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PARTICIPANT INFORMATION SHEET: RVF001

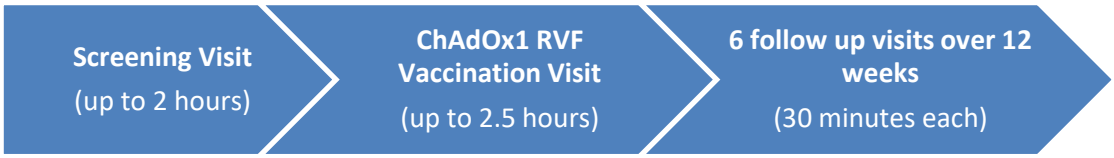
A study to assess a new Rift Valley Fever Virus vaccine in healthy adults

"A phase I study to determine the safety and immunogenicity of the candidate Rift Valley Fever Virus (RVFV) vaccine ChAdOx1 RVF in UK healthy adult volunteers"

We would like to invite you to take part in a research study. Before you make a decision, it is important you take the time to understand why we are doing this research and what it would involve. Please read the following information carefully and discuss it with friends, relatives and your General Practitioner (GP) if you wish.

- Part 1 tells you the purpose of the study and what will happen if you take part.
- Part 2 tells you more general information about how we run the study.

Please ask us if there is anything that is not clear, or if you would like more information. Take time to decide whether or not to take part.



Who can take part?	Healthy adult volunteers aged 18-50
Number of study visits:	8 in total (1 screening visit, 1 vaccination visit, 6 follow up visits)
Study Duration:	12 weeks
Compensation:	Up to £370
Benefits of participation:	Participating in this trial will help our research into an effective rift valley fever vaccination.
Risks of participation:	We expect side effects to be like those of similar vaccines i.e. usually mild. See below for full details. The study does not involve any risk of developing rift valley fever at all.

The rest of this document covers the above areas in more detail, plus additional areas such as how we will protect your personal information, what to do if you have any problems, and where to get more information or make a complaint.

PART 1

What is the purpose of this research study?

The purpose of this study is to test a new vaccine against the Rift Valley Fever Virus (RVFV) in healthy volunteers.

Rift Valley Fever (RVF) is an emerging disease caused by a virus and it's transmitted through a mosquito bite. It affects mainly cattle and livestock animals but has catastrophic consequences to human health as it can also be transmitted to people. The disease has serious implications for livestock agriculture and trade as up to 90% of young animals affected by the disease will die. Although initially restricted to Africa, the virus can be transmitted by several different mosquito species that are more widely distributed than the virus itself, leading to concerns of disease spread as has occurred in the Arabian Peninsula and Madagascar. Humans can get infected through either infectious mosquito bites or contact with virus-contaminated tissues and fluids. In humans, RVFV infection usually shows itself as a sudden illness with fevers, but more serious symptoms can occur including severe bleeding or brain and nervous system problems. In previous human outbreaks in East Africa and Saudi Arabia, 30% of the people who had the disease died and some of the survivors had long-term health problems (e.g. impaired vision).

Although vaccines against RVFV exist for livestock, there is currently no similar vaccines or specific treatment that can be used in human patients.

RVFV is considered a global health threat with significant potential for international spread and use in bioterrorism and it has been prioritised for vaccine research and development by the World Health Organisation (WHO), the National Institute of Allergy and Infectious Diseases (NIAID) and the UK Vaccine Research & Development Network (UKVRDN).

This study will enable us to assess the safety of a new vaccine called ChAdOx1 RVF and record the extent of the immune response in healthy volunteers. We will do this by giving participants one dose of the vaccine in addition to doing blood tests and collecting information about any symptoms that occur after vaccination. This is the first trial to use this vaccine in humans and we plan to recruit a maximum of 15 participants to be vaccinated.

This study is conducted as part of a student post-graduate degree (MD or PhD).

What is the vaccine we are testing?

The vaccine we are testing in this research study is called ChAdOx1 RVF.

ChAdOx1 RVF is made from a virus (ChAdOx1), which is a weakened version of a common cold virus (adenovirus) from chimpanzees that has been genetically changed so that it is impossible for it to grow in humans. To this virus we have added genes that make proteins from the RVFV called Gn and Gc, which play an essential role in the infection pathway of the RVFV. By vaccinating with ChAdOx1 RVF, we are hoping to make the body recognise and develop an immune response to the Gn and Gc proteins that will help stop the RVFV from entering the human cells and therefore prevent infection.

Adenovirus vaccines have previously been trialled in human volunteers, protecting against different diseases. These were not associated with serious side effects. Vaccines made from the ChAdOx1 virus have been given to millions of people to date following government roll-outs of COVID-19

vaccinations, and have been shown to be safe and well tolerated, although they can cause side effects. In very rare cases a serious blood clotting disorder have been seen after the Oxford/AstraZeneca COVID-19 vaccine which is based on the same ChAdOx1 "viral vector" technology (see section *Are there any risks from taking part in the trial?*). As part of its manufacture, the ChAdOx1 vector is grown in a human-derived cell line called HEK 293 (human embryonic kidney cells 293).

We will give you an injection with the vaccine into the muscle around the shoulder region; this is the most commonly used route for vaccination.

Until now this vaccine has only been tested on laboratory mice and other animal species, but this is the first time that the vaccine will be given to humans. There might be side effects that we don't yet know about. If any new side effects are identified, from this trial or from animal studies, we will tell you.

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 a follow up appointment for safety reasons.

Can I take part?

In order to be involved in the study you must:

- Be a healthy adult aged between 18 and 50 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.
- Practise continuous effective contraception for the duration of the study (women only).
- 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.
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- You have had antibody infusions and/or any blood products (such as a blood transfusion) in the 3 months preceding your involvement in this trial.
- You have any bleeding disorders
- You have problems with your immune system.
- You are pregnant, breast feeding or intend to become pregnant in the 3 months following receiving the vaccine.
- 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 recreational drugs at any time in the last 5 years

- You have hepatitis B, hepatitis C or HIV infection.
- Prior exposure to RVFV
- Cough, fever, loss of sense of smell or taste or diagnosed COVID-19 infection within 28 days of receiving the study vaccine
- You have ever had a major blood clot (e.g. deep vein thrombosis (DVT), pulmonary embolism (PE), or cerebral venous sinus thrombosis), have ever been diagnosed as having antiphospholipid antibodies, or have ever received unfractionated heparin

Mild conditions that 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 will happen if I decide to take part?

If you decide you would like to take part in this trial, you will need to attend a screening visit up to 3 months before the vaccination day. This should last for about 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), Churchill Hospital, Oxford.

At the screening visit you will be met by one of the Investigators who will go through this information sheet with you to ensure you understand what to expect by taking part, the risks involved and what side-effects you might expect to experience. You can of course expect to receive full and comprehensive answers to any questions you may have.

Once you are happy that you understand what the trial involves, and the Investigator is happy that you have understood everything, you will be asked to a consent form. You will be asked to agree to allow the Investigators to contact your own Doctor (GP) to make sure there are no medical reasons why you should not participate. You will also be asked to agree to being registered on the confidential TOPS (The Over-Volunteering Prevention System) database which is set up to prevent people entering into multiple studies or trials at the same time.

Having signed the appropriate forms, the Investigator will go through a few questions for administrative purposes and detailed questions related to your health. This will be followed by a brief medical examination. Your blood pressure, pulse and temperature will also be recorded.

A number of blood tests will also be carried out which include tests for anaemia, tests to see how your liver and kidneys are functioning and tests to see if you have been exposed to HIV (the virus that leads to AIDS), Hepatitis B or Hepatitis C (viruses which affect the liver). In the event of you testing positive to any of these infections, we would inform you of the result and, with your permission, offer referral for medical review, confirmation of the result, and treatment if necessary. You will also be asked to provide a urine sample to check for glucose (to exclude diabetes), protein and blood (which can indicate kidney disease). Women will also have a urine pregnancy test performed.

Sometimes minor abnormalities can be found with the blood tests. In this situation you may be asked to return for a repeat blood test so that it can be checked again. If the test results are still abnormal you may not be able to participate and we will ask your permission to contact your GP or a specialist doctor, whichever is the most appropriate, to ensure the abnormality will be followed up.

Once all your test results have been checked and no problems have been highlighted, you will be contacted to arrange a date to start the trial.

COVID-19 arrangements

Due to the ongoing COVID-19 pandemic you will be asked to wear a face mask during your visits and observe social distancing. Staff carrying out your visits will be wearing face masks, gloves and aprons. We will maintain social distancing but certain procedures will involve being in closer proximity to staff for short periods for example to take blood samples or measure your blood pressure. Equipment and rooms will be cleaned between volunteers. We require you inform us if you develop COVID-19 during the study period and that you follow the latest government public health guidance in place in Oxfordshire. A separate information sheet detailing our covid-19 additional measures will also be provided.

Length of research

If you decide to take part in this study, you will be involved in the trial for approximately 3 months.

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 vaccine being tested is safe during pregnancy. For this reason, it is important that all women use adequate contraception during the trial period, for at least 3 months after your vaccination. This will be discussed with you at the screening visit. If you were to become pregnant during the trial you must tell us immediately and you will be withdrawn from the study, although we will ask to follow you up for safety reasons. Male participants with female partners are not required to use barrier methods for the purposes of contraception, as the risks of vaccine excretion are negligible.

How is the trial going to work?

The main focus of this study is to find a safe dose that won't cause unacceptable side effects. For this reason the doses given to participants will initially be very low. The first person in the study will only have one tenth of the dose that we expect to be tolerated. The dose will then be increased in a step-wise fashion.

For this trial we plan to recruit a maximum of 15 people. We will allocate volunteers into 3 different groups of 3-6 participants each.

Group 1: Volunteers will receive a low dose of ChAdox1 RVF (5×10^9 vp).

Group 2: Volunteers will receive an intermediate dose of ChAdox1 RVF (2.5×10^{10} vp).

Group 3: Volunteers will receive a higher (standard) dose of ChAdox1 RVF (5×10^{10} vp).

vp= Viral particles

If you qualify to be in the trial, we will ask you to attend in the morning on the vaccination day (Day 0). We will ask you a few questions to check there have been no new problems since screening. We will check your blood pressure, pulse and temperature (observations) and we will take blood samples. All women will have a urinary pregnancy test before vaccination.

We will give you an injection with the vaccine into your arm and we will cover the vaccine site with a dressing. We will need to keep an eye on you in the waiting room of the department for 1 hour after the vaccine. After this period, we will check your observations again and the injection site inspected. We will give you a thermometer, tape measure and an E-diary account to record all your symptoms and your temperature every day for 7 days after vaccination. After these 7 days we will ask you to record if you feel unwell or take any medications over the next 3 weeks. Overall the vaccination visit will take about two and a half hours.

	Screening	**Day 0**	**Day 2**	**Day 7**	**Day 14**	**Day 28**	**Day 56**	**Day 84**
Vaccination		X						
Blood Tests	X	X	X	X	X	X	X	X
Urine Test	X	(X)						
Time Required	1.5h	2.5h	15-30min	15-30min	15-30min	15-30min	15-30min	15-30min

(X) female volunteers only

Following vaccination, we will ask you to attend 6 follow-up visits (lasting 15-30 minutes) as detailed in the table above.

Two days after the vaccination, you will need to attend a short visit to ensure everything is fine, to check your symptoms, the injection site and to have blood tests done. A similar visit will take place one week after vaccination.

There will be further follow-up visits as in the table above. At 14 days, 4, 12 and 26 weeks after vaccination we will check your observations, take a blood sample, and review your completed E-diary. During the course of the trial you may be asked to attend for an extra visit, for example, if a blood test needs to be repeated. You will be compensated for the time and inconvenience of any extra visits. After the last visit, your participation in the trial will be complete.

We may ask to photograph your vaccination site and you can choose whether or not to agree to this when you sign the consent form. You will not be identifiable in these photographs, as only the vaccination site and your unique trial number will be visible. These photographs may be shown to other professional staff, used for educational purposes, or included in a scientific publication.

What should I avoid during the trial?

You should not donate blood during the trial or take part in other studies that involve blood sampling or the administration of drugs or vaccines. If during the trial you require any vaccinations for health, travel, or occupational reasons, you should inform the Investigators beforehand. We will discuss with you the most appropriate time to receive them.

Are there any risks from taking part in the trial?

The risks and side effects of the proposed vaccinations and trial procedures are detailed here:

a) Blood samples

Drawing blood may cause slight pain and occasionally bruising at the site where the needle enters. Rarely, people feel light-headed or even faint. During the course of the trial we will need to take up to 60mL of blood (approximately 4 tablespoons) at a single visit. The total amount we will take over the period of the trial is approximately 300mL which is less than the amount taken if you donate blood. The volume of blood taken at each visit ranges from 5 to approximately 60mL.

The following blood tests will be performed;

- Tests for Hepatitis B, Hepatitis C and HIV are done at the screening visit.
- HLA typing, a test of a component of the body's immune system may be done at the first vaccination visit.
- Tests of red and white blood cells, liver and kidney function are done at the screening visit and most of the other visits (including the vaccination day), in order to check the vaccines are safe.
- Tests of the immune responses to vaccines are done at most of the visits.

The blood samples we collect will be stored after testing, and may be used in future research. Samples will be de-identified (i.e. samples will only be identified by a unique study number) and you can request that your samples are destroyed at any time. You will be asked to consent specifically for your blood to be stored.

If abnormal results or undiagnosed conditions are found in the course of the study these will be discussed with you and, if you agree, your GP (or a hospital specialist, if more appropriate) will be informed. Any newly diagnosed conditions will be looked after within the NHS.

b) Vaccination Side Effects

It is likely that you will experience some symptoms at the vaccination site as well as general symptoms due to vaccination. It is important to remember these are vaccines in the early stage of development and the amount of safety data available is limited. For this reason, there is a chance you could experience a side effect that is more severe than what is described below, or that has not been seen before.

Although the vaccine is being tested for the first time, other ChAdOx1 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. The RVFV proteins it carries cannot cause RVF disease.

c) Local Reactions at vaccination site

You may experience some discomfort at the injection site as the vaccination is given. This usually gets better within 5 minutes. Later, you might experience pain resulting in some difficulty moving your arm, but this should resolve within a few days. In addition to pain, you may experience redness, swelling, itchiness or warmth at the injection site.

d) General reactions

During the first 24-48 hours after vaccination you may experience flu-like symptoms such as muscle aches, joint aches, feverishness, chills, headache, nausea, tiredness and/or feeling generally unwell. These symptoms should usually resolve within a few days.

Note: If you develop fever that starts and resolves within 48 hours of vaccination <u>without</u> cough, loss of sense of smell or sense of taste then the current national guidance is that you wouldn't be required

to self-isolate. If you are unsure whether post-vaccination symptoms might require you to self-isolate then you can contact the study team for advice at any time.

e) How common were reactions in other clinical trials using ChAdOx1 based vaccines?

In a study of-over 10,000 healthy adult volunteers, the percentage of volunteers experiencing the following symptoms after ChAdOx1 COVID-19 vaccine were: vaccination arm tenderness (83%) or pain (67%), fatigue (70%), headaches (68%), feeling generally unwell (61%), muscle aches (60%), chills (56%), feeling feverish (51%), fever of at least 38°C (18%). The dose used in that study was the same as the highest dose we plan to use for this study (group 3). Other ChAdOx1 vaccines have also been used in smaller clinical trials, where similar rates of side effects were seen when using that dose.

f) Serious Reactions

With any vaccination there is a risk of rare serious adverse events, such as an allergic reaction. These may be related to the immune system or to the nervous system. Severe allergic reactions to vaccines (anaphylaxis) are rare, but can be fatal. In case of this unlikely event, medication for treating allergic reactions is kept in the clinic room and the investigators are appropriately trained in the management of anaphylaxis. Reactions in the nervous system are also extremely rare, but can cause an illness called Guillain-Barré syndrome, a condition in which people can develop severe weakness and can be fatal. These adverse events have not previously been seen following administration of similar vaccines using ChAdOx1 as a viral vector.

A case of a neurological condition called transverse myelitis was diagnosed 14 days after vaccination in a participant of the Oxford/AstraZeneca COVID-19 vaccine trials. This was reviewed by an independent expert panel who could not completely rule out a possible link to vaccination, however this condition has not appeared as a safety issue following the vaccine rollout and dosing of millions of individuals.

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 14th April 2021 there have been 168 UK reports of these blood clots and unfortunately 32 people have died. By 31 March 2021 21.2 million first 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, occurring following less than 1 in 100,000 vaccinations.

After investigation, the UK Medicines Healthcare Regulatory Agency concluded there was evidence of a link between these cases and the Oxford/AstraZeneca COVID-19 vaccine although more work was needed to establish this. 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. The same rare blood clotting problems have also been reported after the Janssen COVID-19 vaccine, which is another adenovirus based vaccine, and the European Medicines Agency have concluded that a link with the vaccination is likely.

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. Additionally, two adenovirus vaccines are approved in the USA for use in US military personnel and have been administered to at least 1.3 million individuals over the last 10 years, with no similar blood clotting problems reported to regulators with those vaccines.

These events remain extremely rare (in the UK it is estimated to affect less than 1 in 100,000 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 E-Diary 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.

g) Potential interaction with other adenoviral vectored vaccines (e.g. Oxford/AstraZeneca and Janssen COVID-19 vaccines)

The 'vector' (ChAdOx1), the vehicle part of the vaccine, used in the ChAdOx1 RVF experimental vaccine 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 RVF vaccine may reduce the benefit of subsequent administrations of certain vaccines such as the Janssen 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 RVF 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.

h) Unexpected side effects

With any new medicine or vaccine there is always a possibility of an unexpected side effect. You will be provided with a 24h study mobile number. If you experience unexpected 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 too.

What are the advantages of taking part?

You will not necessarily gain any direct benefit from the trial, but the information gained from the study might help to develop an effective vaccine against RVFV. If in the future you become exposed to RVFV, you should not assume that the experimental vaccine you received in this study will give you any protection against RVF.

Will I be paid for taking part in this trial?

You will be compensated for your time, the inconvenience of having blood tests and procedures, and your travel expenses. The total amount compensated will be approximately **£370** depending on the exact number of visits and whether any repeat or additional visits are necessary.

Trial reimbursement will be made by bank transfer within six weeks of your completion of the trial, so please bring your bank details with you to your screening visit (no cash payments can be made). Should you decide to withdraw from the trial before it is completed, payment will be *pro rata* (you will receive a proportion of the total amount).

PART 2

What if new information becomes available?

Sometimes during the course of a trial, new 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. If you withdraw from the study, any data collected until that point will still be used in the study analysis.

What if something goes wrong?

The investigators recognise the important contribution that volunteers make to medical research, and make every effort to ensure your safety and well-being. The University of Oxford, as the research Sponsor, has arrangements in place in 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.

Complaints statement

If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you should contact the research investigators who will do their best to address your concerns by sending us an email to 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, Oxford University Hospitals NHS Trust, government regulatory agencies and the Sponsor (University of Oxford), who can ask to access 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, and 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.

Involvement of the General Practitioner/Family doctor (GP)

In order to enrol into this study, you will be required to sign a form documenting that you consent for us to contact your GP. This is to inform them that you are interested in being involved in the study, and to check there are no medical reasons that they are aware of that would make your participation inadvisable. Your GP may be asked to share information about your medical history and give access to any other medical records as required. The researchers will not enrol you in the trial if your GP has relevant concerns about your eligibility or safety. We will write to your GP to let them know about your enrolment and study completion status, so they can update your medical records accordingly.

Prevention of 'Over-Volunteering'

Volunteers participating in this study must not be concurrently receiving investigational medications or vaccines in another study at the same time. In order to check this, you will be asked to provide your National Insurance or Passport number. This will be entered on to a national database which helps prevent volunteers 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.

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. 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 identifiable information about you such as contact details for a minimum of 5 years after the study has finished. The need to store this information for longer in relation to licensing of the vaccine 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 15 years after the end of the study, subject to adjustments in clinical trials regulations. In addition to the anonymised 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

What will happen to any samples I give?

If you consent, some of your leftover blood samples will be stored indefinitely at the Oxford Vaccine Centre Biobank and may be used for further studies of the human body's immune response and/or the vaccines used in this study, and/or your safety. Any such tests will have an appropriate ethical review. Upon your request at any time, your remaining blood samples will be destroyed. Your participation in this study will not be affected by your decision whether to allow storage and future use of your leftover samples. More information around the procedures for long term storage of your samples is available in the Oxford Vaccine Centre Biobank information booklet and you will be asked to sign a separate consent form if you agree to have your samples stored for future use in ethically approved research.

To avoid repeat testing, if you are not enrolled into this study and you apply to enter another study conducted by the Jenner Clinical Vaccine Trials Group based at the CCVTM, the results from your screening visit blood tests may be used to determine whether you are eligible for the trial you applied for.

Your study visit blood tests will be analysed in the hospital laboratories and Oxford University research laboratories. Other blood tests to look at the response of your body to the vaccine will be done with collaborating laboratories in the UK and in other countries. Any samples or data sent to them would be de-identified.

Blood samples taken in this study may later be used for research involving animals and for the creation of immortalised cell lines or specific antibodies ("monoclonal antibodies").

Will any genetic tests be done?

We may do genetic tests on your blood samples to look at the patterns of genes that regulate your own individual immune response (these are called Human Leukocyte Antigen genes). Doing this helps us to work out which aspects of the immune response to vaccines are due to genetic differences between individuals. We may also look at the expression of certain genes which relate specifically to the immune response to RVFV, but no genetic tests concerning diseases or conditions other than RVF. We do not plan to look at participants entire genetic code (whole genome sequencing).You can opt out of 'genetic tests' on the consent form if you wish, without any effect on your participation in the trial.

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. Data from this study may be used as part of a student post-graduate degree, for example a MD or PhD.

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.

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 to Oxford University from the UK Department of Health. Neither your GP nor the researchers are paid for recruiting you into this study.

Who has reviewed the study?

This study has been reviewed by the National Research Ethics Service (NRES) – East of England - Cambridge East Research Ethics Committee 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**:

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