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PARTICIPANT INFORMATION SHEET

A study of a new vaccine against Crimean-Congo Haemorrhagic Fever (a life-threatening tick-borne viral disease)

We plan to recruit 46 people aged 18-55 years to take part in a study for the development of a new vaccine against **Crimean-Congo haemorrhagic fever virus**. Our vaccine is called **ChAdOx2 CCHF** and this study will be the first time in which it has been used in humans.

Everyone taking part in the study will be given two doses of ChAdOx2 CCHF vaccine. All participants will be followed up over a 1-year period.

There is no risk of contracting Crimean-Congo haemorrhagic fever virus from the vaccine itself, and participants will not be exposed to the virus at any point during this study.

What is the purpose of this study?

The purpose of this study is to test a new vaccine (ChAdOx2 CCHF) in healthy adult volunteers. The study vaccine has been developed by The University of Oxford, using similar technology to the Oxford/AstraZeneca COVID-19 vaccine.

This study will be the first time this vaccine has been given to people and will allow us to assess:

1. The safety of the vaccine
2. The immune response to the vaccine

The study will also look at whether the immune response to the new vaccine is affected by having received a previous dose of the Oxford/AstraZeneca COVID-19 vaccine (or other similar vaccines).

Before you decide on whether to participate in this study, it is important that you take the time to understand why the research is being done and what it would involve. Please read this information sheet carefully. If you have any further questions about the study, please do not hesitate to contact us (contact details are on the final page).

What is Crimean-Congo haemorrhagic fever?

Crimean-Congo haemorrhagic fever (CCHF) is caused by a virus which can result in severe illness and death. Cases occur in many parts of the world, including southern Europe, the Middle East, Africa and south-west Asia. The World Health Organisation estimates that 3 billion people live in areas at risk, and the CCHF virus infects up to 15,000 people per year, causing 500 deaths. CCHF is one of twelve diseases currently listed by the WHO as a priority disease for research and development, based on its risk to public health, epidemic potential.

The virus is transmitted by ticks, which can live on many domestic and wild animals, including cattle, sheep and goats. Humans usually become infected after a tick bite, although the virus can also be caught from close contact with infected animals or humans. In some people infection causes no symptoms, but in others it can cause very serious illness with impaired blood clotting, which can lead to severe bleeding. Up to 40% of people admitted to hospital with the infection die. There are currently no specific, effective treatments and there is no approved vaccine. The only vaccine for humans was developed in the early 1970s in Russia; it is not suitable for widespread use.

Summary

Who can take part?	Adults aged between 18 and 55 years in good health.
Vaccine being tested	Two doses of ChAdOx2 CCHF vaccine, 12 weeks apart, given as an injection.
Study Aims	To assess safety and immune response to the vaccine.
Chief Investigator	Dr Katrina Pollock
Principal Investigator	Dr Katrina Pollock
Trial Site	Oxford Vaccine Group, University of Oxford Centre for Clinical Vaccinology and Tropical Medicine Churchill Hospital, Headington, Oxford, OX3 7LE
What happens in the study?	All participants will attend a screening visit, to decide their eligibility to take part, and to obtain their consent to take part. At the next visit the first study vaccination will be given; the second will be given 12 weeks later. Any symptoms after the vaccinations will be recorded in an electronic diary. All participants will be followed up for one year after the first vaccination. The first six participants will attend a total of 15 study visits (1 screening, 2 vaccination and 12 follow up visits). The remaining participants will attend a total of 11 study visits (1 screening, 2 vaccination and 8 follow up visits). All visits will include a blood test.
Reimbursement	The first 6 participants (15 visits): total £1,470 The remaining 40 participants (11 visits): total £1,110
Risks of participation	Short-lived post-vaccine symptoms, such as mild discomfort of the arm and fever, may occur. The vaccine has been made using similar technology to the Oxford-AstraZeneca Covid vaccine, which has been associated with rare disorders including abnormal blood clotting. A full discussion of risks, including potential rare but serious reactions, can be found on page 12. As this is the first time the vaccine has been used in people, we will monitor the safety of all participants closely.
Benefits of participation	By participating in this study, you will help research into the development of a safe and effective vaccine to protect against Crimean-Congo haemorrhagic fever virus, but you will not directly receive any personal health benefit from the study or its procedures.

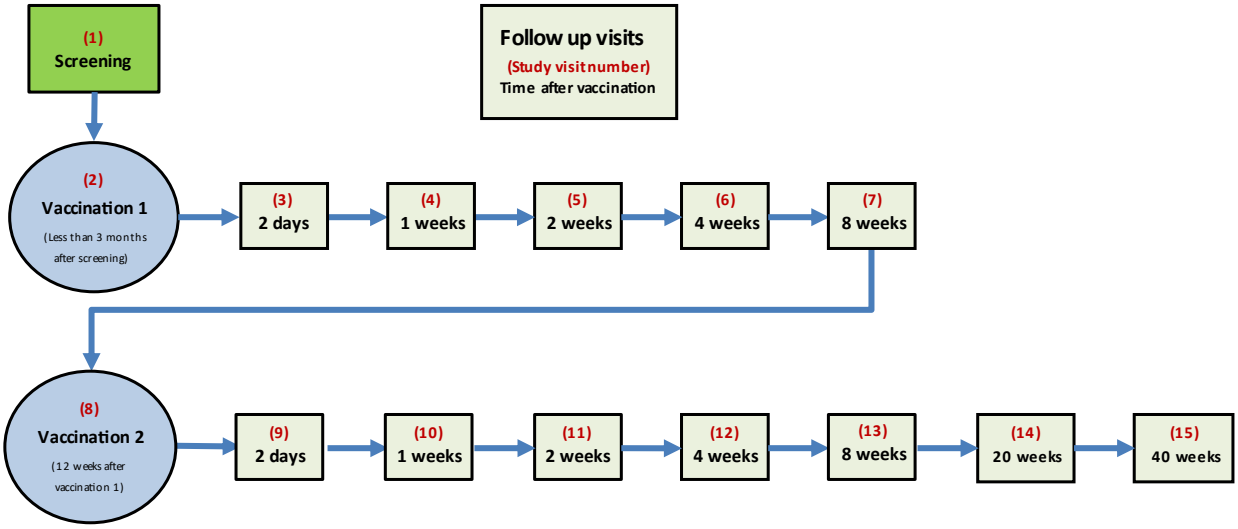
Study visits

The first six people recruited into the study will be in a group called "**Cohort 1**". They will have a total of 15 visits: 1 screening visit, 2 vaccination visits and 12 follow up visits.

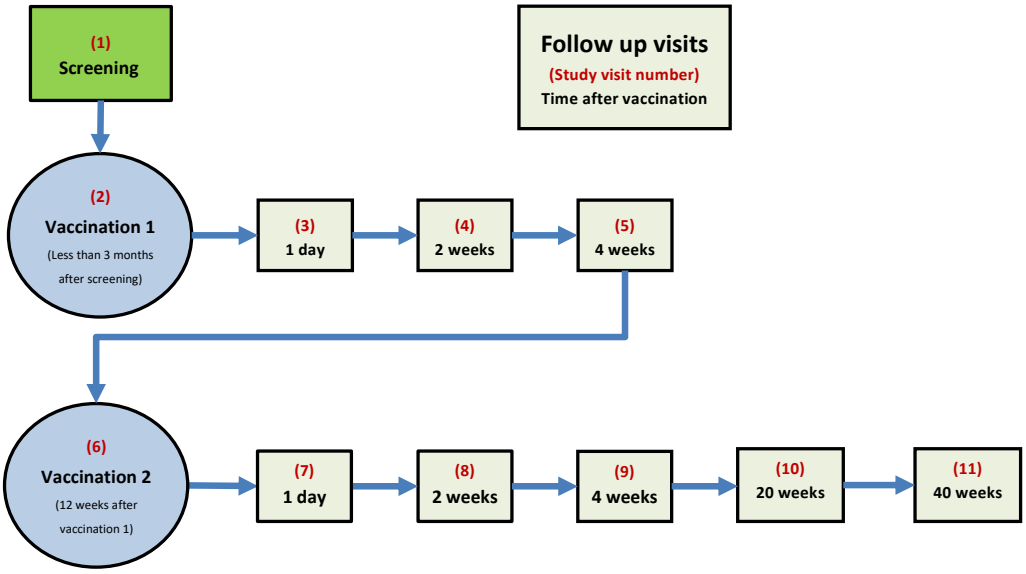
All other participants will be in "**Cohort 2**". They will have a total of 11 visits: 1 screening visit, 2 vaccination visits and 8 follow up visits.

The study visits are shown in the diagrams below.

Study Visits Cohort 1



Study Visits Cohort 2



Brief details of each study visit

Visit	**What to expect**
Pre-screening phone call	Phone discussion about your medical history and to answer any questions about the trial you may have. We will ask you to complete a consent form to retrieve a summary of your medical and vaccination records. This information will be kept confidential.
Screening visit	Consent discussion and sign a consent form, ID check, review your medical history, physical examination, vital signs (temperature, pulse, blood pressure), blood tests and urine pregnancy test (if appropriate).
Vaccination Visit	Vital signs, brief physical examination, blood tests and urine pregnancy test, (if appropriate), receive vaccine, remain in clinic for at least 30 minutes post vaccine and go through eDiary set-up. (COHORT 2 ONLY: optional return stool sample by post)
Follow up	Follow-up medical questions, vital signs, eDiary review and blood tests. A urine pregnancy test (if appropriate) at the last study visit (COHORT 2 ONLY: optional return stool sample by post)

What happens in the study?

1. Recruitment and eligibility screening

We plan to recruit up to 46 people aged between 18 and 55 years to take part in this study at the Oxford Vaccine Group. Volunteers will be asked to complete an initial online questionnaire, followed by a phone call from the study team, to assess whether they are eligible to take part. After this, volunteers will be invited to attend a screening visit which will include a medical assessment, and, if eligible to take part, they will then be invited to attend the first vaccination visit.

2. Allocation to a study group

Everyone in the study will be given two doses of ChAdOx2 CCHF, 12 weeks apart.

Cohort 1

The first 6 people to be enrolled into the study ("Cohort 1") will attend a total of 15 study visits.

Cohort 2

The remaining 40 people in the study ("Cohort 2") will attend a total of 11 study visits. We wish to compare the immune response to the study vaccine in people who have previously been given the Oxford/AstraZeneca COVID-19 vaccine (or other similar vaccines) with the response in those who have not. To do this, we plan to recruit 20 people who have had the Oxford/AstraZeneca COVID-19 vaccine (Group A), and 20 who have not (Group B). Once we have enrolled 20 people into one of these groups, we will only continue to recruit people who are eligible for the other.

3. Follow up

All participants in the study will be followed up for one year after the first vaccination.

All follow up visits will include a blood test, to ensure safety and assess the immune response to the vaccine. In addition to visits, participants will be asked to complete a symptom diary for the first 28 days after each vaccine dose.

Who is sponsoring, organising and funding the research?

The study is organised and sponsored by the University of Oxford. The study is funded by UK Research and Innovation, which is sponsored by the Department for Business, Energy and Industrial Strategy and whose legal status is "non-departmental public body".

How long would I be in the study?

If you are eligible to take part, we will enrol you into the study for 12 months starting from your first vaccination visit. You may decide to withdraw from the study early (What happens if I don't want to carry on with the study? page 15).

Can I take part?

To take part in the study, all the following **must apply** to you**:**

You must--

Be aged between **18 to 55 years** at the time of your screening visit
Be **in good health** without a history of serious ongoing medical conditions
Be able and willing to **comply with all study requirements** including attending all follow up visits
Be willing to **allow your past medical and vaccination history to be checked by the study team** (either by allowing us to discuss your medical history with your GP, or by giving us a medical history summary)
Be willing to **register with TOPS** (The Over-volunteering Protection System)
Agree to **refrain from blood or blood product donation** during the study
Tell us about any **vaccinations** you may have received recently or expect to receive soon
(**For participants who could potentially become pregnant**) Use **contraception** for the duration of the study *and* have a **negative pregnancy test** at the screening visit and vaccination visits

You must NOT have-

Current and Past Medical Problems
A serious long-term illness *e.g*. a condition that requires hospital or specialist follow-up.
A history of **neurological** or **immune system disorders**
A history of either a **major blood clot**, **blood clotting disorder**, or **bleeding disorder**
A history of **thrombosis with thrombocytopenia syndrome** (TTS, also known as VITT)
A history of **capillary leak syndrome**
A history of **angioedema**
A history of **cancer**
A history of **hepatitis B**, **hepatitis C** or **HIV infection**
A **serious ongoing mental health condition** if this may affect your participation in the study
A history of a **severe allergic reaction to a vaccine, including hypersensitivity**
Previously **injected recreational drugs** (within the last 5 years)
A history of **COVID-19 infection** within **14 days** of study vaccines
A history of a **blood transfusion** or "**Immunoglobulin infusions"** within 3 months of the trial
An intake of more than **42 units of alcohol per week** on average (The NHS recommends the following calculator: https://alcoholchange.org.uk/alcohol-facts/interactive-tools/unit-calculator)
A history of **Crimean-Congo haemorrhagic fever** infection
Other Vaccines
You cannot receive **flu or COVID-19 vaccines within 14 days** (before or after) of each study vaccine. This extends to **30 days for any other vaccine**. You must also be willing to inform the study team if you are offered or receive any **COVID-19 vaccine** during the study. If you receive the Oxford-AstraZeneca COVID-19 vaccine, you will be withdrawn from the study.
Other Clinical Trials

You must NOT participate in **another clinical trial** that involves receiving a drug or vaccine in the 30 days before the study starts and for the duration of the study
(In applicable participants only) Pregnancy/Breast Feeding During the Study
You must NOT be pregnant or breastfeeding during the study

If you are unclear whether you might be eligible to be involved in the study, you can contact the study team (details at the end of this information sheet).

What is the vaccine being tested?

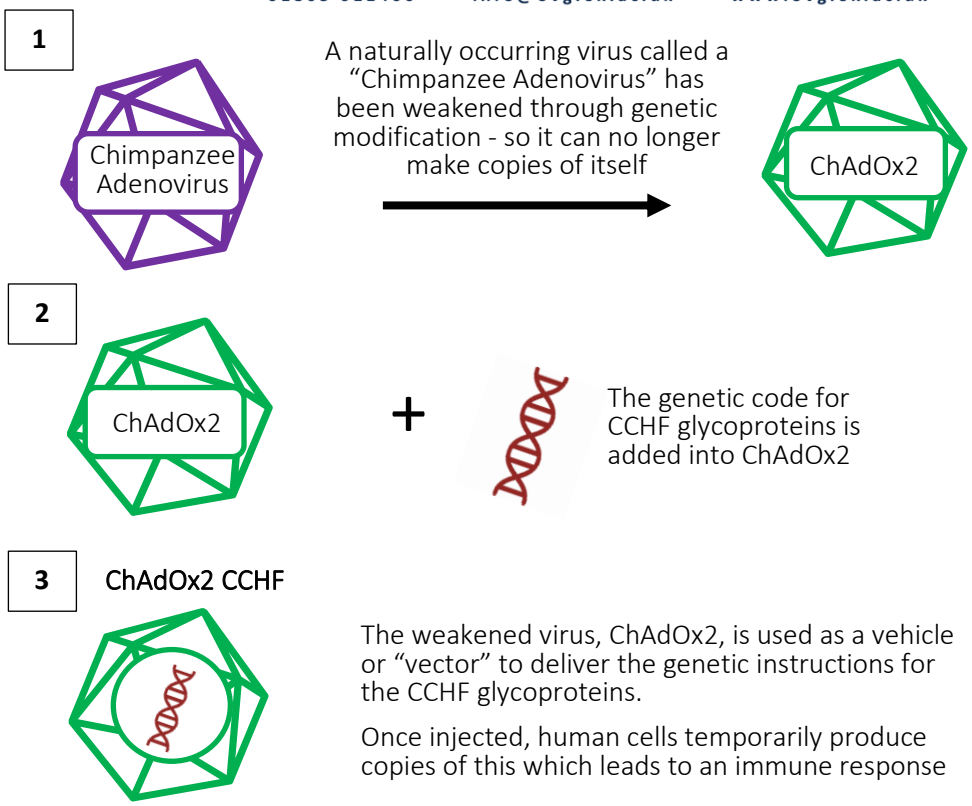
ChAdOx2 CCHF consists of a weakened version of a virus called a *chimpanzee adenovirus.* Chimpanzee adenoviruses are naturally occurring viruses that are completely unrelated to the CCHF virus. The natural, unmodified versions of chimpanzee adenoviruses can cause mild cold/flu-like symptoms in chimpanzees.

We have developed a weakened version of a chimpanzee adenovirus through genetic engineering. This modified version of the virus is completely unable to reproduce inside the human body. This means it cannot copy itself in humans and it cannot cause infections or be spread from person to person. We call this modified virus 'ChAdOx2' which stands for 'Chimpanzee Adenovirus Oxford 2'.

We took the weakened virus and inserted a gene from the CCHF virus. This gene provides the instructions for two important components of the CCHF virus, called 'Glycoprotein G' and 'Glycoprotein N'. These glycoproteins coat the surface of the CCHF virus and enable it to invade cells and cause infection. We want to investigate whether people who are vaccinated with ChAdOx2 CCHF will make an immune response against the glycoproteins.

The genetic code for CCHF glycoproteins is the only component of CCHF virus in the vaccine. The virus itself is not used to manufacture the ChAdOx2 CCHF vaccine, so there is no chance of being exposed to CCHF virus at any point during this study. **You cannot catch CCHF from the vaccine**.

This ChAdOx2 vaccine technology used in the CCHF vaccine under investigation in this clinical trial is similar to that used to make the Oxford/AstraZeneca COVID-19 vaccine (which used another modified chimpanzee adenovirus, ChAdOx1).



As part of its manufacture, ChAdOx2 is grown in a laboratory using modified cells that were originally derived from a sample of human tissue. These cells are called HEK 293 (human embryonic kidney 293) cells. More information on the use of human-derived cell lines in the manufacture of vaccine is available at https://vk.ovg.ox.ac.uk/vk/vaccine-ingredients#Human%20cell%20strains.

What dose of vaccine is used in this study?

The dose we will give is $5x10^{10}$ viral particles per vaccination. This is based on experience with similar vaccines, and is equivalent to the approved dose that is used for the Oxford/AstraZeneca COVID-19 vaccine. This dose is expected to give a satisfactory immune response without causing too many unwanted side effects.

Will there be any placebo vaccines?

No. All doses of vaccine given in this study will be ChAdOx2 CCHF.

Previous experience with ChAdOx1-based vaccines

Although ChAdOx2 CCHF is still in early development, as are some other vaccines based on ChAdOx2, there is now a lot of experience in humans with ChAdOx1-based vaccines, which are similar.

Oxford/AstraZeneca COVID-19 vaccine

The Oxford/AstraZeneca COVID-19 vaccine is made using ChAdOx1 virus technology. This has been shown to be safe for the vast majority of individuals and highly effective at protecting against severe COVID-19. However, following administration of the vaccine to millions of people, a very rare but serious side-effect of blood clots in combination with low platelets has now been associated with the vaccine. It is currently unknown why this vaccine appears to lead to this clotting disorder. Further

details of this are included in this information sheet ("Are there any risks from the ChAdOx2 CCHF vaccine?" page 12).

Other ChAdOx1 vaccines

Our research institute has also carried out trials of ChAdOx1 based vaccines against many other diseases such as flu, malaria, meningitis B, TB, HIV and Zika virus. Over 500 individuals have received these other ChAdOx1 vaccines (not including the Oxford/AstraZeneca COVID-19 vaccine). The other ChAdOx1 vaccines were shown to be safe during these trials and they were also found to create strong immune responses against the viruses, bacteria or parasites being targeted.

Do I have to take part?

No. It is up to you to decide whether 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 (it will be sent electronically but you can request a paper copy) and will be asked to sign a consent form.

What will happen if I decide to take part?

Online pre-screening questionnaire

If you decide that you would like to take part in this study, then you will need to complete a short set of online questions that cover some of the key criteria for participation in the trial. If you are suitable at this point, we will contact you to provide further instructions on the next steps.

Pre-screening phone-call

If you express an interest in taking part and you appear suitable from the pre-screening questionnaire, a member of the study team will contact you by telephone to discuss the study and answer any questions you may have. We would also like to ask you a few more detailed questions to further assess your eligibility.

Medical records consent

If you remain interested and are suitable for the study, we will arrange for you to come to our clinic for a screening visit. In addition, we would send you a consent form (paper or electronic) asking your permission for the study team to access your medical records to obtain information via the electronic patient records or through your GP. We would then ask you to return a copy of the signed consent form (paper or electronic). A countersigned form will be provided at the screening visit. This consent form is only to allow access to your medical records, and not the consent for enrolment into the study. If you choose to participate in the study, a separate consent will be taken (see below).

Screening visit

This may take place up to 3 months before the vaccination day. This, and all other study visits, will take place at the Oxford Vaccine Group.

At the screening visit, you will meet with study staff who will discuss this information sheet with you and answer any questions you might have about the study. If you then decide to take part, and the study team consider that you have understood the information, you will be asked to sign the study consent form.

This will be followed by a physical examination, which will involve the doctor listening to your heart and lungs with a stethoscope and examining your abdomen. Your vital signs (blood pressure, pulse, and temperature) will also be measured, and blood samples will be taken (approximately 10ml; if you happen to have had the relevant blood samples taken recently, for another study that you did not

subsequently take part in, we may be able to use these results instead). If applicable, a urine sample may also be taken to perform a pregnancy test.

Vaccination visits

If you qualify to be in the study after the screening visit eligibility checks, we will arrange for you to attend to receive the first dose of ChAdOx2 CCHF. We will check there have been no new problems since your screening visit. Your blood pressure, pulse and temperature (vital signs) will be checked, and blood samples taken (approximately 55-60ml). If appropriate, you will have a urinary pregnancy test before vaccination.

The vaccine will then be given as an injection into your (non-dominant) upper arm. We will temporarily cover the vaccine site with a dressing. We will need to monitor you in a waiting area for 30-60 minutes after the vaccine. After this period, your vital signs will be checked again, and the injection site inspected. We will then allow you to go home. The second vaccination visit (12 weeks after the first) will follow the same steps. Overall, the vaccination visits will each take about two hours.

Electronic symptom diary 'eDiary' *(to be completed at home)*

During the vaccination visits you will be given access to an online symptom eDiary. This will be set up using your personal e-mail address. We will ask you to record any symptoms or illnesses you experience in the 28 days following each vaccine, even if you think these are unrelated. For the first 7 days we will also ask you to measure and record your temperature at the same time each day, and if you feel feverish at any time in the 28 days following vaccination, using an oral thermometer that we will provide. We will also give you a tape measure, so that you can measure and record symptoms you may experience at the injection site, such as skin redness or swelling (see "Vaccine site – 'local' reactions" page 12). If you forget to fill in the diary, you will receive automatic reminders; you may also be contacted by a member of the study team.

Follow up visits

After each vaccination, you will attend the clinic for several short follow up visits, as shown in the diagrams on page 3. The last visit will be one year after starting the study. The visits are for us to check if you are experiencing any problems after the vaccine, review your injection site and check your eDiary. At each visit you will have a blood test.

During the study, you may also be asked to attend for an extra visit, for example, if a blood test needs to be repeated.

OPTIONAL: Home stool sampling

As an optional part of the study, we are asking participants in Cohort 2 provide stool (poo) samples at four timepoints during the study (at the first vaccination, two weeks after both the first and second vaccinations, and at the end of the study). If you agree to this, you will be provided collection kits and instructions on how to collect samples, which you will do at home. The study staff will explain to you how to collect and return the samples. However, if you prefer not to provide stool samples, you can opt out without otherwise affecting your participation in the study.

We will test these samples for microscopic organisms such as bacteria, parasites and fungi that naturally occupy your gut to see if the mix of these microscopic organisms are influenced by the study vaccines.

What other medical matters are relevant to the study?

Other vaccinations or medications during the study

If during the study you require any vaccinations for health, travel, or occupational reasons, you should inform the study team beforehand. We ask you not to receive any other vaccines within 30 days

(before and after) of receiving each study vaccine, EXCEPT for flu and COVID-19 vaccines (apart from the Oxford-AstraZeneca COVID-19 vaccine), which can be given 14 days or more before or after a study vaccine. Please note that if you receive the Oxford-AstraZeneca vaccine whist you are in the study, you will no longer be able to continue as a participant.

If you are prescribed any new medications during the study, please inform the study team.

Private insurance

If you have private medical insurance or travel insurance, participation in a study will often not affect your cover for any conditions unrelated to the study; however, to be certain, you must tell your insurer you are planning to participate.

Contraception

There are no data on the use of this vaccine in pregnancy or whilst breast feeding. It is therefore a requirement of participation that volunteers who could become pregnant must use contraception (exceptions to this are below).

Female participants where any of the following apply will not be required to use contraception:

- Post-menopausal
- Surgical sterilisation
- Complete abstinence from sex with a male partner

Acceptable contraception methods include:

- Oral, injected or implanted hormonal contraceptives that prevent ovulation
- Intrauterine device (IUD)
- Intrauterine system (IUS)
- Sole sexual partner is a vasectomised male

Note that barrier methods of contraception are not sufficiently reliable.

Male participants in the trial are not required to use barrier methods for the purposes of contraception. There is no evidence that the vaccine can be shed into semen.

Pregnancy

If you were to become pregnant during the study, you should tell us immediately so that we can review certain study procedures, such as blood sampling. With your consent, we would continue to follow you up for safety reasons but you will not be given any further vaccines as part of the trial. We would follow up your baby for up to three months after birth.

What should I avoid during the study?

Blood donation

Under current UK regulations, participants must refrain from blood donation during their involvement in the study. However, you will be able to restart blood donation once the last study visit has been completed.

Taking part in other clinical trials

You should not take part in other clinical trials in which drugs or vaccines are administered, or which involve repeated blood sampling, whilst participating in this study.

Are there any risks from the ChAdOx2 CCHF vaccine?

We can predict, from experience with other ChAdOx vaccines, what the symptoms should be like with this new vaccine. However, it is important to remember this vaccine is in a very early stage of development and has not been used in humans before. For this reason, there is a chance you could experience an unexpectedly severe side effect or a new side effect that has not been seen before. Potential risks are summarised below:

Vaccine site - 'local' reactions

As with any vaccine, you may experience some discomfort at the injection site. Usually this is mild, but sometimes individuals experience more significant pain which might interfere with their usual activities. Post-vaccination arm pain usually resolves completely within a few days, although it may occasionally persist up to a week or even longer.

Other less common, but possible, symptoms around the injection site might include redness, swelling, itchiness or a feeling of warmth.

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 feeling generally unwell. We would expect these symptoms to resolve within a few days.

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

Vaccine reaction symptoms were measured in volunteers in the large Oxford/AstraZeneca COVID-19 vaccine trials involving over 10,000 volunteers. The percentage of volunteers experiencing symptoms after vaccination is shown below. Symptoms were mostly described by volunteers as mild, although a minority described temporary moderate or severe-intensity symptoms. The dose given to those individuals is equivalent to the dose we plan to use in this study (What dose of vaccine is used in this study? page 9).

Percentage of participants reporting side effects in trials of the Oxford/AstraZeneca COVID-19 vaccine	
Vaccine site reactions	**General reactions**
Vaccination site tenderness (68%)	Fatigue (53%)
Vaccination arm pain (58%)	Headaches (53%)
	Feeling generally unwell (44%)
	Muscle aches (44%)
	Feeling feverish (34%)
	Joint pains (27%)
	Nausea (22%)
	Fever 38°C and over (8%)

An analysis of symptoms following the Oxford/AstraZeneca COVID-19 vaccine by the UK's medical regulator, the MHRA, has shown that individuals tend to have fewer and milder symptoms after their second dose.

The other ChAdOx vaccines that have been used in smaller clinical trials had similar rates of side effects when used at the equivalent dose.

Post-vaccination symptoms completely resolved within a few days in the vast majority of people in all previous ChAdOx1 trials.

Serious rare blood clot disorder with similar vaccines

The Oxford/AstraZeneca COVID-19 vaccine has been associated with a very rare but serious blood clot condition that can lead to death or serious long-term disability. The condition consists of unusual types of blood clots together with low levels of platelets in the blood (thrombosis with thrombocytopenia syndrome). Most of the clots were a rare brain blood clot known as a 'cerebral venous sinus thrombosis'. Unusual blood clots occurring in other organs, together with low blood platelets, were also reported. Most of these cases occurred within the first 3 weeks after vaccination.

This condition is not predictable and has occurred in previously healthy people, although it appears slightly less common in older people. The available data from the independent UK drug regulator (MHRA) shows that approximately 1 out of every 100,000 people who receive the Oxford/AstraZeneca COVID-19 vaccine develop this rare reaction. Approximately 1 in 5 patients who develop this condition unfortunately die.

Very low levels of blood platelets (immune thrombocytopenia), that can be associated with serious bleeding, (including internal bleeding) have also been reported very rarely, usually within the first four weeks following vaccination with the Oxford/AstraZeneca COVID-19 vaccine.

We do not know whether these rare reactions may also occur with other ChAdOx vaccines, such as the ChAdOx2 CCHFvaccine used in this study. We therefore advise you to seek urgent medical advice from the study team if you experience the following in the first 28 days after each of your study vaccines:

- Sudden severe headache that does not improve with usual painkillers 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 24-hour study mobile number. If you experience any of the above events or become in any way concerned, you can use this to contact the study doctors at any time.

Capillary leak syndrome

Cases of capillary leak syndrome (CLS) following vaccination with the Oxford/AstraZeneca COVID-19 vaccine are extremely rare (less than one case per million doses). Some affected patients had a previous diagnosis of CLS. CLS is a serious, potentially fatal condition causing fluid leakage from small blood vessels (capillaries) resulting in rapid swelling of the arms and legs, sudden weight gain and feeling faint (low blood pressure). Seek immediate medical attention from the study team if you develop these symptoms following vaccination.

Other serious vaccine reactions

With any vaccination there is a risk of rare serious adverse events. Severe allergic reactions to vaccines (anaphylaxis) are extremely rare but can be fatal. In case of this unlikely event, medication for treating allergic reactions is kept in the clinic room and the study team are appropriately trained in the management of anaphylaxis. Nervous system reactions are also extremely rare but have been reported with vaccinations in the past. A rare neurological illness called Guillain-Barré syndrome (GBS)

has previously been associated with a flu vaccine used in the USA during a swine flu outbreak in 1976. This is a condition in which people can develop severe weakness; it can be fatal. Cases of GBS have been reported after COVID-19 vaccinations and GBS is possibly a very rare side effect of the Oxford/AstraZeneca COVID-19 vaccine (about 10 cases per million doses of vaccine).

Unknown/unexpected side effects

With any new medicine or vaccine that is in early development, there is always a possibility of an unpredicted or unexpected side effect occurring. This could include something severe. If you experience concerning or unexpected symptoms, you should phone the 24-hour study contact number and speak to a study doctor.

Potential interaction with similar vaccines

When people are vaccinated with ChAdOx2 CCHF they should make the intended immune response against CCHF viral glycoproteins. However, they may also make an immune response against the ChAdOx part of the vaccine. Some scientists believe that having a strong immune response against ChAdOx might interfere with future doses of ChAdOx-based vaccines, preventing them from working as well. The same potential interference might also apply to other adenovirus-based vaccines (*e.g.* the Janssen COVID-19 vaccine), although these are not currently in widespread use in the UK. This means that it is possible that receiving the study vaccine may reduce the effectiveness of similar vaccines (such as the Oxford-AstraZeneca COVID-19 vaccine) which you may be given in future. One of the purposes of this study is to investigate whether having had a previous ChAdOx-based vaccine may interfere with the response to ChAdOx2 CCHF.

Are there any other potential risks from taking part in the study?

Blood samples

Blood sampling may cause slight pain and occasionally bruising. Occasionally, people feel light-headed, nauseous or faint. At most visits we will take about 55ml of blood, which should be well tolerated by healthy adults. The **total** amount of blood we will take from each participant over the whole trial period is approximately 600 ml. For comparison, a *single* donation to the NHS blood bank would be approximately 470ml.

Incidental medical findings

Since we carry out several medical tests throughout the study, it is possible that we detect previously unknown health issues (*e.g.* high blood pressure, abnormal blood results). If abnormal results or undiagnosed conditions were to be found during the study, these would be discussed with you and, if you agreed, your GP would also be informed. We would refer any newly diagnosed conditions to your GP for further follow-up. If you were diagnosed with Hepatitis B or C these would be reported by your GP to Public Health England.

Sometimes incidental medical findings require your GP to carry out further investigations such as blood tests, scans or referral to specialists.

What are the advantages of taking part?

You will not gain any direct personal benefit from the trial as you are unlikely to be at immediate risk from CCHF virus. You should not assume you have gained protection from future CCHF virus infection by receiving the study vaccine.

Will I be paid for taking part in this study?

Study participants would be reimbursed for their time, travel and inconvenience of taking part in the study. Reimbursement for all participants will be based on the following figures:

- Travel expenses:: £30 per visit
- Inconvenience of blood: £20 per blood donation
- Time: £40 per hour
- Diary card completion: £30 per fully completed diary card

The sum reimbursed is based on the number of visits you attend. If you choose to withdraw part-way through the study, we will calculate your reimbursement based on the visits you have attended. The maximum reimbursement for any volunteer who completes the study is £1,470 for participants in Cohort 1 and £1,110 for those in Cohort 2.

Payments are made directly by bank transfer in instalments during the study. For this reason, we require participants to provide their bank details at screening. Bank details are kept confidential. Personal information such as your name, bank details and national insurance number may be shared with the University finance team to process or verify your reimbursement payments. Financial auditors may also audit the records where this information is held. All confidential data will be stored according to the UK General Data Protection Regulation (see below).

You may also receive reimbursement for any unscheduled visits you attend. You would be reimbursed £90 per unscheduled visit.

What if new information becomes available

Sometimes during a study, new information relevant to the study becomes available (such as results from this or other studies). If this were to happen, we would tell you about it and discuss whether you would want to, or should, continue in the study. If you decided to continue to take part, you would 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.

If any new information or safety concerns were to arise during the trial in relation to ChAdOx2, this would be reviewed, and you would be kept fully updated.

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

At any time during the study, you are entirely free to change your mind about taking part, and to withdraw from the study. This would not result in any penalty. Unless you state otherwise, any blood taken whilst you have been in the study would continue to be stored and used for research, as detailed below. You may request that your blood samples are destroyed at any time during or after the study. Anyone of child-bearing potential should continue to practice effective contraception for at least 18 weeks after their last study vaccination, even if they withdraw from the study. For safety, if you withdraw, we may still ask to follow up any medical problems you might have experienced whilst in the study.

In exceptional circumstances, your participation in the study might also be stopped early by the study doctor or the sponsor of the trial.

What will happen to any samples I give during the study?

Your samples will be assigned a code and will only be identifiable by this code number. Any samples given to researchers outside of the study clinic will not have information that identifies you. The blood and urine samples (and, if applicable, stool samples) collected during this study will be analysed in the Oxford Vaccine Group and University of Oxford research laboratories. We may also send de-identified samples to other researchers working with us on this research project. This may include researchers in other countries, including outside of the European Union. All samples you provide will be tested in a de-identified form. However, as your DNA is unique, samples can never be completely anonymous.

If you choose to take part in this study, we will be asking for your separate permission to store your samples (including cells and DNA), in a collection of samples called the Oxford Vaccine Centre Biobank. Details of this will be provided in a separate booklet after you are enrolled into this study, and you are free to decline the Biobank and continue to take part in this study if you wish. If you consent to your samples being stored as part of the Biobank, a copy of your informed consent form for the Biobank (which contains your personal information) will be stored, in the same way as your consent form for the vaccine study. If you do not wish for your samples to be stored in the Biobank, they will be destroyed 12 months after the end of the study.

The following tests will be performed on your samples:

- Blood tests for blood cell counts and liver and kidney function.
- Blood tests for Hepatitis B, Hepatitis C and HIV (at the screening visit).
- A blood test for glucose (at the screening visit).
- A blood test for HLA typing, a genetic test of components of the body's immune system.
- Tests of immune responses following vaccination looking at your antibodies and immune cells.
- If you opt in, bloods samples in this study will be stored in the Oxford Vaccine Centre Biobank and may be used in future vaccine research studies.
- If you opt in, blood samples taken in this study may be used for research involving the creation of specific antibodies called 'monoclonal antibodies.'
- If you are in Cohort 2 and opt in, stool samples will be analysed with genetic testing or 'sequencing' of the bacteria, parasites and fungi that naturally occupy your gut. Collectively these are known as the gut 'microbiome'.

Will any genetic tests be done?

We will 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 (HLA) genes. This will help us to work out which aspects of the immune response to vaccines are due to genetic differences between individuals. We may also try to identify and study the genes that appear to be important in your immune response to the vaccination. Other genetic tests may be done if you consent to your samples being stored in the Biobank (as described in more detail in the Biobank leaflet). You will not receive the results of any genetic tests performed.

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 study.

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. If you are referred to the NHS during the study, then NHS indemnity operates in respect of the clinical treatment which may be provided.

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 at info@ovg.ox.ac.uk. Alternatively, you may contact the sponsor organisation of this study (University of Oxford) at the Research Governance, Ethics and Assurance (RGEA) team office on 01865 616480 or email RGEA.Sponsor@admin.ox.ac.uk .

Would my taking part in this study be kept confidential?

All information that is collected about you during the research will be coded with a study number and kept strictly confidential. Any information about you that leaves the clinic would have your name and address removed so that you could not be recognised, except for your signed consent form and letters sent to your own GP. To enrol into this study, you are required to consent for us to contact your GP.

We will write to your GP to inform them when you enrol in the study and when you complete it, so they can update your medical records accordingly. Your GP may also be asked to share information about your medical history and give access to any other medical records as required to ensure there are no medical reasons that would prevent you from taking part. We would only notify your GP of the results of any medical tests with your permission.

Responsible members of the University of Oxford, the relevant NHS Trusts involved in the research and the regulatory agency responsible for clinical trials in the UK, the MHRA, may also be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations. No one else will be told that you are involved in the study.

What will happen to my data?

Data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest.' The University of Oxford is the 'data controller' and is responsible for looking after your information and using it properly. We will be using information from you and your medical records to undertake this study.

We will use the minimum amount of personally identifiable information. Data will be collected and held by the Oxford Vaccine Group. It will be accessible to staff at the Oxford Vaccine group, responsible staff from the University of Oxford who may monitor/audit the data collection process, and inspectors from the regulatory agency responsible for clinical trials in the UK (the MHRA). The database servers are held by the sponsor. 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. De-identified research data will be stored indefinitely.

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 in exceptional

circumstances concerning your safety. A photocopy of your ID (driver's licence, passport or national ID card) and either your national insurance or passport number for "TOPS Database Registration" (page 17) and payment processing will be taken at the screening visit. We will securely retain copies until the end of the study. Your bank details will be stored for 7 years in line with local site policy. If you only complete online screening or telephone screening (before informed consent) your data will only be kept to the end of the trial.

Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited 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

TOPS database registration

Volunteers participating in this study must not be enrolled in another study that involves receiving investigational medications or vaccines at the same time. 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*.

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 can take approximately 2 years after the study is completed. Your individual results would not be identifiable, nor would you be identified in any report or publication. If you contact the researchers in the future, you can obtain a copy of the results.

The de-identified research 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 or licence vaccines in the future or make profits in other ways. You would 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.

Who has reviewed the study?

This research has been checked by an independent group, the Research Ethics Committee, who protect participants' interests. This study has been reviewed and approved by London – Harrow REC Committee.

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 given you enough information to decide whether to volunteer for this study. 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 are interested in taking part in this study, then please complete the online pre-screening questionnaire at: https://trials.ovg.ox.ac.uk/trials/cchf

If you have further questions about the study that you would like to discuss with our team, please contact us at:

Email: info@ovg.ox.ac.uk

Tel: 01865 611400

Thank you for your interest in taking part in this study.