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# PARTICIPANT INFORMATION SHEET

## A study of a new mRNA vaccine against COVID-19

You are invited to take part in a study to test a new vaccine against COVID-19. Before you decide to take part, it is important that we explain why this research is being done and what it will involve.

We plan to recruit 36 participants aged 18-64 years to take part in a study of a newly developed experimental messenger RNA (mRNA) platform formulation called NeomiVac. To test that the NeomiVac platform is safe and to identify the optimal dose to obtain a satisfactory immune response, it is being used in this study as a vaccine against COVID-19 (SARS-CoV-2) Omicron B.1.1.529 variant. This study will be the first time this vaccine has been tested in humans with pre-clinical data derived from studies on animals and results from similar vaccines.

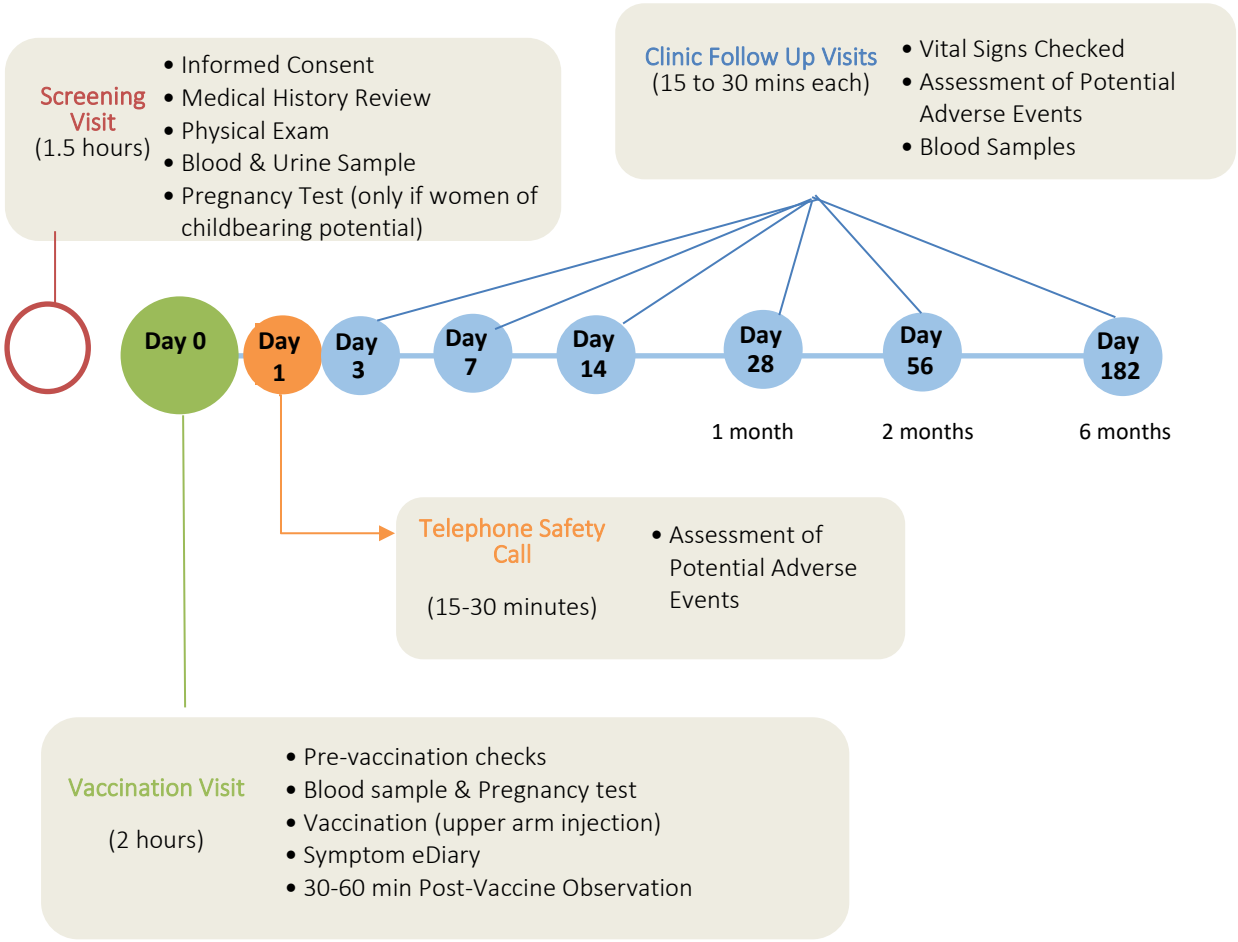
Eligible volunteers will receive one dose of vaccine, a safety follow up call the day after the vaccination, and then will return to clinic for 6 follow up visits over 6 months. mRNA vaccines cannot cause infection with the virus that causes COVID-19 or other viruses. mRNA from these vaccines do not enter the nucleus of the cell where our DNA (genetic material) is located, so it cannot change or influence our genes.

**Before you make a decision on whether to participate in this trial, please take time to read the following information carefully to understand why the research is being done and what it would involve. You can discuss it with friends, relatives or your GP if you wish. Please contact us if there is anything that is not clear or if you would like more information (contact details are on the final page).**

## Study Summary

| | |
|---|---|
| **Study Name** | NeomiVac001 |
| **Who can take part?** | Healthy adult volunteers aged 18-64 in good health (Full criteria inside) |
| **Vaccine being tested** | A single dose of NeomiVac, a new mRNA vaccine at either: a low, medium, or higher dose |
| **Total participants** | 36 participants |
| **Study Aims** | To test safety and immune responses to this vaccine |
| **Trial Site** | Centre for Clinical Vaccinology and Tropical Medicine (CCVTM), University of Oxford, Churchill Hospital, Oxford, OX3 7LE |
| **What happens in the study?** | After obtaining informed consent, all participants will attend a screening visit, to assess their eligibility to take part in the trial. Once a volunteer is deemed eligible and confirms their willingness to take part in the research, a vaccination visit is scheduled. NeomiVac will be administered as an intramuscular injection in the non-dominant arm. Any symptoms after the vaccination will be recorded in an electronic diary for 7 days. Any other health issues experienced after 7 days should be reported to the study team. All participants will be provided with a telephone number in case they have to contact a study doctor out of hours. All participants will be followed up for 6 months after vaccination. Participants will receive a safety phone call the day after the vaccination and will attend a total of 8 in clinic study visits (1 screening, 1 vaccination, and 6 follow up visits) and 1 safety follow up call. All clinic visits will include a blood test. |
| **Reimbursement:** | Up to £975 |
| **Risks of participation:** | From studies on similar vaccines, we expect participants might experience short-lived post vaccine symptoms such as pain in the injection site, malaise and fever. A full discussion of risks, including potential rare but serious reactions is contained within (page 15). As this is the first time the vaccine has been used in people, there might be side effects we are not aware of, and we will monitor the safety of all participants closely. |
| **Benefits of participation:** | Although you will not directly benefit from this trial, participating will help research into the development of new safe and effective vaccines against infectious diseases. |
| **Investigator** | Dr Paola Cicconi (Chief Investigator) |

## Study Visits



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**What is the NeomiVac Vaccine?**

NeomiVac is a next generation messenger RNA (mRNA) vaccine that is being tested in this study against COVID-19. It works by using mRNA to give your cells instructions to make the full-length Spike (S) proteins that are found on the surface of the COVID-19 virus. This causes your body to create antibodies which will fight the virus and protect you from serious disease.

To have a clinical effect from an mRNA vaccine, mRNA needs to enter into our cells where it can be processed. However, mRNA cannot enter cells on its own and is readily broken down by human enzymes. Therefore, mRNA needs to be enveloped in a protective delivery system which can enter human cells and then release the mRNA once inside the cell. The NeomiVac platform aims to achieve this by using lipid nanoparticles (LNPs) which are little balls of fat that can envelope the mRNA. LNPs are also used in the Pfizer-BioNTech and Moderna mRNA COVID-19 mRNA vaccines. The LNPs protect mRNA from degradation enzymes and carry the mRNA into human cells. Once inside the cells the LNPs open and release the mRNA.

The mRNA can then instruct your cells to begin making the target proteins and displaying them on cell surfaces.

After delivering instructions, the mRNA is immediately broken down. <u>It never enters the nucleus of your cells, where your DNA is kept, so it cannot change or influence our genes. NeomiVac cannot cause infection with the virus that causes COVID-19 or other viruses.</u>

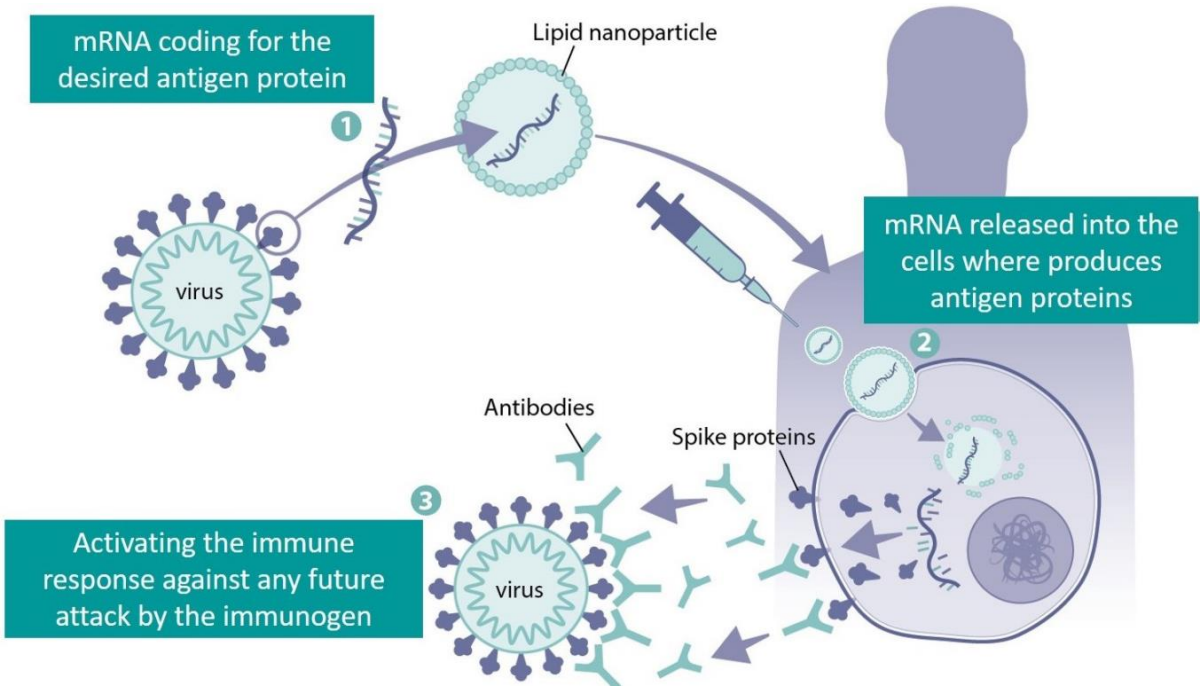


*Figure 1. How mRNA vaccines work: mRNA molecules that carry instructions for making a specific protein (e.g. Spike protein) is made and enveloped in a lipid nanoparticle (little balls of fat) that protect and deliver mRNA into our cells. Once the LNP enters our cells, it releases the mRNA. The mRNA then instructs our cells to make the target protein (e.g. COVID-19 S protein). The proteins then get presented on the outer surface of the cells which causes your immune system to produce antibodies against them. If you then become infected with COVID-19 in future, your body will already have antibodies ready to fight it.*

In this study, the mRNA used in NeomiVac targets the Omicron BA.1 variant of COVID-19. If NeomiVac is shown to be safe and capable of inducing an immune response, then the mRNA molecule will be updated to tackle newer variants of concern (as has been done with the Pfizer-BioNTech and Moderna vaccines) and/or different diseases.

To help understand this principle, we can use the 'doughnut analogy'. Here you can think of LNPs containing mRNA as a filled doughnut, whereby the LNP is the 'dough' and the mRNA molecule is the 'filling'. A baker can create many different flavours of doughnut by using the exact same dough recipe but changing the filling that is added (e.g. by filling the doughnut with strawberry jam, raspberry jam, custard, chocolate etc). The same principle may be applied to some LNPs where the same LNP ('dough') recipe could be filled with different mRNA molecules ('fillings') that may target different viruses/diseases or variants of the same virus.

Indeed, NeoVac, the drug company who is the Sponsor of this study, is working on a pipeline of mRNA vaccines, including vaccines against antibiotic resistant bacteria, that could potentially use the same or similar LNP recipe that is used for NeomiVac. This could rapidly accelerate the vaccine development and greatly reduce the time taken for new mRNA vaccines to reach patients without sacrificing quality.

Whilst NeomiVac is frozen and stored at -80 °C, it may have the potential to be stable for longer at fridge temperature compared with existing mRNA vaccines. Early research and development (R&D) studies have shown that when the ingredients used in NeomiVac are combined they can form LNPs that are stable for up to 1 year at 2-8 °C (fridge temperature) and up to 1 month at 25 °C (room temperature). This would simplify the use and distribution of mRNA vaccines in low- and middle-income countries where there may be limited facilities and infrastructure available. It is important to note that further research is required to validate the long-term stability of NeomiVac.

**What is the purpose of this trial?**

The purpose of this study is to test NeomiVac 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 at incrementing doses
2. The immune response to the vaccine

The purpose of measuring the immune response is that it provides some initial evidence that the lipid nanoparticles (LNPs) in NeomiVac can protect and deliver mRNA into the cells as they are supposed to.

**How is the trial going to work?**

We plan to recruit 36 people to take part in this study. All participants will be given **one dose**

of NeomiVac vaccine. We are testing three different doses of the vaccine in the trial and participants will be allocated into the following groups:

- Group 1: **LOW DOSE** (25% of the higher dose)
- Group 2: **MEDIUM DOSE** (50% of the higher dose)
- Group 3: **HIGHER 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 concerns 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.

We will not vaccinate all participants in the same group at the same time. Instead, the first participant in each group will be vaccinated alone ahead of any other participant in their group. The safety and health of the participant will then be reviewed at least 48 hours after vaccination to check there are no safety concerns with the tested dose. If there are no safety concerns, a further two participants will be vaccinated at least 1 hour apart from each other. The second and third participants will also then be reviewed for safety at least 48 hours after vaccination. If there are no safety concerns, then the remaining participants in the group will be vaccinated. Once all participants in the group have been vaccinated, there will be a safety review at least 7 days after the last participant in the group was vaccinated to determine if it is safe to proceed to vaccinating the next group with a higher dose. This review of the first and then second and third participants safety data, within a dosing group will be repeated at each dosing level, and dosing will only go ahead if safe to do so, as agreed by the safety committee.

The safety committee will include an independent expert who is not part of the research team. The independent expert and the clinicians will hold the decision-making power on whether it is safe to dose further participants within a group and also whether it is safe to proceed to vaccinate the next group at a higher dose.

**Who is sponsoring, organising and funding the research?**

The study is sponsored and funded by NeoVac Ltd. NeoVac is a UK-based biotechnology company with a mission to produce a range of mRNA vaccines and medicines against various diseases.

The Chief Investigator for this study is Dr Paola Cicconi, a senior researcher at the University of Oxford and an Infectious Disease consultant at Oxford University Hospital. The study is being carried out by Oxford University researchers based at the Clinical Trial Unit of the Jenner Institute, the Centre for Clinical Vaccinology and Tropical Medicine, Oxford.

**How long will I be in the study?**

If you are eligible to 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 (week 26). You may also decide to withdraw from the study early without this having any effect on your future medical care (What will happen if I don't want to carry on with the trial? Page 19).

**Can I take part?**

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

**You must:**

| |
|---|
| Be aged **18 to 64 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 donation** throughout the study (From vaccination to final follow up visit) |
| 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 visit |

**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 **bleeding disorder** |
| A history of **myocarditis, pericarditis** or other **active known heart disease** |
| A **serious ongoing mental health condition** if this may affect your participation in the study |
| A history of **allergic disease or reactions** likely to be exacerbated by any component of the vaccine |
| A history of **allergy to polyethylene glycol (PEG)** |
| A history of a **severe allergic reaction to a vaccine, including hypersensitivity** |
| A history of **cancer** (except basal cell carcinoma of the skin and cervical carcinoma in situ) |
| A history of **Hepatitis B**, **Hepatitis C** or **HIV infection** |
| A history of **hereditary angioedema**, **acquired angioedema**, or **idiopathic angioedema** |
| Previously **injected recreational drugs** (within the last 5 years) |
| A history of **COVID-19 infection** within **30 days** of the study vaccination |
| A history of a **blood transfusion** or '**Immunoglobulin infusions'** within 3 months of the trial |

| |
|---|
| Any medical, psychiatric, or occupational condition, including reported history of **drug** or **alcohol** abuse, that, in the opinion of the Investigator, might pose additional risk due to participation in the study or could interfere with the interpretation of study results |
| ***Other Vaccines*** |
| Receipt of any COVID vaccine during the 3 months before and planned receipt of any COVID vaccine vaccines for at least 3 months after receiving the trial vaccine |
| Planned or actual receipt of any non-COVID vaccines administered within 14 days (before or after) enrolment EXCEPT for live vaccines which must not be given within 30 days of the trial vaccine |
| ***Other Clinical Trials*** |
| Participating in **another clinical trial** involving receipt of an investigational product during, or within 90 days of the vaccine visit of this study |
| ***(Females of Childbearing Potential) 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 (details at the end of this information sheet). 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 doses of vaccine are used in this trial?**

The doses we will use are chosen based on data in animals and experience with similar vaccines. The 'higher' dose is equivalent to the approved primary series dose that is used for the Moderna mRNA-1273 COVID-19 vaccine/Spikevax.

The doses that we are using in this trial are:

| Group<br>(number of participants in each group) | Dose of NeomiVac (mRNA) |
|---|---|
| 1<br>(n=6) | 25 microgram |
| 2<br>(n=15) | 50 microgram |
| 3<br>(n=15) | 100 microgram |

**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 covers 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 you questions about your health and any medications you are taking and give you a physical examination. Your pulse rate, blood pressure and temperature will be recorded. A blood sample will be taken in order to confirm that you are eligible to take part. This will include a pregnancy test for women of childbearing potential (WOCBP), as well as tests for HIV, Hepatitis C, and Hepatitis B infections, as well as markers to show you do not have any bleeding disorders. These tests will be explained to you in detail. In case of a new diagnosis of viral hepatitis or HIV emerges during the screening process, you will be referred to the NHS for further assessment and management.

Urine samples will also be taken to check for protein, blood and glucose in your urine.

You will have an electrocardiogram (ECG) to check your heart's rhythm and electrical activity.

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

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

We will ask you to refrain from participating in other clinical trials at the same time. In addition we will register you on the TOPS database (www.tops.org.uk), which is a confidential national

database of healthy volunteers that identifies volunteers participating in studies, to minimise the risks that can come from over-volunteering. We will enter into the database only:

- your National Insurance number (if you have one)

- your passport number and country of origin (if you are not a UK citizen and don't have a National Insurance number)

- the date of your last dose of study vaccine

Vaccination Visit (Day 0)

If you qualify to be in the trial after the screening visit eligibility checks, we will arrange for you to attend and receive the NeomiVac vaccine. Your blood pressure, pulse and temperature (vital signs) will be checked, and blood samples taken. A COVID-19 nasal swab will be taken. Women of childbearing potential will have a urinary pregnancy test before vaccination.

If you are still happy to be enrolled in the trial and there you are still eligible, the NeomiVac vaccine will then be given as an injection into the muscle of 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 30 minutes after the vaccine (60 minutes if you are the first participant in your group). After this period, your vital signs will be checked again, your lymph nodes around your neck and armpits will be examined as these are involved in your body's immune response to vaccination and it is important to monitor any swelling, and the injection site inspected. We will then allow you to go home. After vaccination we will give you a telephone number you can use to contact a study doctor if you have concerns out of normal office hours. 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. From the first day of vaccination until 6 days after vaccination, you will need to record symptoms you might experience. We will also ask you to measure and record your temperature at the same time each day using an oral thermometer that we will provide. We will also give you a tape measure so that you can measure local side effects such as skin redness or swelling at the injection site (see 'Vaccine Reactions around the injection site – local reactions' page 15). If you forget to fill in the diary, you will be contacted by a member of the study team.

Follow up Visits

After you have received the vaccination, you will receive a safety telephone call from the study team one day after vaccination. There will be 6 more follow-up visits in clinic. During the follow up visits, we will check your vital parameters, we will do a physical examination if required and we will take some blood tests as per the schedule indicated in the trial visit

timeline. At vaccination visit and Day 28, we will also perform a nasal swab for COVID-19 lateral flow test. Information about your Covid status will help us interpret the immune response to the vaccine.

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.

**Trial Visit Timeline**

| **Visit** | **What to expect at the visit** |
|---|---|
| Screening Visit | Informed Consent, consent to contact the GP, registration on TOPS, medical history, physical examination, ECG, vital signs, blood test (including pregnancy test if WOCBP) and urine sample |
| Vaccination Visit (Day 0) | Physical examination, vital signs, blood test, (urine pregnancy test if WOCBP), nasal COVID-19 lateral flow test, receive NeomiVac vaccine, remain in clinic for 30 minutes post-vaccine observation (60 minutes if you are the first participant in your group) |
| Day 1 Safety telephone call | Clinical assessment |
| Day 3 Follow up (in clinic) | Clinical assessment, vital signs, blood tests |
| 1 Week (Day 7) Follow up (in clinic) | Clinical assessment, vital signs, blood tests |
| 2 Weeks (Day 14) Follow up (in clinic) | Clinical assessment, vital signs, blood tests, nasal COVID-19 lateral flow test |
| 1 Month (Day 28) Follow up (in clinic) | Clinical assessment, vital signs, blood tests, nasal COVID-19 lateral flow test |
| 2 Months (Day 56) Follow up (in clinic) | Clinical assessment, vital signs, blood tests |
| 6 Months (Day 182) Follow up (in clinic) | Clinical assessment, vital signs, blood tests (including pregnancy test if WOCBP), final study visit |

**What should I consider before taking part in this study?**

Having a COVID-19 Vaccination during the study

You should not have had a COVID-19 vaccine within 3 months from receiving the trial vaccine and planning to receive one for at least three months after the trial vaccine. We are not suggesting participants should delay their NHS COVID-19 booster 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.

Having a COVID-19 infection during the study

This study is not designed to assess efficacy of the NeomiVac vaccine, however information on symptomatic and asymptomatic infections will help us with the interpretation of the immunological tests. For this reason, we will perform COVID-19 lateral flow tests during the study at Vaccination visit, Day 14 and Day 28. As part of your continued medical assessment, we will ask you to report any changes in your medical history at every follow up visit, this will include information on asymptomatic or symptomatic COVID-19 infection that might occur during the study period. We will ask you to follow the most updated government guidelines in case of COVID-19 infection.

Private Insurance

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

Contraception

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

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 affect 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. This will be 14 days before or after the study vaccination and 30 days in case of a live vaccine.

**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, you will be able to restart blood donation once your last study visit has been completed.

Taking Part in Other Clinical Trials

You should not take part in other clinical trials where investigational drugs or vaccines are administered during this study. You should also not take part in studies that involve repeated blood sampling, whilst participating in this study.

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 NeomiVac vaccine?**

We expect mild local and systemic, self-resolving side effects after vaccination based on pre-clinical studies of the study vaccine and on past experience with similar mRNA vaccines. 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 side effects we are not aware of.

Injection site- 'Local' Reaction

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 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.

After vaccination with mRNA vaccines, nodes swelling and tenderness of the underarm glands on the same side as the injection site have also been reported.

How common were reactions after administration of other mRNA based COVID-19 vaccines according to the information leaflet?

**Moderna mRNA-1273 COVID-19 vaccine/Spikevax®**

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 10).

| **Very common: may affect more than 1 in 10 people** | **Common: may affect up to 1 in 10 people** | **Uncommon: may affect up to 1 in 100 people** |
|---|---|---|
| • Swelling/tenderness of the underarm glands on the same side as the injection site<br>• Headache<br>• Nausea<br>• Vomiting<br>• Muscle ache, joint aches, and stiffness<br>• Pain or swelling at the injection site<br>• redness at the injection site (some of which may occur approximately 9 to 11 days after the injection)<br>• Feeling very tired<br>• Chills<br>• Fever | • Diarrhoea<br>• Rash<br>• Rash or hives at the injection site (some of which may occur at a median of 4 to 11 days after the injection) | • Itchiness at the injection site<br>• dizziness<br>• stomach pain<br>• raised, itchy rash (urticaria) (which may occur from the time of injection and up to approximately two weeks after the injection) |

**Pfizer BioNTech COVID-19 BNT162b2 vaccine Comirnaty®**

The dose given to those individuals was 5 µg higher than the group 'low dose' we plan to use in this trial but lower than the dose planned for group 'medium dose' and 'higher dose' (What doses of vaccine are used in this trial? page 10).

| Very common: may affect more than 1 in 10 people | Common: may affect up to 1 in 10 people | Uncommon: may affect up to 1 in 100 people |
|---|---|---|
| • injection site: pain, swelling<br>• tiredness<br>• muscle pain<br>• headache<br>• chills<br>• joint pain<br>• diarrhoea<br>• fever | • redness at injection site<br>• nausea<br>• vomiting<br>• enlarged lymph nodes | • feeling unwell<br>• arm pain<br>• insomnia<br>• injection site itching<br>• allergic reactions such as rash or itching<br>• feeling weak or lack of energy/sleepy<br>• decreased appetite<br>• dizziness<br>• excessive sweating /night sweats |

The information leaflets of both vaccines report other rare and very rare side effects:

**Rare (estimated to affect between 1 in 10,000 up to 1 in 1000 people)**

- Temporary one-sided facial drooping (Bell's palsy)
- Swelling of the face (Swelling of the face may occur in patients who have had facial cosmetic injections.)
- decreased sense of touch or sensation
- unusual feeling in the skin, such as tingling or a crawling feeling (paraesthesia)

**Very rare (may affect up to 1 in 10,000 people)**

There have been rare cases of inflammation of the heart (myocarditis and pericarditis) reported after COVID-19 vaccination. The reported rate appears to be highest in those under 25 years of age and in males, and after the second dose. Onset is within a few days of vaccination and most cases are mild and have recovered without any long term complications.

Symptoms of myocarditis/pericarditis include: chest pain, shortness of breath, a fast-beating, fluttering or pounding heart (palpitations).

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.

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.

Guillain-Barré Syndrome (GBS) is a condition affecting the nervous system, in which people can develop severe weakness and can be fatal. Cases of GBS are also severe but extremely rare, and have been reported after vaccinations in the past.

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 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 study?**

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 trial period is approximately 500ml**.** The maximum amount of blood taken at a single visit would not exceed 80ml. 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 / similar to the amount of blood donated by regular blood donors over the same period. (For comparison, a *single* donation to the NHS blood bank would be approximately 470ml)

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 gain any direct personal benefit from the trial, but the information gained from the study might help to develop improved mRNA vaccines against COVID-19 and other

diseases (e.g. via the doughnut analogy outlined in section: 'What is the NeomiVac Vaccine?').

**Will I be paid for taking part in this trial?**

The total reimbursement you would receive for the trial will be up to **£975**. 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.

Reimbursement for all participants will be based on the following figures:

Screening visit: £75
Vaccination visit: £130
Safety Telephone call: £20
Follow up visit: £90 x 6 = £540
Full completion of the Diary: £30 x7 = £210

Trial reimbursement will be made by bank transfer in instalments during the study, 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 (i.e., 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 for this at the rate appropriate for the type of visit.

**What if new information becomes available?**

Sometimes in a study, new information relevant to the trial 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 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 NeomiVac, this will be reviewed, and you would be kept fully updated.

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

If, at any time after agreeing to participate, you change your mind about being involved with this study you are free to withdraw without giving a reason. If you withdraw, we would not usually perform any more research procedures, although occasionally we might need to offer you a follow up visit for safety purposes, for example to check the injection site or a blood

result. Your decision will not result in any penalty, and your standard medical care will not be affected.

Unless you state otherwise, any blood taken whilst you have been in the study will continue to be stored and used for research as detailed above. You are free to request that your blood samples are destroyed at any time during or after the study.

**What will happen to any samples I give during the trial?**

The blood tests will include:

- tests for HIV, Hepatitis C, and Hepatitis B infections (only at screening visit)
- a full blood count, blood chemistry and liver function tests at selected visits, to ensure that the vaccines are safe.
- coagulation tests at selected visits to make sure there are no bleeding disorders.
- blood samples taken at each visit for research laboratory tests that will measure your immune response to the vaccine.
- HLA typing, a genetic test of components of the body's immune system

Blood samples will be labelled with your unique study code only, before sending to the appropriate laboratory for analysis. The safety blood samples collected during this study would be stored and analysed in the Oxford University Hospital NHS Foundation Trust and University of Oxford research laboratories in the first instance. However, as part of this project, research samples may be sent to our academic and industrial collaborating partners both within and outside the UK. These samples would be stored with your unique study code only. Your samples will be stored for 12 months after the end of the trial and then will either be destroyed or transferred to a licensed facility for future research related to the product development with your consent.

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

**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. NeoVac Ltd., 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.

We will provide compensation for any injury caused by taking part in this study in accordance. We will pay compensation where the injury probably resulted from:

- A drug being tested or administered as part of the trial protocol;
- Any test or procedure you received as part of the trial.

Any payment would be without legal commitment. (Please ask if you wish more information on this). We would not be bound by these guidelines to pay compensation where the injury resulted from a drug or procedure outside the trial protocol or where the protocol wasn't followed.

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.

**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 or contacting the study team at 01865 611430.

If you would like to make a complaint to an independent body, you can contact the clinical trial monitor by sending an email to ClinicalTrials@neovac.co.uk. The study monitor will liaise with the study Sponsor, NeoVac, to investigate the matter further.

**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, the Sponsor, 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?**

We will need to use information from you, from your medical records and from your GP for this research project. This information will be held by site for research and will include, but is not limited to:

- your full name
- Your date of birth
- NHS number
- Contact details
- National Insurance Number for TOPS registration
- Photocopy of an ID (Passport/Driver's License)

Bank details for reimbursement and next of kin contacts will also be collected.

People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure. Some of your information may be sent to other countries. They must follow our rules about keeping your information safe.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

**What are your choices about how your information is used?**

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

If you choose to stop taking part in the study, we would like to continue collecting information about your health. If you do not want this to happen, tell us and we will stop.

We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

**Where can you find out more about how your information is used?**

You can find out more about how we use your information at www.hra.nhs.uk/information-about-patients/ and by asking one of the research team by sending an email to vaccinetrials@ndm.ox.ac.uk.

**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.

**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 (South Central - Oxford A Research Ethics Committee, Ref. No 24/SC/0136).

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 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 611430

**If you are interested in taking part in this study, then please complete the online pre-screening questionnaire at:** https://app.onlinesurveys.jisc.ac.uk/s/oxford/neomivac001-duplicate

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