal data' means any information that relates to and is capable of identifying a living individual. The University's data protection policy governing the use of personal data by the University can be found on its website (https://www.southampton.ac.uk/legalservices/what-we-do/data-protection-and-foi.page).

This Volunteer Information Sheet tells you what data will be collected for this project and whether this includes any personal data. Please ask the research team if you have any questions or are unclear what data is being collected about you.

Our privacy notice for research participants provides more information on how the University of Southampton collects and uses your personal data when you take part in one of our research projects and can be found at http://www.southampton.ac.uk/assets/sharepoint/intranet/ls/Public/Research%20and%20Integrity%20Privacy%20Notice/Privacy%20Notice%20for%20Research%20Participants.pdf

Any personal data we collect in this study will be used only for the purposes of carrying out our research and will be handled according to the University's policies in line with data protection law. If any personal data is used from which you can be identified directly, it will not be disclosed to anyone else without your consent unless the University of Southampton is required by law to disclose it.

Data protection law requires us to have a valid legal reason ('lawful basis') to process and use your Personal data. The lawful basis for processing personal information in this research study is for the performance of a task carried out in the public interest. Personal data collected for research will not be used for any other purpose.

For the purposes of data protection law, the University of Southampton is the 'Data Controller' for this study, which means that we are responsible for looking after your information and using it properly. The University of Southampton will keep identifiable information about you for 15 years after the study has finished after which time any link between you and your information will be removed.

To safeguard your rights, we will use the minimum personal data necessary to achieve our research study objectives. Your data protection rights – such as to access, change, or transfer such information - may be limited, however, in order for the research output to be reliable and accurate. The University will not do anything with your personal data that you would not reasonably expect.

If you have any questions about how your personal data is used, or wish to exercise any of your rights, please consult the University's data protection webpage (https://www.southampton.ac.uk/legalservices/what-we-do/data-protection-and-foi.page) where you can make a request using our online form. If you need further assistance, please contact the University's Data Protection Officer (data.protection@soton.ac.uk).

Expenses and payments

Volunteers will be compensated for their time and for the inconvenience caused by procedures. Payments are as follows;
Screening - £20 compensation (plus up to £15 travel reimbursement)
Inoculation 1 (Visits D-7 to D28)- £60 compensation (plus up to £15 travel reimbursement per visit).
Re-inoculation (Week 13 to Week 16) - £70 compensation (plus up to £15 travel reimbursement per visit).
Week 18 phone call – pre-arrange phone call with a member of the clinical study team- £25
Bonus payment for attending and completing all inoculation 1 visits, re-inoculation visits and phone call - £150
The maximum volunteers will be compensated is £1,000 and the minimum £20. If extra clinical visits are required then they will be paid at £60 compensation (plus up to £15 travel). Extra visits are defined as visits to the NIHR Southampton CRF which require clinical review with the study doctor or nurse.

Compensation will be paid via bank transfer, up to 6 weeks following the final visit (Final visit defined as Week 18 phone call for participants who decide to opt for the re-inoculation visits) and may be delayed around bank holidays. If volunteers withdraw from the study prior to its completion they will be offered financial re-imbursement corresponding to the number of visits attended.

What if there is a problem?

If you have any concerns or symptoms, you should inform a member of the study team immediately. Following inoculation you will be given contact details for the study team who are available 24 hours a day for emergencies.

The investigators recognise the important contribution that participants make to medical research, and will make every effort to ensure your safety and well-being. In the unlikely event of harm during the research study, the University of Southampton has appropriate insurance in place to cover its legal liabilities. While the University will co-operate with any claim, you may wish to seek independent legal advice to ensure that you are properly represented in pursuing any complaint. At any time during the study you will be entirely free to change your mind about taking part, and to withdraw from the study. This will not affect your subsequent medical care in any way.

What if I wish to complain about the way the study was conducted?

If you have cause to complain about any aspect of the way in which you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you and you are not compromised in any way because you have taken part in a research study.
Contact details for the study team, the Sponsor and the independent Patient Support Service located within the hospital are at the end of this information sheet.

What will happen if I don't want to carry on with the study?

If you wish to withdraw from the study you are free to do so at any time, but you may be asked take a dose of antibiotic treatment to eradicate possible carriage with *B. pertussis* and have a telephone contact follow up for safety reasons. In such an event, we would continue to use any data we collected up to the point of your withdrawal. Your compensation would be paid as a proportion of the total compensation according to the length of your participation.

Prevention of 'Over Participating'

Participants participating in this study must not be concurrently receiving medications or vaccines in another study. In order to check this, you will be asked to provide your National Insurance or Passport number (if you do not have a NI

number). This will be entered on to a national database, which helps prevent participants from taking part in too many clinical trials. More information can be found at www.tops.org.uk. Your national insurance or passport number is also required to allow processing of compensation payments.

Contact for further information

If you are interesting in taking part in this study, please contact the study team:

Email: uhs.recruitmentCRF@nhs.net
Tel: 023 8120 3853 Fax: 023 8120 5023

If you have any questions regarding this research study, please contact the clinical research fellow Dr. Hans de Graaf

Email: h.de-graaf@soton.ac.uk
Tel: 023 8120 4989 Fax: 023 8120 5023

If you are a volunteer participating in the study and you would like to contact us in case of an emergency we can be contacted 24 hours a day, 7 days a week on: 077 71674842

If you have a concern or complaint which you wish to discuss with the Sponsor, please contact the Research Governance Manager at the University of Southampton
Email: rgoinfo@soton.ac.uk
Tel: 023 8059 5058

In the event that you wish to discuss this project with an independent third party, please contact the hospital's Patient Support Service (available 9am to 4.30pm Monday to Friday)

Patient Support Service
C Level Centre Block, Mailpoint 81
Southampton General Hospital
Tremona Road
SO16 6YD, Southampton
Tel no. 023 81 20 6325
Email: PatientSupportService@uhs.nhs.uk