Sisonke Phase 3B open label Study

(VAC31518COV3012)

Each **participant** must read and understand this document **before** consenting to join.

This is an open-label, single-arm phase 3B study to monitor the effectiveness of the single dose Ad26.COV2.S COVID-19 vaccine among health care workers in South Africa.

Sponsor: South African Medical Research Council
Francie van Zijl Drive, Parowvallei, Cape Town;
7505 Tygerberg, South Africa

We are inviting you to take part in a research study called SISONKE (Together)

South Africa is severely affected by the global COVID-19 epidemic, but currently no vaccine has been rolled out. The recent promising results of the 'ENSEMBLE' trial conducted by Janssen in South Africa, and the availability of a limited amount of vaccine doses, provide the rationale for a vaccination study of HCWs to inform the larger vaccine rollout.

- Please take time to read the following information carefully. Discuss it with friends and relatives if you wish. Take time to decide whether or not you wish to take part.
- You are free to decide whether or not to take part in this study. If you choose not to take part, this will not affect the care you get from your own doctors in any way.
- You can stop taking part in the study at any time, without giving a reason.
- Ask us if there is anything that is not clear or if you would like more information.
- Thank you for reading this information. If you decide to take part in the study, you will be asked to consent to take part.

Important things that you need to know

- We want to find out two things:
  - the effectiveness of the vaccine to prevent severe disease and death from COVID19 in health care workers
  - The ongoing safety of this COVID vaccine in vaccinated health care workers
- **This is an open label study: that means everyone in this study will receive a single dose of the Ad26.COV2S COVID19 vaccine. There is no placebo.**
- Like all vaccines, the COVID vaccine used in this study, can have unwanted side effects. The most common side effect is that the injection site may be red, swollen and feel sore for a day or two.
- There may also be symptoms of "reactogenicity", eg fever, fatigue for 1-2 days.
- The study will fit into your normal schedule, so for most people, there are no hospital visits.
- In a subset of HCWs only (approx. 1400), you will need to give a nasal or nasopharyngeal swab and a blood (about 60ml or 10-12 teaspoons) sample before you start, at baseline, six weeks and at six months. If you are breastfeeding, we will also ask for approximately 10mL of breastmilk at these time points. (vaccination day, 6 weeks, 6 months)
- You will be in the study for 2 years.

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1 Why are we doing this study?

This study is carried out to see the effectiveness of Ad26 Covid Vaccine to prevent or reduce the severity of COVID-19 in healthcare workers in a "real world" setting.

What is COVID-19?

A new coronavirus pandemic is sweeping the world and is called COVID-19. This is caused by infection with a virus called SARS-CoV-2. The illness is usually mild, but it can cause a severe chest infection (pneumonia) or death in some people. If you want to know more about COVID-19, please look at the World Health Organisation (WHO) website:

https://www.who.int/emergencies/diseases/novel-coronavirus-2019/

How is COVID-19 usually prevented?

Although some drugs reduce the severity of COVID-19 in hospital patients, vaccines are just being licensed in some parts of the world and this is the wider scale availability of vaccines in South Africa. Physical distancing, quarantine and infection control measures are the only interventions currently available here in South Africa.

What are we trying to find out?

We want to find out three things:

- Whether healthcare workers who do get infected experience a milder disease if they have received the Ad26 vaccine.
- Whether we see less COVID infections in health care workers who have been vaccinated.
- Ongoing safety on this vaccine

2 Why am I being asked to take part?

You are being asked to take part in the Sisonke study because you are a healthcare worker who may be at high risk of being exposed to COVID-19 and may therefore catch the disease.

Do I have to take part?

No, joining the study is voluntary; it is up to you to decide whether or not to take part. If you decide to take part, you can ask for this information sheet or read it on the website and you will be asked to consent to the study.

A decision to not take part will not be held against you and will not affect the standard of care you receive if you become ill at any time.

3 What do I need to know about the vaccine used in this study?

The Jansen COVID-19 vaccine, Ad26.COV2.S, is being administered under study conditions while the regulatory processes are underway in South Africa. This study has been approved by the regulatory authorities. A single-dose regimen of this vaccine has been shown to be 64% effective overall in South Africa and 85% effective overall in preventing severe disease by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). This vaccine also demonstrated complete protection against

COVID-19-related hospitalisation and deaths as from 28 days after receiving the vaccine. The vaccine, although protective against severe disease and hospitalisation in all regions of the world, was found to have less impact on other milder forms of disease because of new circulating virus variants, such as 501Y.V2 in South Africa. Because of this, we will be following you up to evaluate this further.

The Ad26.COV2.S study vaccine is made from a type of common cold virus called Adenovirus. The adenovirus used to make this vaccine is thought to be harmless to people because it has been weakened so it cannot replicate and cause a cold.

The Ad26.COV2.S study vaccine includes genetic material from the SARS-CoV-2 virus. When the vaccine is injected into your body, the genetic material from SARS-CoV-2 gets "translated" to produce so called 'spike proteins' which are small bits of protein specific to SARS-CoV-2. Our bodies then make an immune response against these spike proteins. This immune response is our body's way of fighting the infection. <u>You cannot contract COVID-19 from the vaccine.</u>

J&J is filing for the emergency use of the single dose of the Ad26COV2.S vaccine in various regions of the world, including South Africa. Emergency use approval has now been granted by FDA (USA), the European Authorities and the WHO. This study is being conducted while these processes are ongoing in attempt to offer this as an emergency to health care workers. It will be available once registered later in this year.

4 What will I need to do if I take part?

This is an open-label single arm study. That means that you will receive a single shot of the Ad26 vaccine. There is no placebo. You must be aged 18 years or older, have registered on the national vaccine site, and be willing to attend one of the vaccination centres or research sites to be vaccinated. We would also require your permission to collect hospital and laboratory information from databases.

Can I definitely take part?

Not everyone will be able to take part in this program. We need you to answer some questions first.

You need to be over 18 years and a health care worker.

Women who are pregnant, will be asked to consult their antenatal care provider and bring a recommendation for vaccination. Pregnant women must be between 16 and 34 weeks of their pregnancy in order to enrol.

We recommend that those who intend to get pregnant within three months of entering the trial or those in their 1st trimester or between 34 weeks and delivery defer their vaccination.

Lactating women are eligible to enrol. There are some previous medical conditions below which if you have them, we would like you to call the number below and inform the vaccine centre where you attend prior to vaccination.

If you have had a very severe reaction to a vaccination before,

You have had a severe clotting disorder for example:

- cerebral venous sinus thrombosis (clotting in the brain)
- antiphospholipid syndrome (unusual blood disorders)
- you are on chronic anticoagulation medication, e.g. warfarin.

You may **not** participate if you have a history of thrombocytopenic thrombosis (clotting) with a previous COVID19 vaccine or have had heparin-induced thrombocytopenia

If you have a recent infection or are unwell, you may be asked to wait to be vaccinated.

You will be asked to inform the research staff:

- If you have received another vaccination in the previous 30 days. This may not be a contraindication, but it is important to let us know. We recommend a 14-28 days window between vaccinations.

You will also need to agree to allow access to your healthcare records to 1) confirm medical data if necessary, or 2) to contact us on the number below if you are admitted to hospital during the study or become ill so we can collect study follow up information.

What if I am immunocompromised or living with HIV?

- If you are uncertain of your HIV status or have not had an HIV test within the past 12 months, we would encourage you to test for HIV before joining this study. While Ad26 vaccine is safe for people living with HIV who are not severely immunocompromised, it is important that you know your status prior to joining this trial. If you need information about where you can get tested for HIV, we will provide you with this information. If you know you live with HIV and are on treatment, please let us know. This is not a contraindication to being vaccinated.

What if I have allergies?

You could have an allergic reaction to a vaccine, including a rash, hives, or difficulty breathing. Some allergic reactions can be life-threatening. The study staff will watch you for at least 15 – 30 minutes after each injection.

Always tell the study staff if you have ever had a bad reaction to any injection or vaccine. They may give you medicines in the clinic to treat serious allergic reactions. If you think you're having a severe allergic reaction after you leave the study site, contact the emergency number on the vaccination card (given below) and get medical help right away.

What if the questions show I can take part?

Before you can enter the study, you will need to complete a questionnaire about your health to make sure that this study is suitable for you.

If your answers to the questions show you can take part and you agree to join the Sisonke Study, we will ask you to sign an online consent form or a paper consent at a vaccination site. You will not be able to join the study without a signed consent.

What will happen to me during the study?

Once your suitability in the study is confirmed by the local investigator, and you have signed the eConsent/consent you will be given the vaccination. Data will be collected using routine data sources form the National Department of Health by linking your ID/passport national number, name and other locator information for up to 2 years after receiving the vaccination. If you develop COVID-19 and want to take part in a treatment study, you can do it, but we would like you to inform the study team to ensure your safety and best possible care. We may check your medical and laboratory records if we are alerted to possible breakthrough COVID infection. We ask that if you need routine care, you also mention to your provider that you have been on the Sisonke Study.

In a subset of the healthcare worker population enrolled (about 100 000 volunteers) we will also request a blood test (1 teaspoon = 5ml) at the start to check prior

exposure to SARsCOV2 infection, ie prior immunity. This is voluntary.

In another subset/sub-study of volunteer HCWs (approx. 1000-1400) we will draw a sample of blood (about 12 teaspoons= 60ml) to check for prior COVID19 exposure at the time of vaccination and at 1, 3 and 6 weeks and 6 months. At that time, we will check on your health status and repeat the blood test to rule out COVID-19 infection at this time, and again at 6 months. At the end of the study we may check your medical and laboratory records. We may also conduct nasal swabs for COVID19 if indicated.

What checks and tests will be done?

It is particularly important that if you have a previous history of cerebral venous sinus thrombosis, acquired or hereditary thrombophilia or antiphospholipid syndrome or severe allergy following vaccination we would like you to call the number below or ask to speak with the research team associated with your vaccine centre. This is because we would like to have experts consult on whether it is safe for you to be vaccinated and to advise best procedures to do so. You will also be carefully followed up, should you be vaccinated. This is for your own safety.

During the study, if you develop symptoms of COVID19, including cough, shortness of breath or difficulty breathing, fever, chills, muscle pains, sore throat, or new loss of taste or smell we advise you to follow the NICD guidance and seek care/ advice from your health care provider.

We will be analysing the information we receive regularly throughout the study. If there is clear evidence that the risks outweigh the benefits, we will stop the study early.

Will I get paid to take part?

There is no reimbursement for joining this study.

5 What are the possible side-effects?

What are the most common side-effects?

Pain, tenderness and redness at the injection site, headache, chills, joint pain, muscle pain, tiredness, generally not feeling well, nausea and fever have been seen with this vaccine. These reactions usually start within 1 to 2 days after the injection and most of the reactions get better within 1 to 3 days.

Are there serious side-effects?

It is rare for anyone to have a serious allergic reaction to a vaccine. If this does happen, it usually happens within minutes. The person who vaccinates you will be trained to deal with allergic reactions and treat them immediately. With fast treatment you will make a good recovery.

Vaccines similar to Ad26.COV2.S (that is, Ad26-based vaccines) have been given to participants in studies designed to prevent RSV (Respiratory Syncytial Virus), HIV (Human Immunodeficiency Virus), Ebola/filovirus, Zika Virus, HPV (Human Papillomavirus) and malaria. As of 04 September 2020, Ad26-based vaccines have been administered to approximately 114,000 participants in ongoing and completed studies, including more than 99,000 participants in an ongoing Ebola vaccine study in the Democratic Republic of the Congo and in an ongoing immunization campaign in Rwanda.

The Ad26.COV2.S has been studied in the test tube and in animals with no vaccine-related adverse effects observed. As of 2nd Feb 2021, a single injection of Ad26.COV2.S has been administered to at least 20,800 participants, aged 18 and older. Following administration

of Ad26.COV2.S, fever, muscle aches and headache appear to be more common in younger adults and can be severe. For this reason, we recommend you take a fever reducer or pain reliever if symptoms appear after receiving the vaccination, or upon your study team's recommendation.
RARE CLOTTING DISORDER: Another rare, possibly related serious side effect has recently come to light through international vaccination programs. This is the unusual medical situation where thrombosis (clotting) occurs in major vessels in the presence of a low platelet count (platelets are a part of our blood system that helps with clotting). The condition has become known as vaccine induced thrombocytopenic thrombosis or VITT.
This is exceedingly rare, but cases have been documented in association with some COVID19 vaccines including the vaccine you will receive in Sisonke. Cases of the rare clotting syndrome have occurred within 4-20 days of vaccination (median 8 days).
It is important that if you develop any of the following symptoms during this period after vaccination we advise that you seek care urgently, advise your doctor that you have recently been vaccinated and ask them to contact the Sisonke desk on 0800 014 956.

Symptoms that should prompt you to seek care in this period include:

- new onset seizures; or weakness in a limb
- severe dizziness
- severe unrelenting blinding headaches with vomiting
- severe abdominal pain associated with vomiting
- blurred vision
- breathlessness
- pain in the chest or stomach
- swelling or coldness in a leg,
- after vaccination
- persistent bleeding
- multiple small bruises
- new leg pain reddish and/or purplish spots, or blood blisters under the skin.

When seeking medical care, please ask your practitioner to make immediate contact with the Sisonke desk and avoid heparin until a diagnosis has been established.
There may be other risks associated with Ad26.COV2.S that we don't know about yet. If we learn new information about the vaccine and risks associated with it, we will tell you.

Please remember that we request you to report any side effects or serious medical conditions that occur after vaccination. The Sisonke safety desk will also send you an SMS after vaccination at weekly until 3 weeks post vaccination to remind you.

If you become concerned about any side-effects, please call the number on your vaccination card and listed below as soon as possible.

Pregnancy and Breast Feeding

Animal studies have shown that Janssen's licensed Ad26-based vaccine against Ebola did not raise concerns in preclinical reproductive toxicity studies. These are studies in pregnant animals that received the vaccine, and then delivered animal babies. Therefore, ongoing studies with the Ebola vaccine allow pregnant women and women planning to become pregnant to receive that vaccine. While we gain more understanding about this we would ask you about your pregnancy status at the vaccination visit. If you are pregnant, you may be enrolled and vaccinated if

- You are 16-34 weeks pregnant.

- You bring a letter of recommendation from your antenatal care provider to establish

how many weeks pregnant you are and whether they support vaccination for you

- Sign an additional consent to vaccination at site

If you suspect that you have become pregnant within 3 months of receiving the vaccine, please notify the number of your vaccination card. The Sisonke team will collect data about the wellbeing of your pregnancy and baby after birth. If you do not wish to be followed, you can withdraw your consent at any time by informing your doctor.

The vaccine is safe to use in women who are breastfeeding for both mother and baby.

If you are pregnant or breastfeeding we urge you to report how you feel post vaccination through the adverse event link that will be sent to you via sms. When you complete this form please indicate that you are pregnant or breastfeeding (as applicable) when you complete this form. We will therefore ask you about your pregnancy status at the vaccination visit.

If you suspect that you have become pregnant within 3 months of receiving the vaccine, please notify the number of your vaccination card. The Sisonke team will collect data about the wellbeing of your pregnancy and baby after birth. If you do not wish to be followed, you can withdraw your consent at any time by informing your doctor.

6 What are the possible benefits of taking part in this study?

The information we get from this study will help us understand COVID vaccines and their effectiveness in South Africa.

You will receive access to an emergency use of this vaccine while we are awaiting regulatory approval. The single-dose Ad26.COV2.S vaccine regimen has been shown to be 64% effective overall in South Africa and 85% effective overall in preventing severe disease by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). This vaccine also demonstrated complete protection against COVID-19-related hospitalisation and deaths as from 28 days after receiving the vaccine.
You can choose to wait until the South African Health Products Regulatory Authority (SAHPRA) approves it for general use.

7 What are the possible disadvantages and risks of taking part?

There are no disadvantages to taking part in this study. Whilst there is a risk of study participation disclosure at the time of vaccination, all data will be anonymised before reporting.

8 More information about taking part

Who is organising and funding the study?

The study is funded by the SA MRC and National Dept of Health. The vaccines have been supplied by Johnson and Johnson.

The principal investigators (PI) are not receiving any money or other payment for asking you to be part. As local representative of the international sponsor, the SA Medical Research Council has overall responsibility for the conduct of the study in South Africa. The

SAMRC is responsible for ensuring the study is carried out ethically and in the best interests of the study participants.

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.

A decision to stop taking part at any time will not affect the standard of care you receive if you become ill.

If you agree to take part in the sub study, you will have the option to take part in future research using your data saved from this study. If you do, we will request and hand signed informed consent for this.

How will we use information about you?

We may need to use information from your medical records, your hospital and/or your healthcare provider/laboratory for this research study. This information will include where appropriate, your ID number, name, date of birth, postcode, contact details and healthcare information related to this study. We are not allowed to gather information about you that does not directly inform this study. People will use this information to do the research or to check our 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.

We will keep all information about you safe and secure.

Some of your information will be shared with researchers from other countries from across the world. This includes researchers from countries taking part in the study as well as those who might request use of your anonymous study information after the study is complete.

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 will happen to the results of the Sisonke study?

When the study is completed, we will publish a summary of the results.

We will also publish the results in a medical journal, so that other doctors can see them. You can ask the study team for a copy of any publication. Your identity and any personal details will be kept confidential. No named information about you will be published in any report of this study.

Who has reviewed the Sisonke study?

The study has been reviewed by international scientists. It has been approved by all relevant research ethics committees and written approval has been granted by those committee.

It has been authorised by the South African Health Products Regulatory Authority (SAHPRA). These groups have been involved in the planning and preparation of the study and will not have access to your information.

The study has been structured in accordance with the Declaration of Helsinki (last updated: October 2013), which deals with the recommendations guiding doctors in biomedical research involving human participants. A copy may be obtained from the PI if you wish to review it.

What if new information becomes available during the course of the study?

Sometimes during a study, new information becomes available about the vaccines that are

being studied. If this happens, the research team will tell you about it.

What happens if the Sisonke study stops early?

Very occasionally a study is stopped early. If it happens, the reasons will be explained to you.

What if something goes wrong for me?

If you become ill with COVID19 you will be referred to a COVID19 hospital for care. Please tell your treating doctor that you are enrolled in this study. Your treating doctor or you can contact the numbers below for more information.

Every care will be taken in the course of this study. However, in the unlikely event that you are injured by taking part, compensation may be available.

SAMRC insurance will provide compensation for reasonable medical expenses incurred as a result of study-related injury or illness, or death determined according to the guidelines laid down by the Association of the British Pharmaceutical Industry (ABPI Compensation Guidelines Version 2014), and Guidelines for Good Practice in the Conduct of Clinical Trials in Human Participants in South Africa. http://www.abpi.org.uk/media/1607/compensation_guidelines_2014.pdf

Please notify the investigator immediately of any complications, side effects and/or injuries during the study and the nature of the expenses to be covered.

If a research related injury occurs, you have not waived any of the legal rights which you otherwise would have as a participant in this study by signing this form.

The insurance does not cover medical treatment of other injuries or illnesses or injury caused by non-observance of the protocol.

The investigator is indemnified conditional on compliance with the protocol, SAHPRA and related research committees and is not a substitute for medical malpractice insurance.

Please note that if you have a life insurance policy you should enquire whether your insurance company requires notification of your intention to participate in a study like this. Information to date is that it should not affect any life insurance policy taken out. Nevertheless, you are strongly advised to clarify it with the company concerned.

9 Contacts for further information

If you want further information about the Sisonke study, contact: 0800 014 956

More information is also available on this website. http://sisonkestudy.samrc.ac.za/

If you have any concerns about the way you have been approached or treated during the study, please talk to the Sisonke desk at

0800 014 956.

After you have consulted your doctor or the ethics committee and if they have not provided you with the answers to your satisfaction, you should write to the South African Health Products Regulatory Authority (SAHPRA):

The Chief Executive Officer
South African Health Products Regulatory Authority (SAHPRA)
Department of Health
Private Bag X828
Pretoria, 0001
E-mail: Boitumelo.Semete@sahpra.org.za

Tel: 012 501 0410

Thank you for taking the time to consider taking part in this study.