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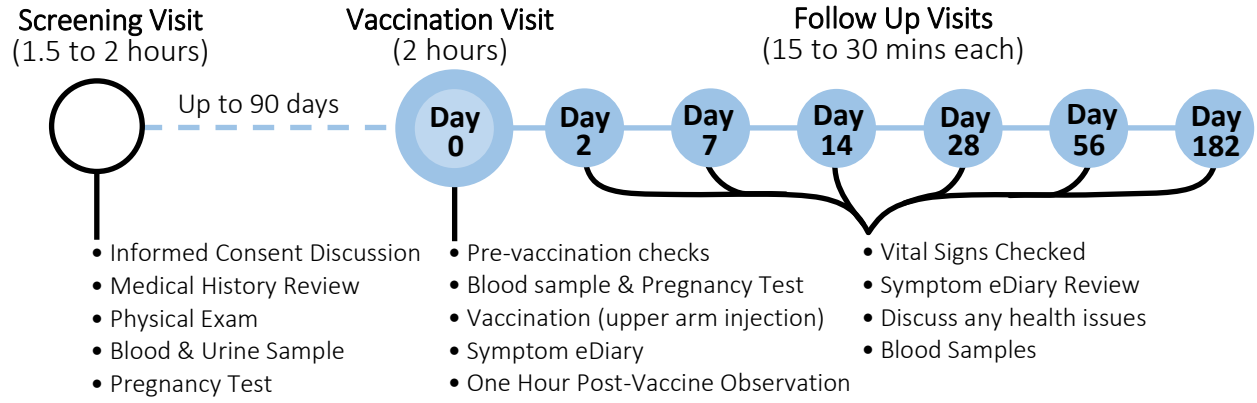
PARTICIPANT INFORMATION SHEET: EBL07

A study of a new vaccine against two types of Ebola

We hope to recruit 26 participants to take part in a study of our newly developed experimental Ebola vaccine called **ChAdOx1 biEBOV**. Eligible volunteers will receive a single dose of vaccine then return for 6 follow up visits over 6 months. The study will be the first time this vaccine has been tested in humans. **There is no risk of contracting Ebola from the vaccine, and you will not be exposed to viruses that cause Ebola at any point during this study.**

Study Name	EBL07
Who can take part?	Healthy adult volunteers aged 18-55 that have **not** had the Oxford/ AstraZeneca COVID-19 Vaccination (Full criteria inside)
Vaccine being tested	A single dose of ChAdOx1 biEBOV, our new "double acting" Ebola vaccine at either: a low, medium, or higher dose.
Total participants	Approximately 26 participants
Study Aims	To test safety and immune responses to this vaccine
Trial Site	Centre for Clinical Vaccinology and Tropical Medicine (CCVTM), Churchill Hospital, Oxford, OX3 7LE
Reimbursement:	£370
Risks of participation:	Short-lived post vaccine symptoms such as arm pain and fever may occur. A full discussion of risks, including potential rare but serious reactions is contained within (page 10). As this is a phase 1 study, we will monitor the safety of all participants closely.
Benefits of participation:	Participating in this trial will help our research into the development of a safe and effective vaccine against Ebola virus disease.
Investigators	Dr Paola Cicconi (Chief Investigator) Dr Daniel Jenkin (Principal Investigator) Professor Teresa Lambe (Lead Scientific Investigator) Professor Sarah Gilbert (Scientific Co-Investigator)



Before you make a decision on whether to participate in this trial, it is important 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 trial please do not hesitate to contact us.

What is the purpose of this trial?

Ebola is a highly lethal disease that occurs in periodic outbreaks in Sub Saharan African countries. Ebola outbreaks can be catastrophic. Healthcare workers are at particular risk of exposure and death during when they occur.

Rather than being caused by a single species of virus, **Ebola is caused by several distinct species** of virus. Collectively these are known as "**Ebolaviruses**".

There have been very recent advances in Ebola vaccine development which have led to the approval of the first vaccines against Ebola by international medical regulators. However, these vaccines are currently only authorised for protection against a ***single*** Ebolavirus species. It is currently thought that a vaccine that only targets a single species of Ebolavirus might not fully protect against other Ebolavirus species.

This study involves testing a **new** vaccine that is designed to simultaneously target ***two*** Ebolavirus species. The vaccine, ChAdOx1 biEBOV, targets the two deadliest Ebolaviruses: "**Zaire Ebolavirus**" and "**Sudan Ebolavirus**". These have been responsible for **nearly all Ebola outbreaks and deaths.**

The purpose of this study is to test ChAdOx1 biEBOV in a small group of healthy adult volunteers in the UK. This study will be the first time this vaccine has been given to humans and will allow us to assess:

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

How is the trial going to work?

We plan to recruit 26 people to take part in this study. All participants will be given **one dose** of ChAdOx1 biEBOV vaccine. We are testing three different doses of the vaccine in the trial and will split participants into the following groups:

- Group 1: **LOW DOSE** group: 6 participants (dose = 10% of the higher dose)
- Group 2: **MEDIUM DOSE** group: 6 to 9 participants (dose = 50% of the higher dose)
- Group 3: **HIGHER DOSE** group: 11 to 14 participants (dose = 100% of the higher dose)

Recruitment into these groups will happen in a stepwise manner, starting with the low dose group. We will vaccinate individuals in the low dose group first and review them for safety before starting any of the medium dose group vaccinations. Likewise, the medium dose participants will be vaccinated and reviewed for safety before we start vaccinating the higher dose group.

After vaccination, all participants will return to the clinic for 6 follow up visits over 6 months. They will be assessed at each visit for safety and to take blood tests to measure their immune responses.

Who is sponsoring, organising and funding the research?

The study is organised and sponsored by the University of Oxford. It is being carried out by Jenner Institute researchers based at the Centre for Clinical Vaccinology and Tropical Medicine, Oxford. The study is funded by Innovate UK, a UK Government research funding body.

Will there be any placebo or "dummy" vaccines?

There are no placebos or dummy vaccines in this trial. All participants will receive an actual dose of ChAdOx1 biEBOV (either at the low, medium or higher dose).

Length of your participation in the study

If you are eligible take part we will enrol you into the study for 6 months starting from your vaccination visit (Day 0) until your last scheduled follow up visit (Day 182). You may also decide to withdraw from the study early (What will happen if I don't want to carry on with the trial? Page 13).

Can I take part?

In order to be involved in the study the following **must apply** to you**:**

Aged **18 to 55 years**
You are **in good health** without a history of serious ongoing medical conditions
Able and willing to **comply with all study requirements** including attending all follow up visits.
Willing to **allow your past medical 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.
Agree to **refrain from blood donation** throughout the study (Day 0 to Day 182 visit)
Tell us about any **vaccinations** you may have received recently or expect to receive soon
(**Females only/ if applicable**) Use **contraception** for the duration of the study *and* have a **negative pregnancy test** at the screening visit and vaccination visit

You **cannot** participate in this study if any of the following apply to you:

Past Medical Problems
Have 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)
A history of capillary leak syndrome
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 **30 days** of the first study vaccination
A history of a **blood transfusion** or "**Immunoglobulin infusions"** within 3 months of the trial.
Drink 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)
Other Vaccines
You have previously received any doses of the **Oxford/AstraZeneca COVID-19 vaccine** *(Note: Previous other COVID-19 vaccines e.g. Pfizer/Moderna/Novavax **are permitted**)*
May receive the Oxford/AstraZeneca COVID-19 vaccine in the **three months *after* the first study vaccination** (Note: *You can still have other COVID-19 vaccines during the study)*
Receipt of any **other adenovirus-based vaccines** prior to enrolment (e.g. in clinical trials)
Received any doses of any Ebola vaccines in the past (e.g. in clinical trials)
Other Clinical Trials
Participating in another clinical trial during, or within 30 days of the vaccine visit, of this study
(Females Only) Pregnancy/Breast Feeding During the Study
Current or planned pregnancy and/or breast feeding during the study

Having a mild condition which is 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 very happy to advise you. The criteria above will be discussed with you in detail at the screening visit by a study doctor to make sure that you are eligible to take part.

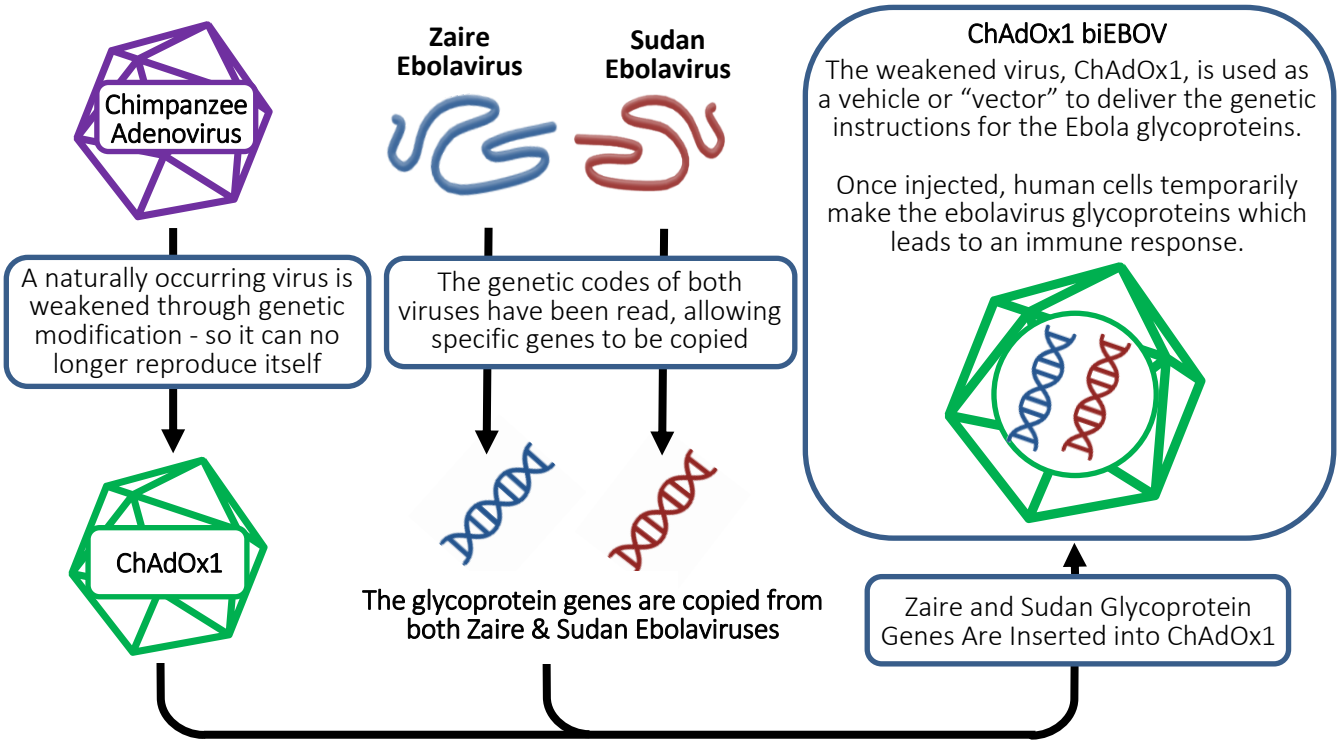
What is the vaccine being tested? (ChAdOx1 biEBOV)

ChAdOx1 biEBOV consists of a virus (ChAdOx1), which is a weakened version of a virus called a *chimpanzee adenovirus (ChAd).* Chimpanzee adenoviruses are naturally occurring viruses that are **completely unrelated to Ebolaviruses**. The natural, unmodified versions of ChAd viruses can cause mild cold/flu-like symptoms in chimpanzees.

We have developed a profoundly weakened version of the ChAd virus 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 "ChAdOx1" which stands for "Chimpanzee Adenovirus Oxford 1".

We then took the weakened virus and inserted **two versions** of an Ebolavirus gene. These genes provide the instructions for an important component of Ebolaviruses called the Ebola "glycoprotein". Ebola glycoproteins are used by viruses to let them invade cells and cause infection. Each Ebolavirus species has a **different version** of the Ebola glycoprotein gene. We therefore copied the **two versions** of this gene from the **two** deadliest Ebolaviruses**: Zaire Ebolavirus** and **Sudan Ebolavirus**.

The vaccine is called biEBOV as it targets two ("**bi**") **EBO**la**V**iruses. We hope that when people are vaccinated with ChAdOx1 biEBOV they will make an immune response against ***both*** the Zaire Ebolavirus and Sudan Ebolavirus.



As part of its manufacture, ChAdOx1 is grown in a lab using modified cells that were originally derived from a sample of human tissue. These cells are called HEK 293 (human embryonic kidney 293) cells.

What doses of vaccine are used in this trial?

The doses we will use are chosen based on experience with similar vaccines, and the "higher" dose is equivalent to the approved dose that is used for the Oxford/AstraZeneca COVID-19 vaccine. We measure the dose of these vaccines in a unit called "viral particles" which refers to the total number of ChAdOx1 biEBOV particles in the dose. The doses in viral particles that we are using in this trial are:

- Group 1: **LOW DOSE** ChAdOx1 biEBOV 5×10^9 viral particles
- Group 2: **MEDIUM DOSE** ChAdOx1 biEBOV 2.5×10^{10} viral particles
- Group 3: **HIGHER DOSE** ChAdOx1 biEBOV 5×10^{10} viral particles

Previous experience With Other ChAdOx1-based Vaccines

Although this will be the first time ChAdOx1 biEBOV has been given to people, there is now a lot of experience with other *ChAdOx1* based vaccines in humans.

ChAdOx1: Oxford/AstraZeneca COVID-19 Vaccine

The Oxford/AstraZeneca COVID-19 vaccine is made using the same ChAdOx1 virus technology that is used for ChAdOx1 biEBOV. 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 major blood clots in combination with low platelets has now been associated with the vaccine. It is currently unknown why these vaccines appear to lead to this clotting disorder. Further details of this are included in this information sheet ("Are there any risks from taking part in the trial?" Page 10).

Other ChAdOx1 Vaccines

Our research institute has also carried out small scale trials of ChAdOx1 based vaccines against many other diseases such as flu, malaria, meningitis B, TB and Zika virus. Around 400 individuals have received these other (non-COVID-19) ChAdOx1 vaccines. The other ChAdOx1 vaccines were shown to be safe across these multiple trials. They were also able 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 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.

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 invite you to attend an in-person screening visit.

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 Centre for Clinical Vaccinology and Tropical Medicine (CCVTM) at the Churchill Hospital, Oxford.

At the screening visit you will be met by one of the study doctors who will go through this information sheet with you again and answer any questions you might have about the trial. If you then decide to take part and the study doctor is happy that you have understood the trial information you will be asked to sign the study consent form. We will ask to check and photocopy a form of photo ID for identification purposes at this visit.

The study doctor will then ask about your health including any past medical problems. This will be followed by a physical examination which will involve the doctor listening to your heart and lungs with a stethoscope, examining your abdomen as well as feeling for lymph nodes around your neck and in your armpits. Your vital signs (blood pressure, pulse, and temperature) will also be measured, and blood and urine samples will be taken.

We will also need to review a copy of your medical records, usually in the form of a medical summary printout from your GP practice, before we can complete our eligibility assessment and invite you to the vaccine visit.

Vaccination Visit

If you qualify to be in the trial after the screening visit eligibility checks we will arrange a morning for you to attend to receive the ChAdOx1 biEBOV vaccine (Day 0). You will be asked a few questions to check there have been no new problems since your screening. Your blood pressure, pulse and temperature (vital signs) will be checked and blood samples taken. If appropriate, females will have a urinary pregnancy test before vaccination.

The ChAdOx1 biEBOV 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 keep an eye on you in the waiting room of the department for 1 hour 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. Overall, the vaccination visit will take about two hours.

Electronic symptom diary "eDiary" *(completed at home)*

During the vaccination visit you will be given access to an online symptom eDiary. **We will ask you to record any symptoms or illnesses you experience in the 28 days following your vaccine even if you think these are unrelated**. For the first 7 days we will also ask you to measure and record your temperature each evening using an oral thermometer that we will provide. We will also give you a tape measure so that if you experience any redness around the injection site you have something to measure this with (see "Vaccine Reactions around the injection site – local reactions" page 10).

Follow up Visits

After you have received the vaccination, you will attend the clinic for several short follow up visits. The first visit takes place two days after vaccination to check if you are experiencing any problems after the vaccine, review your injection site, check your eDiary and have a blood test. There will be further follow-up visits at 7 days, 14 days, 4 weeks, 8 weeks and 6 months after vaccination. 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.

We may ask to photograph your vaccination site(s) 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.

OPTIONAL: Home Stool Sampling

Optional stool (faecal) samples may be collected at three occasions during the study. However, if you do not agree to this 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. You will be given materials to collect stool samples. You will collect the samples at home and either return the sample to the clinic or send it to our laboratory in a pre-stamped pre-addressed envelope. The study staff will explain to you how to collect and return the samples.

The stool samples will be collected before the first vaccine is administered, two weeks after the trial vaccine and at the end of the study. We will test to see if the mix of these microscopic organisms influences your response to the study vaccines.

Trial Visit Timeline

Visit	What to expect at the visit
Screening Visit	Consent discussion and sign consent form, ID check, discuss medical history, physical examination, vital signs, blood test and urine sample (including pregnancy test if female)
Day 0 Vaccination Visit	Vital signs, blood test, (urine pregnancy test if female), receive ChAdOx1 biEBOV vaccine, remain in clinic for 1 hour post-vaccine observation
Day 2 Follow up	Follow up medical questions, eDiary reviewed by investigator, vital signs, blood tests
Day 7 Follow up	Follow up medical questions, eDiary reviewed, vital signs, blood tests
Day 14 Follow up	Follow up medical questions, eDiary reviewed, vital signs, blood tests
Day 28 Follow up	Follow up medical questions, eDiary reviewed and stopped, vital signs, blood tests
Day 56 Follow up	Follow up medical questions, vital signs, blood tests
Day 182 Follow up	Follow up medical questions, vital signs, blood tests, Final Study Visit

Considerations before taking part in this study

Having a COVID-19 Vaccination during the study

As explained above, you will not be able to enrol into this study if you have had any doses of the Oxford/AstraZeneca COVID-19 vaccine. The reason for this is this could **potentially interfere with the vaccine in this study as it uses the same ChAdOx1 viral vector**. It is also possible that if you had the ChAdOx1 biEBOV vaccine and then went on to receive the Oxford/AstraZeneca vaccine shortly afterwards it might dampen the protective immune response to COVID-19 from that vaccine. (see "Potential interaction with other adenoviral vectored vaccines" Page 12).

There are no theoretical risks of interference of ChAdOx1 biEBOV with mRNA or protein COVID-19 vaccines (such as Moderna, Pfizer, Novavax) so these **can be given at least 2 weeks before or after the study vaccine without issue**.

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. You should tell the study team if you are offered a COVID-19 vaccine during the trial period so we can record this and give you advice if needed.

Other 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 to 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.

If you develop a post-vaccination fever (see "General Reactions" page 10) that starts and resolves within 48 hours of vaccination **without** cough, loss of sense of smell or sense of taste, then the current national guidance is that you should not be required to self-isolate. If you are unsure whether any early post-vaccination symptoms might require you to self-isolate then you can contact the study team for advice at any time.

Private Insurance

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

Contraception

There is no data on the use of this vaccine in pregnancy. We therefore require female volunteers to use contraception to participate (exceptions to this are below). Acceptable contraception methods include:

- Oral, injected or implanted hormonal contraceptives
- Intrauterine device (IUD) intrauterine system (IUS)
- Condoms or occlusive cap with spermicide
- Sole sexual partner is a vasectomised male

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

- Complete abstinence from sex (with a male partner)
- Exclusively have female sexual partners
- Post-menopausal
- Surgical sterilisation

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.

Other (non-COVID-19) Vaccinations

If during the trial you require any vaccinations for health, travel, or occupational reasons, you should inform the study team beforehand. We will discuss with you the most appropriate time to receive them, usually 30 days after the study vaccination will be fine.

What should I avoid during the trial?

Blood Donation

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

Taking Part in Other Clinical Trials

You should not take part in other clinical trials where drugs or vaccines are administered during this study. You should also not take part in studies that involve repeated blood sampling at the same time as this trial.

Pregnancy (Female Participants)

If you were to become pregnant during the trial you should tell us immediately so that we can stop non-essential trial procedures such as blood sampling. With your consent we would continue to follow you up for safety reasons.

Are there any risks from the ChAdOx1 biEBOV vaccine?

We can predict from past experience with other ChAdOx1 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 tested 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 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/or 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 ChAdOx1 COVID-19 vaccine trials involving over 10,000 volunteers. The percentage of volunteers experiencing the following symptoms after ChAdOx1 COVID-19 vaccine 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 was equivalent to the group 3 "higher dose" we plan to use in this trial (What doses of vaccine are used in this trial? page 5).

Symptoms Reported in trials of the Oxford/AstraZeneca (ChAdOx1-based) COVID-19 vaccine	
Vaccine Site Reactions	**General Reactions**
Vaccination site tenderness (64%)	Fatigue (53%)
Vaccination arm pain (54%)	Headaches (52%)
	Feeling generally unwell (44%)
	Muscle aches (44%)
	Feeling feverish (34%)
	Joint pains (26%)
	Nausea (22%)
	Fever over ≥38°C (8%)

The other ChAdOx1 vaccines that have been used in smaller clinical trials had similar rates of side effects when also used at the equivalent dose. Lower doses were also tested in those trials, equivalent to the low and medium doses that we will use in this trial (What doses of vaccine are used in this trial? page 5). Lower doses were associated with fewer reactions in these trials.

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

Serious Blood Clots in Combination with Low Platelets

The ChAdOx1 part of ChAdOx1 biEBOV is **also used in the Oxford/AstraZeneca COVID-19 vaccine**. In the Spring of 2021 concerns were raised of a rare types of blood clots occurring after the large-scale use of the Oxford/AstraZeneca COVID-19 vaccine. This led some countries to pause its use.

The cases were of unusual types of **blood clots together with low levels of platelets in the blood**. Most of the clots were a rare brain blood clot known as a "cerebral venous sinus thrombosis". Unusual blood clots occurring in other organs along with low blood platelets were also reported. Both the UK drug regulator, known as the Medicines and Healthcare products Regulatory Agency (MHRA) and the European Medicines Agency (EMA) carried out extensive reviews of these cases.

After investigation, the MHRA and EMA concluded there was evidence of a link between these cases and the Oxford/AstraZeneca COVID-19 vaccine and that this should be listed as a possible rare side effect of the vaccine. The MHRA and EMA also looked at the overall rate of blood clots occurring without a low platelet count. Both agencies concluded that the available evidence **does not suggest** that the Oxford/AstraZeneca vaccine increases the risk of **blood clots without a low platelet count.**

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 .

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 at an approximate rate of around **1 in every 100,000** vaccinations. Cases are still being collected and the estimate of how frequently the condition occurs may change.

The MHRA have received a proportionally higher number of reports from younger compared to older people that have received the vaccine. Cases also appear slightly more common in females than males. However, it is important to note that there is currently no way of predicting who will go on to develop this condition and that cases have been reported in individuals across all adult age groups, and in both males and females.

The same rare blood clots with low levels of platelets in the blood have also been reported after the Janssen COVID-19 vaccine, which is another **adenovirus-based** vaccine. The EMA has concluded a link between the Janssen COVID-19 vaccine and these rare blood clotting cases is also likely.

We currently don't know whether this rare clot disorder is related to the ChAdOx1 part of the vaccine, or whether it is related to the COVID-19 virus component of the vaccine (the "spike protein"). The rare blood clotting problems have not been seen in trials of other ChAdOx1 vaccines, however the number of people in those trials has been small. Two adenovirus vaccines are currently approved in the USA for use in US military personnel. These have been administered to at least 1.3 million individuals over the last 10 years, with no blood clotting problems identified by vaccine regulators.

As we do not know if this issue could affect other ChAdOx1 vaccines yet we advise you to be alert for the following possible blood clot symptoms in the first 28 days after your 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 the study doctors at any time.

Potential Interaction with Other Adenovirus-based Vaccines (e.g. Oxford/AstraZeneca and Janssen COVID-19 vaccines)

When people are vaccinated with ChAdOx1 biEBOV they should make the intended immune response against the two Ebolavirus glycoproteins. However, they are also likely to make an immune response against ChAdOx1 itself. In theory, an immune response against ChAdOx1 might interfere with future doses of ChAdOx1-based vaccines and prevent them working as well. The same potential interference issue might also apply to other adenovirus-based vaccines. This **theoretical risk** could mean **reducing the protection offered by Oxford/AstraZeneca or Janssen COVID-19 vaccines if they were received soon after ChAdOx1 biEBOV**.

Reassuringly, our earlier research showed immune responses from the Oxford/AstraZeneca COVID-19 vaccine were not reduced in people who had previously received a different experimental ChAdOx1-based vaccine one year earlier. Other research suggests that leaving a gap of three months or more between administrations of two adenovirus-based vaccines reduces the risk of any interference. For this reason, we advise participants to wait at least three months after receiving the ChAdOx1 biEBOV vaccine before receiving the AstraZeneca or Janssen COVID-19 vaccines.

Other Serious Vaccine Reactions

With any vaccination there is a risk of rare serious adverse events. 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. 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 and can be fatal. However, these adverse events have not previously been associated with adenovirus-based vaccines.

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 even potentially be something severe. If you experience concerning or unexpected symptoms, you should phone the 24hr study contact number and speak to a study doctor.

Are There any Other Potential Risks from Taking Part in the Trial?

Blood samples

Blood sampling may cause slight pain and occasionally bruising. Occasionally, people feel light-headed, nauseas or faint. The **total** amount of blood we will take over the whole 6 month trial period is **334ml**. We will take around 50ml at most visits. These are fairly small amounts of blood and should be well tolerated by healthy adults. The amount of blood taken during the trial is less than the amount of blood donated by regular blood donors over the same period. (A *single* donation to the NHS blood bank would be approximately 470ml by comparison)

Incidental Medical Findings

As we carry out several medical tests throughout the trial it is possible that we pick up previously unknown health issues (e.g. high blood pressure, abnormal blood results). If abnormal results or undiagnosed conditions are found during the study these would be discussed with you and, if you agreed, your GP would also be informed of these results. We would refer any newly diagnosed conditions to your GP.

Sometimes incidental medical findings might 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 necessarily gain any direct personal benefit from the trial, but the information gained from the study might help to develop an improved vaccine against Ebola.

Will I be paid for taking part in this trial?

The total reimbursement you would receive for the trial will be **£370**. We have calculated this amount based on: the time you will have to set aside to take part in this trial, any potential travel costs you might incur and the inconvenience of having blood tests and other trial procedures.

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). If you were unable to attend some of the visits, decide to withdraw from the trial before it is completed, have to be withdrawn from the trial for another reason or the trial is stopped early you will receive a proportion of the total reimbursement amount based on the actual number of visits that you attended (e.g. on a "pro rata" basis).

If you are asked to attend an extra in-person visit over and above the scheduled visit listed in the Trial Timeline you will receive further compensation.

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.

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

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

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 will continue to be stored and used for research as detailed below. You are free to request that your blood samples are destroyed at any time during or after 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 trial?

Your samples will be assigned a code and will only be identifiable by this code number. Any samples given to researchers outside of the clinic will not have information that identifies you. The blood and stool samples collected during this study will be analysed in the Oxford University Hospitals 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 say no to the BioBank and continue to take part in this study if you wish. If consent to your samples being stored as part of the Biobank, a copy of your informed consent form (which contains your personal information) will also be stored. If you do not wish for your samples to be stored in the Biobank, they will be destroyed 12 months after the last participant has completed the study.

The following tests will be performed on your samples:

- Blood tests of for blood cell counts and liver and kidney function
- Tests for Hepatitis B, Hepatitis C and HIV (at the screening visit)
- 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, 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). 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 try to identify and study the genes that appear to be important in your immune response to the vaccination. 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 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. 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 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 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 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 letters sent to your own GP. In order 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 about your enrolment and study completion status, 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 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 in order to undertake this study.

We 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, and to oversee the quality of the study. The only people who will have access to information that identifies you will be staff at the University of Oxford who need to contact you to conduct the study or monitor/audit the data collection process and inspectors from the regulatory agency responsible for clinical trials in the UK, the MHRA.

Your information would be stored on a secure server hosted by the University of Oxford, and paper records will be held by at the Centre for Clinical Vaccinology and Tropical Medicine in a locked cabinet. Your data is retained in case we need to contact you regarding any study related matters. We will also ask for you to optionally consent to us securely storing your details in order to inform you of future research studies you may be interest in.

The University of Oxford will keep identifiable information about you from this study for at least 5 years after the study has finished. We will securely store the anonymised research data and any research documents with personal information, such as consent forms, for at least 5 years after the end of the study. The need to store this information for longer in relation to licensing of the vaccine will be reviewed every 5 years.

Once the study has been completed, all documents would be archived in a secure facility. Files will be confidentially destroyed if storage is no longer required. For effective vaccines that may be licensed, secure storage of research data may be required for at least 15 years after the end of the study, subject to adjustments in clinical trials regulations. Your bank details will be stored for 7 years in line with University financial policy.

A photocopy of your ID (drivers licence, passport or national ID card) and either your national insurance or passport number (for "TOPS Database Registration" page 15 and payment processing) will be taken at the screening visit. We will securely retain copies until the end of the study.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible. Further information about your rights with respect to your personal data is available at:

http://www.admin.ox.ac.uk/councilsec/compliance/gdpr/individualrights/

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. 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*.

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 up to 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 looked at by an independent group of people, called a Research Ethics Committee, to protect participants' interests. This study has been reviewed and given favourable opinion by Fast-track Research Ethics 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 make decision on 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://oxford.onlinesurveys.ac.uk/ebl07-pre-screen-questionnaire

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

Email: Vaccinetrials@ndm.ox.ac.uk

Tel: 01865 611419