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PARTICIPANT INFORMATION SHEET: HIV-CORE 0052 (Group 2)

A study to assess new candidate HIV vaccines in HIV-1/2-negative adults

"A phase I open label trial to assess safety and immunogenicity of candidate T-cell vaccines ChAdOx1.tHIVconsv1 and MVA.tHIVconsv3+MVA.tHIVconsv4 given in combination to HIV-1/2 negative adults in Oxford, UK."

You are invited to take part in a study to test a new vaccine against HIV. Before you decide to take part, it is important that we explain why this research is being done and what it will involve.

You should be aged 18-65 years, HIV-negative and healthy. Women who are interested in participating should not be pregnant, breast-feeding or intending to become pregnant during the study period.

Participating in this trial **does not** mean that you will become immune to HIV. It is important that you continue to protect yourself against HIV infection. During the trial you will be counselled on reducing your risk of infection and receive information on available methods to reduce your risk.

Please take time to read the following information carefully and discuss it with friends, relatives or your GP if you wish. Please ask us if there is anything that is not clear or if you would like more information.

Key Information for You to Consider

- **Voluntary Consent**. You are being asked to volunteer for a research study. You can choose to participate or not. There are no penalties for not participating, or if you decide to leave once you have joined the study
- **Purpose**. This study is to test whether three potential vaccines against HIV are safe; to learn how the immune system responds to them; and to learn if any side effects are experienced and how severe those side effects might be.
- **Study overview.** 13 healthy individuals will be sequentially allocated into two groups. The first three volunteers (Group 1) will receive, by injection, a very low dose of one study vaccine (called ChAdOx1.tHIVcons1) because this vaccine has not been administered to humans before. In this group we will only assess if the vaccine is safe and what kind of side effects (if any) are experienced. Group 2 participants will receive a dose of ChAdOx1.tHIVconsv ten times higher than participants in Group 1. In previous studies

on similar vaccines, this higher dose is believed to stimulate an immune response with no additional side-effects. Participants in Group 2 will also receive two other vaccines by injection (called MVA.tHIVconsv3 and MVA.tHIVconsv4), four weeks after the first vaccination. Participants of Group 2 will be assessed for safety, tolerability, and how their immune systems respond to the vaccinations.

- **Duration.** The study will last for a total of five months for group 2 participants.
- **GP contact.** With your permission your GP will be informed about your participation in the trial, and asked to share with the study team your medical information, in order to assess if it's safe for you to take part.
- **Reimbursement.** You will be reimbursed for time, travel and inconvenience of taking part in the trial.
- **Procedures and Activities.** Blood, urine tests and medical examinations will be carried out to check your general health and ensure you meet all the requirements to participate. If eligible and you agree to participate, you will receive three study vaccines on two occasions. During each vaccination visit you will receive 2 injections, one in each arm. We will ask you to come to the clinic for follow up visits. We will ask you to record in a diary any signs or symptoms that you experience after vaccination.
- **The vaccines used in this study will not protect you from HIV infection. It is important for you to avoid exposure to HIV during and after the study. It is absolutely impossible to get HIV infection or AIDS from this vaccine.**

What is the purpose of this trial?

Approximately 36.9 million people are living with HIV, the virus that causes AIDS, and it is estimated that over 1.8 million new infections occurred in 2017. At present, there is no licensed vaccine to prevent HIV infection available. Vaccination is the most effective way to prevent infection, but it has proved extremely difficult to develop an effective vaccine against HIV. One of the main reasons for this is the extraordinary ability of the virus to change itself so that the human immune system does not recognise it and the virus escapes detection.

Oxford University researchers have developed second generation vaccine candidates for HIV. These follow on from similar first generation vaccines which have been given to several hundred healthy volunteers, and to a smaller number of HIV infected patients. In all these studies the vaccines have been shown to be safe and well tolerated.

Preclinical studies on the vaccines we assess in this trial have been performed in small animals, without safety concerns. However, this is the first time that these particular vaccines will be given sequentially to people.

The purpose of this study is to find out if the study vaccines are safe and how your immune system responds to them. In addition, we hope to learn what kind of side affects you may experience after receiving the study vaccines, and how severe those side effects will be.

What are the vaccines being tested?

The vaccines used in this trial are called ChAdOx1.tHIVconsv1, MVA.tHIVconsv3 and MVA.tHIVconsv4.

They consist of two parts:

1) Each vaccine contains segments of the genes of the HIV virus (tHIVconsv1; tHIVconsv3 and tHIVconsv4). These HIV segments are completely synthetic and do not contain live HIV, therefore they cannot give people HIV infection or AIDS. These segments were chosen because HIV cannot easily change them to escape from the immune system. The aim is to direct the body to respond to these parts.

2) The second part is known as a carrier (also called a 'vector'). The vectors used in this trial are a chimpanzee adenovirus called ChAdOx1and a modified vaccinia virus Ankara (MVA), neither of which can multiply in the human body or cause disease in people. These vectors have been safely used in research vaccine studies against many different infections in Oxford and more widely.

It is absolutely impossible to become infected with HIV or AIDS from these vaccines.

Do I have to take part?

No. It is up to you to decide whether or not to take part. Your decision will not result in any penalty, or changes to your standard medical care. If you do decide to take part, you will be given this information sheet to keep (or be sent it electronically) and will be asked to sign a consent form. You are free to withdraw at any time and without giving a reason, but you may be asked to return to the clinic for follow up for safety reasons.

Can I take part?

In order to be involved in the study you must:

- Be a healthy, HIV-negative adult aged between 18 and 65 years
- Be able and willing (in the Investigator's opinion) to comply with all study requirements
- Allow the Investigators to discuss your medical history with your GP
- Practice continuous effective contraception for the duration of the study
- Refrain from blood donation during the course of the study

You cannot participate in this study if:

- You have participated in another research study in the last 30 days
- You are planning to participate in another study at the same time as this study
- You have previously received an Adenoviral vectored vaccine likely to impact on interpretation of the trial data (e.g. Oxford AstraZeneca or Janssen Covid-19 vaccines)
- You are due to receive an Adenoviral vectored vaccine (e.g. Oxford AstraZeneca or Janssen Covid-19 vaccines) in the three months after the first study vaccination.

- You have had immunoglobulins and/or any blood products (such as a blood transfusion) in the 3 months preceding your involvement in this trial
- You have received a live attenuated vaccine (a vaccine containing a weakened version of a live virus; for example mumps, measles, rubella [MMR], varicella [chickenpox], or yellow fever vaccines) in the 60 days preceding your involvement in this trial or plan to receive it within 60 days after study vaccination
- You have received another vaccine including influenza vaccine in the 14 days preceding your involvement in this trial or plan to receive it within 14 days after study vaccination
- You have a history of angioedema (swelling of the skin – usually affecting eye, lips, genitals, hands, feet, which may be caused by an allergic reaction)
- You have any bleeding disorders
- You have problems with your immune system
- You are pregnant, breast feeding or intend to become pregnant during the study
- You have a history of a severe allergic reaction to a vaccination
- You have a history of cancer
- You have a history of a serious psychiatric condition that may affect participation in the study
- You have any other serious long-term illnesses requiring hospital follow-up
- You drink on average more than 42 units of alcohol a week (a pint of beer is 2 - 3 units, a small glass of wine (125mL) one unit and a shot of spirits (25mL) one unit)
- You have injected drugs at any time in the last 5 years
- You have HIV, hepatitis B, hepatitis C or untreated syphilis infection
- You report high-risk behaviour for HIV-1 infection

Mild conditions which are well-controlled, would not automatically exclude you from participating. If you are unclear whether you are eligible to be involved in the study you can contact the study team who will be able to advise you.

You must be able to comply with all of the trial requirements and be able to attend all of the follow up visits.

What would I be vaccinated with?

During this study, 13 individuals will be sequentially allocated into two groups. The first group of 3 individuals have received a very low dose of ChAdOx1.tHIVconsv1 by injection. This approach was required because this vaccine had never been administered to humans before. The safety and tolerability of the vaccination have been reviewed by an independent safety monitor (a clinician not involved in the study) who gave their favourable opinion, to proceed with the enrolment of Group 2.

You are invited to be enrolled in the second group of 10 individuals who will receive a higher dose of ChAdOx1.tHIVconsv1 (two injections with half a dose in each arm). Group 2 participants will receive a dose of the ChAdOx1.tHIVcons1 vaccine which is ten times higher

than participants in Group 1. According to results of previous studies on similar vaccines, the dose to be administered to participants in Group 2 is believed to be able to stimulate the immune system without significant side effects. To ensure the safety of the participants, the first participant receiving the higher dose of ChAdOx1.tHIVconsv1 will be vaccinated alone. A safety and tolerability review will be carried out 48 hours after the vaccination by an independent safety monitor (a clinician not involved in the study), and if there are no safety concerns, another two participants will be vaccinated. Another safety review will be carried out by the safety monitor 48 hours after the second and third participants are vaccinated who, in the absence of safety concerns, will then give their favourable opinion to enrol the remaining seven participants. MVA.tHIVconsv3 and MVA.tHIVconsv4 vaccines will be administered four weeks after ChAdOx1.tHIVconsv1 vaccination, given together by injection (one vaccine per arm), following the same staggered vaccination. The purpose of the second vaccination is to increase the effect on the immune response of the first vaccine. MVA.tHIVconsv3 and MVA.tHIVconsv4 have been used in previous trials and a dose escalation is not required for these vaccines.

How often do I need to attend?

You will be asked to attend for a screening visit and 11 study visits over a period of 5 months.

What do I have to do if I agree to take part?

Screening Visit

If you decide you would like to take part in this trial, you will need to attend a screening visit up to 6 weeks before the first vaccination day that can last for up to two hours. The screening visit, the vaccination and all of the post-vaccination follow-up visits will take place at the Centre for Clinical Vaccinology and Tropical Medicine (CCVTM), at the Churchill Hospital in Oxford.

On the first visit (screening visit) the study doctor or nurse will discuss the study in detail with you to make sure that you fully understand what the study is about and what is involved if you decide to take part, and that you are happy to give written consent to take part in the study.

If you decide to take part we will give you a copy of the consent form that you have signed which you can keep for your records together with this information sheet. We will give you an appointment schedule for the study visits. If appropriate, we will ask you to ensure that you use effective contraception throughout the study.

We will ask you questions about your health and any medications you are taking and give you a physical examination. Your pulse rate, blood pressure and temperature will be recorded. We will also ask questions to ensure that you are not at risk of HIV infection. A blood sample will be taken in order to confirm that you are eligible to take part. This will include tests for HIV, Hepatitis C, Hepatitis B and syphilis infections. These tests will be explained to you in detail.

If we identify any reason that would prevent you from taking part in this study this will be discussed with you. If a minor abnormality is noted on a screening blood test, a repeat test might be required to verify it.

With your permission, we will inform your GP of your participation in the study and request a copy of your medical summary from your GP to confirm you do not have any reasons to be excluded from the study. You will be asked to sign a letter addressed to your GP in order to consent them to release relevant medical information about you. If you do not give your permission to contact your GP about your participation, you will not be able to take part in the study. You will be notified within two weeks to inform you whether or not you are eligible to take part.

We will ask you to refrain from participating in other clinical trials at the same time. In addition we will register you on the TOPS database (www.tops.org.uk), which is a confidential national database of healthy volunteers that identifies volunteers participating in studies, to minimise the risks that can come from over-volunteering. We will enter into the database only:

- your National Insurance number (if you have one)
- your passport number and country of origin (if you are not a UK citizen and don't have a National Insurance number)
- the date of your last dose of study vaccine

Considerations before taking part in this study

Blood Donation: Under current UK regulations, participants will not be able to donate blood during the course of the study.

Private Insurance: If you have private medical or travel insurance you are advised to contact your insurance company before participating in this trial, as involvement may affect the cover provided.

Contraception: It is currently unknown whether the vaccines being tested in this study are safe during pregnancy and there is currently no information on the possible effects of the study products on an unborn child. If you are a female capable of getting pregnant, you must not be pregnant or breastfeeding, and you must be willing to use a hormonal contraceptive or intrauterine device (IUD) from at least two weeks prior to receiving the study vaccine until 4 months after the last study vaccination. Barrier methods of contraception (condom or occlusive cap with spermicide) have a <1% failure rate. They are therefore not considered acceptable forms of contraception for this study. You must be willing to undergo urine pregnancy tests and to receive the results during the clinical study. This will be discussed with you at the screening visit.

Male participants with female partners are required to use barrier methods for the purposes of contraception until 4 months after the last vaccination.

Vaccination Visits

On the vaccination visit you will be given two injections into the muscle over the shoulder region of each arm. We will monitor you for 30 minutes at the clinic to ensure that there is no

serious reaction to the vaccine. First participants in each study group will be observed for 60 minutes.

Before going home, you will be given the log in for a web based electronic diary and telephone number(s) to call the doctor or nurse in case you have any side effects or any concerns about the vaccine.

During the next six days you will be asked to keep a daily record of your temperature and any 'flu'-like symptoms that you might experience, using the web based electronic diary.

During the vaccination visit, blood samples will be collected. On three instances (at the first vaccination visit, and 1 and 4 weeks after the second vaccination), we ask you to collect your faeces. For this, you will be given a pot (at the screening visit) in order to collect faeces at home (you can collect faeces up to 24h before coming to the visit and store in the fridge in the provided storage system).

Subsequent Visits

On every subsequent visit we will ask questions about your health and, if necessary, we will carry out a physical examination. Blood will be taken at each visit, including the vaccination visit. The amount of blood taken at each visit will vary as different amounts are required to assess your response to the vaccine over time. You will have up to approximately 130 ml of blood taken at each visit with a total of approximately 600 ml taken over a period of 5 months, about the same as the amount that would be taken from regular blood donors at one visit to a Blood Donation Centre.

There might be a case in which your blood needs to be retested or a urine sample taken to confirm test results. In this case, the study staff would take a sample of your blood and collect urine samples, as needed. This may happen during a scheduled visit or you may be asked to come back to the clinic for an additional visit.

Telephone visit

The visit at day 14 will be conducted by phone; however you might need to attend the clinic at the discretion of the investigator. If you need to attend the clinic, the visit will be recorded as an unscheduled visit.

The chart below gives a summary of the visits involved in the study:

For Group 2 of this trial we plan to recruit a maximum of 10 people. Each volunteer will receive one dose each of the three vaccines (both MVA vaccines will be given on the same day).

Number of visits	12: screening, **Day 0 (C1 vaccination)**, Day 1, Day 7, Day 14 (phone call only), **Day 28 (M3M4 vaccination)**, Day 29, Day 35, Day 42, Day 56, Day 84, Day 140
Duration of study	5 months
Vaccination visits	2 (Day 0 and Day 28)
Blood samples	11
Faeces sample	3

What are the risks of taking part?

The vaccines used in this trial have either not been tested in humans before (ChAdOx1.tHIVconsv1) or have only been tested on only a small number of humans (MVA.tHIVconsv3 and MVA.tHIVconsv4). Similar vaccines using the same vectors have been given to many volunteers with no significant or serious side effects; however, there may be particular risks associated with the use of these vaccines we are not aware of.

Risks of vaccination

Side effects of Vaccination

Although ChAdOx1.tHIVconsv1 has not been tested in humans before and the MVA.tHIVconsv3 and MVA.tHIVconsv4 vaccines have only been tested on a small number of humans, other ChAdOx1 and MVA viral vector vaccines have previously been administered in many other clinical trials. We can predict from past experience what the symptoms should be like with this new vaccine. We expect that symptoms will be mild in strength most of the time, although symptoms may also be moderate or severe. All symptoms should resolve completely within a few days. The chimpanzee adenovirus has been weakened so that it cannot grow in human cells and therefore it is harmless.

Local reactions

After the first vaccine with the adenoviral vector (ChAdOx1.tHIVconsv1), we expect local reactions to occur in most people. Local pain, redness, warmth, and swelling are the most likely local reactions. In general these side effects are expected to be mild. After the second vaccine with the MVA vector we expect the same local symptoms to occur in approximately 60% of the participants, but these may be more intense in nature. However, these symptoms should resolve within a few days.

General Reactions

After the first vaccine with the adenoviral vector, we expect general adverse events to be

observed in the majority of people. Fatigue, headache, and malaise are the most common general reactions. Other symptoms include fever, chills, joint and muscular pain. The majority of these adverse events are expected to be mild to moderate in severity and to have resolved by 72 hours post vaccination.

After the second vaccine with the MVA vector we expect the same systemic symptoms to be more intense. In addition, after the MVA vectored vaccine, gastrointestinal symptoms as nausea and abdominal cramps have been reported by approximately one third of the recipients. However, these symptoms should resolve within a few days.

Severe Reactions

The risk of severe adverse outcomes in this trial is very low. However, unexpected outcomes are possible.

With any vaccination, there is a risk of rare serious adverse events, which may be related to the nervous system, or the immune system, like an allergic reaction.

An allergic reaction can be recognized by itchy skin rash, swelling of the face, difficulties in breathing and swallowing or by a sudden drop in blood pressure. If such reactions occur, they usually start very soon after vaccination. That is why it is important that you stay at the study site for at least 30 minutes after vaccination, where all medical equipment and personnel are available to treat an allergic reaction.

Reactions in the nervous system are also extremely rare following vaccination and can cause an illness called Guillain-Barré syndrome. Guillain-Barré syndrome is an illness in which people can develop severe weakness and can also be fatal. These adverse events have been described after administration of certain vaccines but have not happened with other similar adenovirus or MVA based vaccines. If you experience unexpected events, or become in any way concerned you should contact the Investigator using the contact details provided in this information sheet.

Other potential very rare severe reactions

The ChAdOx1 part of the vaccine (the “viral vector” or “backbone”) is the same as has been used in a recently developed COVID-19 vaccine (ChAdOx1 nCoV-19 - commonly known as the Oxford/AstraZeneca vaccine or Vaxzevria). In the Spring of 2021, some countries that were using this vaccine for their national COVID-19 immunisation programmes temporarily paused the use of the vaccine due to concerns that rare blood clotting conditions could be associated with the vaccine. Following these reports, a review has been undertaken by the MHRA (Medicines and Healthcare products Regulatory Agency) and the EMA (European Medicines Agency). The reports were of a very rare type of blood clot in the brain, known as cerebral venous sinus thrombosis (CVST), and also of clots in some other organs together, with low levels of platelets (thrombocytopenia). Up to and including 31 March 2021 there have been 79 UK reports of these blood clots and unfortunately 19 people died. By 31 March 2021 20.2 million doses of the ChAdOx1 nCoV-19 vaccine had been given in the UK. This means

the overall risk of these blood clots is extremely rare, approximately 4 people in a million who receive the vaccine.

After investigation, the UK Medicines Healthcare Regulatory Agency concluded, based on the data currently available to them, they could not say that there was a definite link between the vaccine and the rare clotting events. The MHRA statement on this can be found here: https://www.gov.uk/government/news/mhra-issues-new-advice-concluding-a-possible-link-between-covid-19-vaccine-astrazeneca-and-extremely-rare-unlikely-to-occur-blood-clots

The European Medicines Agency concluded that unusual blood clots with low blood platelets should be listed as very rare side effects of this vaccine.

Both agencies concluded that there wasn't enough evidence at present to say what the risk factors (e.g. age, gender, or other medical conditions) might be for having one of these rare clotting problems.

We don't yet know whether these rare clotting problems might be related to the vaccine vector virus (ChAdOx1), or to the SARS-CoV-2 part of the vaccine (the spike protein). The ChAdOx1 vector has been used in other clinical trials since 2012 (influenza, tuberculosis, prostate cancer, malaria, meningitis B, chikungunya, Zika and HIV vaccine trials). These rare blood clotting problems have not been seen in participants in these trial, however the number of people in this trials has been relatively small. These events remain extremely rare (in the UK it is estimated to affect 4 in a million people who receive a vaccine dose), and all medical regulators are collecting and analysing further data on them. We don't know whether these rare clotting problems could be related to the ChAdOx1 part of the vaccine, we would advise you to be particularly alert to the following symptoms in the first 28 days after you have a trial vaccine:

- Sudden severe headache that does not improve with usual pain killers or is getting worse
- An unusual headache which seems worse when lying down or bending over, or may be accompanied by blurred vision, nausea and vomiting, difficulty with speech, weakness, drowsiness or seizures
- New and unexplained pinprick bruising or bleeding
- Shortness of breath, chest pain, leg swelling or persistent abdominal pain

You will be provided with a 24h study mobile number. If you experience any of the above events or become in any way concerned you can use this to contact one of the study doctors at any time. We will ask you to record these symptoms in the eDiary too.

If any new information, or any other new safety concern, arose during the trial in relation to ChAdOx1, this would be reviewed, and you would be kept fully updated.

Potential interaction with other Adenoviral vectored vaccines

The 'vector' (ChAdOx1), the vehicle part of the vaccine, used in the ChAdOx1.tHIVconsv1 experimental vaccine (the first vaccination in this study) is the same as the one used in the Oxford AstraZeneca and similar to the one used in the Janssen (Johnson and Johnson) Covid-19 vaccines. There is a theoretical risk that receiving the experimental ChAdOX1.tHIVconsv1 vaccine may reduce the benefit of subsequent administrations of certain vaccines such as the Janssen (Johnson & Johnson) or the AstraZeneca Covid-19 vaccines. This may be more likely to happen if the vaccines are given at short intervals.

The immune response to the AstraZeneca Covid-19 vaccine was not affected in those who received another experimental ChAdOx1 vectored vaccine (similar to the one used in this study) one year earlier. Other studies suggest that an interval of three months between administrations of two adenoviral vectored vaccines reduces the risk of this interference. For this reason, we advise participants to wait at least three months after receiving the ChAdOx1.tHIVconsv1 vaccine before receiving the AstraZeneca or Janssen Covid-19 vaccines.

We are not suggesting participants should delay their NHS Covid-19 vaccination offer, but we will plan enrolment according to when the deployed vaccine is due.

No such interference will be expected with mRNA or protein vaccines (such as Moderna, Pfizer, Novavax) and these can be given at least 2 weeks before or after each study vaccine. You should tell your study doctor about any vaccines that you received in the last 3 months, and if you plan to receive a vaccine during the study.

Risks of taking blood samples (venepuncture)

Having blood taken may cause discomfort, bleeding or bruising where the needle enters the body and, in rare cases, light-headedness and fainting.

We do not foresee that the amount of blood taken during the study will cause harm to your health. It would not be expected for this amount of blood taken to cause anaemia. However, we will check for anaemia at regular intervals during the study.

Incidental findings

We would notify your GP that you were taking part in this study. If abnormal results or undiagnosed conditions are found in the course of the study these would be discussed with you and, if you agreed, your GP would be informed of these results to arrange further follow-up (we would not report them to your GP or anyone else without your permission).

If at screening, or any time during the study, a blood sample indicates that you may be positive for HIV infection, we will take a second sample to confirm this result. In the event that this is a true positive result we will withdraw you from the trial and discuss the implications with you before referring you for treatment and/or support.

False positive results on HIV tests

As a result of vaccination, there is a theoretical risk you may test positive for antibodies against HIV and these antibodies may persist in the future. In the unlikely event that this happens, it is a result of the vaccination and NOT because of HIV infection. There is a simple blood test which can tell if you have contracted HIV: this test, called polymerase chain reaction (PCR), is able to detect even small amounts of virus in the blood. Before and after the trial we will do PCR to verify that you are not infected with the HIV virus. It is absolutely impossible to contract an HIV infection or AIDS from these vaccines. The presence of antibodies that you might have developed as a result of the vaccination will not alter the result of the PCR test. However, according to the current regulations of National Blood Service, HIV antibody positive tests results will exclude you from being a blood or tissue donor as long as you remain positive, and may impact upon the ability to be an organ donor.

If you do develop antibodies to the HIV virus we will, with your permission, write to your GP explaining this and give a copy of the letter to you to keep for the future. In brief, the letter will state that you have generated antibodies against HIV proteins, as a result of the vaccination. However, this test result should not be taken as a marker of current or previous infection with HIV and has no impact on your health status. You will present no risk of transmission of HIV; this status can be confirmed if necessary by analysis of plasma for HIV viral RNA by PCR. The same result will impact upon the ability to be a blood, tissue and possibly organ donor. Should you be required to share this information with a third party, such as an insurance company, we will be happy to provide verbal or written clarification as needed.

Administration of the study vaccines won't affect your ability to be a blood, tissue or organ donor if antibodies against HIV are not detected in your blood by the standard HIV screening tests.

Will the study benefit me?

You will receive no direct benefit from this study. The aim of the study is to see whether the vaccines are safe, but **it is not intended to grant you protection against HIV, and you must continue to protect yourself against HIV infection**. However, knowledge gained from this trial may in the future help others to avoid HIV infection.

Can I take part in this study if I am pregnant?

If you are pregnant or are planning on becoming pregnant in the very near future, or if you are breast-feeding, you should not take part in this study. The safety of the vaccines in pregnancy is not known. You will be asked to use an effective method of contraception during the study, if this is appropriate and if you are not already doing so. Guidance will be provided to participants on what constitutes an effective method of contraception in the context of this trial. Contraception will need to be continued for the duration of the study. If you become pregnant during the study, you should tell us immediately. Should this happen you will not receive any further vaccinations but would remain under follow up until after delivery.

Will I be able to participate in other trials in the future if I have received this vaccine?

This depends on the specific criteria of each trial and it would need to be discussed on an individual basis.

What if new information becomes available?

Sometimes during the course of a trial, new relevant information relevant to the trial becomes available. If this happens, we will tell you about it and discuss whether you want to, or should, continue in the study. If you decide to continue to take part, you will be asked to sign an updated consent form. On receiving new information, we may consider it to be in your best interests to withdraw you from the study. Your participation in this study may also be stopped at any time by the study doctor or the Sponsor for other reasons.

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

If, at any time after agreeing to participate, you change your mind about being involved with this study you are free to withdraw without giving a reason. If you withdraw we would not usually perform any more research procedures, although occasionally we might need to offer you a follow up visit for safety purposes, for example to check the injection site or a blood result. Your decision will not result in any penalty. Unless you state otherwise, any blood taken whilst you have been in the study will continue to be stored and used for research as detailed above. You are free to request that your blood samples are destroyed at any time during or after the study. If you choose to withdraw from the trial, your standard medical care will not be affected.

What if something goes wrong?

We do not expect you to suffer any injury as a result of participating in this study. Medical care will be organised in the unlikely event that an injury related to the study does occur.

The University of Oxford, as Sponsor, has appropriate insurance in place for the unlikely event that you suffer any harm as a direct consequence of your participation in this trial.

In the event of harm being suffered, while the Sponsor will cooperate with any claim, you may wish to seek independent legal advice to ensure that you are properly represented in pursuing any complaint. The study doctor can advise you of further action and refer you to a doctor within the NHS for treatment, if necessary. NHS indemnity operates in respect of the clinical treatment which may be provided if you needed to be admitted to hospital.

Will I be paid for taking part in this study?

You would be reimbursed for your time, travel and the inconvenience of taking part in the study. The reimbursement for completion of the whole study is £535.00. You would be reimbursed £25 for the screening visit. For subsequent visits you will be reimbursed for your time, travel and the inconvenience based on the following figures:

- Travel expenses: £15 per visit

- Inconvenience of blood tests: £10 per blood donation
- Time required for visit: £40 per vaccination visit and £20 per follow up visit

The sum reimbursed is on a pro rata basis, so if, for example, you choose to withdraw half way through the study we would calculate your reimbursement based on the visits you have attended and samples that have been obtained. You may also receive reimbursement for any unscheduled visits you attend (if blood tests have to be repeated). You would be reimbursed £40 per unscheduled visit.

Complaints statement

If you wish to complain about any aspect of the way in which you have been approached or treated, or how your information is handled during the course of this study, you should contact

Dr Paola Cicconi on 01865 611413 or via email: vaccinetrials@ndm.ox.ac.uk. Alternatively, you may contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 616480, or the head of CTRG, email ctrg@admin.ox.ac.uk.

Would my taking part in this trial be kept confidential?

All information that is collected about you during the course of the research will be coded with a study number and kept confidential. The information is available to the trial team, authorised collaborators, ethical review committees, government regulatory agencies and the Sponsor (University of Oxford), who can ask to assess the trial data. Responsible independent monitors may be given access to data for monitoring and/or audit of the trial to ensure we are complying with regulations. They are bound by the same confidentiality rules. Any information about you that leaves the hospital/clinic will have your name and address removed so that you cannot be recognised from it.

Every effort will be taken to maintain confidentiality. Information about you may be stored electronically on a secure server. This may be outside of the European Economic Area (EEA). The organisation receiving the data is governed by approved contractual confidentiality clauses. Paper notes will be kept in a key-locked filing cabinet at the CCVTM – Churchill Hospital, University of Oxford. Trial results will be published in a scientific journal but nothing that could identify you will be included in any report or publication.

Taking part in future vaccine related research

With your consent, we would like to keep your contact details after your participation in this study is complete, so we may inform you of opportunities to participate in future vaccine related research. This is entirely optional and your participation in this study will not be affected by your decision to allow or not allow storage of your contact details beyond your participation in this trial.

Your details will be stored electronically on a secure server and only authorised individuals at the CCVTM will have access to it. We will not, under any circumstances, share your contact

details with any third party institutions without your permission. Being contacted does not oblige you to agree to take part in future research and you can ask us to have your contact details removed from our database at any time.

What will happen to any samples I give?

The blood tests will include a full blood count, blood chemistry and liver function tests at selected visits, to ensure that the vaccines are safe. In addition, a blood sample will be taken at each visit for research laboratory tests that will measure your immune response to the vaccine. Blood samples will be labelled with your unique study code only, before sending to the appropriate laboratory for analysis.

The safety blood samples collected during this study would be stored and analysed in the Oxford University Hospital NHS Foundation Trust and University of Oxford research laboratories in the first instance. However, as part of this project, research samples may be sent to our collaborating partners both within and outside the UK. These samples would be stored with your unique study code only.

If you choose to withdraw from the study, all the samples collected prior to withdrawal will be analysed. No further samples or information will be requested from you after the date of withdrawal, unless required for safety reasons.

At the end of the study with your consent, blood and faecal samples may be stored long-term for future research use in the Oxford Vaccine Centre Biobank as described in a separate information sheet. You will be asked to sign a separate consent form for this. If you choose not to allow the future use of your remaining samples, you may still participate in this study and your samples will be destroyed at the end of the trial, in accordance with local SOPs and the Human Tissue Act 2004.

What will happen to my data?

We will be using information from you and your medical records in order to undertake this study. Research is a task that we perform in the public interest and is our legal basis for processing your data. The University of Oxford, as sponsor, is the data controller. This means that we, as University of Oxford researchers, are responsible for looking after your information and using it properly. We will use the minimum personally-identifiable information possible. We will keep information about you for at least 5 years after the study has finished. The need to store this information for longer in relation to licensing of the vaccines will be subject to ongoing review. For effective vaccines that may be licensed, we may store research data securely at the University of Oxford for at least 20 years after the end of the study, subject to adjustments in clinical trials regulations. In addition to the de-identified scientific data, we will also store documents containing personal information that you provide when registering for the trial (including contact details), medical information and signed consent forms during this archiving period.

The study team will use your name and contact details, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, in relation to your health during the study and to oversee the quality of the study. At the completion of the study, unless you consent otherwise (e.g. if you request to be informed of other trials), your personal details will not be used to contact you other than exceptional circumstances concerning your safety. If you consent to take part in another study carried out by the Jenner Institute, personal information and medical information including blood test results may be accessed to avoid unnecessary repetition. Your bank details will be stored for 7 years in line with university financial policy.

Your rights to access, change, or move your personal information may be limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at: https://compliance.web.ox.ac.uk/individual-rights

or you can contact the University of Oxford's Data Protection Officer via data.protection@admin.ox.ac.uk.

What will happen to the results of the research study?

The results of this research study may be presented at scientific meetings or conferences and published in a scientific medical journal. This may not happen until 1 or 2 years after the study is completed. If you contact the researchers in the future, you can obtain a copy of the results. You will not be identified in any report or publication.

The de-identified data from this study will be shared with the collaborating partners who are organising and funding this research work. Data from this study may be used to file patents, licence vaccines in the future or make profits in other ways. You will not be paid for any part of this.

Who is sponsoring, organising and funding the research?

The study is organised and sponsored by the University of Oxford. The study is funded through financial support from the European Commission within the Horizon 2020 research programme.

Who has reviewed the study?

This study has been reviewed by the National Research Ethics Service (NRES) –20/EE/0036 and has been given a favourable ethical opinion. The Medicines and Healthcare products Regulatory Agency (MHRA), which regulates the use of all medicines in the UK, has reviewed the study design and has granted permission to use this unlicensed vaccine in this clinical study.

Further information and contact details

We hope this information sheet has answered all of your questions. If you would like further information about participating in research please visit the following website:

http://www.nhs.uk/conditions/Clinical-trials/Pages/Introduction.aspx. For independent advice about participating in this trial you may wish to contact your GP. If you would like to speak to one of our team members to discuss any aspect of this trial or **if you are interested in taking part in the study, please contact us**:

Recruitment Coordinator
Centre for Clinical Vaccinology & Tropical Medicine
Churchill Hospital, Old Road, Headington, Oxford, OX3 7LE
Telephone: **01865 611406**
Email: **vaccinetrials@ndm.ox.ac.uk**