Patient Information Sheet

EudraCT number:	2021-003214-40
IRAS ID:	301103
Study Number:	MVX0004
Study Title:	A multicentre, multinational, parallel group, observer-blind, randomised, placebo-controlled study on the Group B Streptococcus vaccine (GBS NN/NN2), investigating the immunogenicity and safety of four vaccination regimens in pregnant woman, assessing IgG specific to AlpN proteins in cord blood and maternal blood, and the safety profile in mother and infant up to 6 months post-delivery
Short Title:	Study of 4 regimens of Group B Streptococcus vaccine (GBS-NN/NN2) in pregnant women
Sponsor:	MinervaX Aps Ole Maaløes Vej 3 DK-2100 Copenhagen N. Denmark
Study Doctor:	Dr Paul Heath

INVITATION TO TAKE PART IN A RESEARCH STUDY

We are inviting you to take part in a research study. Before you decide, it is important for you to understand why the study is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. If anything is not clear or if you would like more information, please ask the study doctor.

WHY HAVE I BEEN INVITED TO TAKE PART?

You are being invited to take part in this study of a new vaccine because you are pregnant.

Group B Streptococcus (GBS) is a type of bacteria that many people carry in their bodies. A pregnant woman may transfer GBS to her baby in the womb or during delivery. GBS generally lives in the body of healthy adults without causing harm, but it can cause severe, potentially fatal infections in babies such as meningitis (infection of the lining covering the brain and spinal cord) and pneumonia (lung infection). GBS in pregnant women can also lead to poor growth of the baby in the womb, early delivery of the baby, miscarriage, or stillbirth.

A new vaccine (called GBS-NN/NN2) is being studied to prevent these problems caused by GBS. It is given as an intramuscular injection to women while they are pregnant.

Approximately 270 women will be asked to take part in the study in the UK, Denmark and South Africa.

WHY IS THIS STUDY BEING DONE?

This study is being done to see if this new GBS vaccine is safe for a pregnant woman and her unborn baby and if it produces an immune response in the woman that is transferred to the baby.

HOW LONG WILL IT TAKE?

You will start the study at about 20 weeks of pregnancy, and you and your baby will be followed through 6 months after you deliver.

DO I HAVE TO TAKE PART?

No. It is up to you to decide whether or not to take part in this study and you may have as long as you want to think about it although you will need to start the study at about 20 weeks of your pregnancy. Please review this Patient Information Sheet carefully. If you have any questions or concerns, please ask the study doctor.

If you decide to take part, you will be asked to sign the Consent Form (page 11). You will be able to withdraw from the study at any time, and you will not have to give a reason.

If you decide now not to take part in the study or later to withdraw from the study, this decision will not affect the care you get from your doctors.

WHAT VACCINE WILL I BE GIVEN?

GBS-NN/NN2 is made up of 4 protein pieces from GBS bacteria. It does not contain any bacteria and cannot give you or your baby a GBS infection. It is given by an injection in the upper arm, preferably in the non-dominant arm.

In this study, women will be assigned randomly (by chance, like flipping a coin) to 1 of 5 groups and receive 3 injections (each 4 weeks apart) as shown in the table below. You will not be able to choose which group you will be in.

Pregnancy Week	**Group 1**	**Group 2**	**Group 3**	**Group 4**	**Group 5**
	60 women	**60 women**	**60 women**	**60 women**	**30 women**
Week 22	Placebo	GBS-NN/NN2	GBS-NN/NN2	Placebo	Placebo
Week 26	GBS-NN/NN2	GBS-NN/NN2	Placebo	GBS-NN/NN2	Placebo
Week 30	GBS-NN/NN2	Placebo	GBS-NN/NN2	Placebo	Placebo

The placebo does not contain any active ingredient. A placebo is used so that the researchers can tell if the effects seen in the study are a result of the vaccine or not. Neither you nor the study doctor or staff will know which, if any, of the injections you receive are the active vaccine (GBS-NN/NN2) or the placebo.

WHAT IS ALREADY KNOWN ABOUT THIS VACCINE?

Two studies have been completed in non-pregnant women aged 18 to 40 years: one study of this vaccine in 60 women and one study in 240 women of an earlier version of the vaccine

with 2 (rather than 4) of the GBS proteins. In these studies, strong immune responses were seen when vaccinating with the same dose as being given in this study. The vaccine appeared safe and well tolerated in these studies. Side effects occurring at the vaccine injection site (such as pain, redness, bruising, swelling, or itching) were common but were generally mild to moderate and lasted only a short time. No other side effects were observed.

A study in pregnant women is currently being performed in South Africa. Safety information is available so far from 140 pregnant women who have been vaccinated and from 95 new-born babies. An independent safety review committee have reviewed the data from the first 125 women and did not identify any safety concerns.

WHAT OTHER CHOICES ARE THERE?

Whether or not you take part in this study, if you test positive for GBS or are otherwise at high risk of transmission of GBS to your baby, you will be offered antibiotics to prevent the problems caused by GBS as part of your routine health care during pregnancy. These antibiotics are given through a vein for at least 4 hours prior to labour, and they reduce some of the risks caused by GBS infection.

No GBS vaccine is currently available.

WHAT WILL HAPPEN TO ME AND MY BABY IF I TAKE PART?

After you have agreed to take part in the study, we will perform checks to make sure it is appropriate for you to enter the study; this will be at approximately 20 weeks of pregnancy. If it is appropriate for you to enter the study, you will return to the clinic at about 22 weeks of pregnancy and be randomly assigned to 1 of the 5 study groups (as described above). You will receive the first of 3 injections (each 4 weeks apart) on that day . You will return to the clinic 4 days after each injection and 4 weeks after the last injection. After you have your baby, you will return to the clinic for 3 visits with your baby over 6 months. The tables on page 5 show the timing of the visits and the medical procedures that will be performed at each visit for you (first table) and for your baby (second table).

The amount of blood that we will collect from you over the whole study will be approximately 215 mL (about 1/3 of a pint). For your baby, we will collect a sample from the umbilical cord (5 mL = about 1 teaspoon) at delivery and a blood sample either intravenously (2 mL) or by heel prick (½ mL) at 1 month and at 3 months of age.

If you agree, we will collect a small sample of breast milk (½ mL) in the first 2 days after you give birth and a slightly larger sample (2 mL) when your baby is 1 month and 3 months old. You will express the breast milk using a breast pump, similar to what you would use for expressing breast milk for your baby for later use.

We will give you access to a web-based diary to be downloaded to your mobile or computer and completed after each injection. The diary will send notifications or reminders by e-mail or text message using your e-mail address or mobile phone number. We will also give you a thermometer to measure your temperature and a ruler to measure any injection site reaction. Every day for the first 7 days after each injection, you will record your temperature, answer yes or no for a set of symptoms, record the size of any injection site reaction, grade other symptoms by a scale provided in the diary, and record any other symptoms you experience or medications you take. We will explain the diary and review the instructions with you so that you understand how to use it. If you have any concerns when you are completing it, you may also contact one of the research team on the telephone numbers that we will give you.

You will be given a questionnaire to complete about your baby's development at the 3 visits after you give birth.

While you are taking part in this study, you will have the following responsibilities:

- Return to the clinic for all required visits
- Follow the instructions of the study doctor and study staff
- Tell the study doctor about any side effects or health problems that you or your baby may experience during this study
- If you or your baby visit another doctor, tell that doctor that you are in a research study

Medical Procedures for You

Visit Number		1	2	3	4	5	6	7	8	9	10	11
Procedure	Screening	Week 22	4 days after	Week 26	4 days after	Week 30	4 days after	Week 34	Delivery	4 Weeks After Delivery	3 Months After Delivery	6 Months After Delivery
Vaccination		X		X		X						
Physical exam	X	X		X		X				X		X
Obstetric exam	X	X	X	X	X	X	X	X				
Injection site assessment		X	X	X	X	X	X	X				
Height & weight	X							X		X		X
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X
Blood sample	X	X	X	X	X	X	X	X	X			
Urine sample	X	X		X		X			X	X		
Breast milk sample									X	X	X	

Medical Procedures for Your Baby

Procedure	Delivery	4 Weeks After Delivery	3 Months After Delivery	6 Months After Delivery
Apgar score	X			
Physical examination	X	X	X	X
Head circumference	X	X	X	X
Length & weight	X	X	X	X
Vital signs	X	X	X	X
Blood sample	X	X	X	

WHAT ARE THE POTENTIAL BENEFITS OF TAKING PART IN THE STUDY?

You and your baby might not benefit directly from this study. Although non-pregnant women have had an immune response to this vaccine, we do not know if that same immune response will occur in pregnant women or if it will provide protection against GBS for you or your baby.

Your participation in this study will contribute to medical knowledge about the vaccine that may help other women and babies in the future.

WHAT ARE THE POTENTIAL DISADVANTAGES AND RISKS OF TAKING PART?

As happens with other injected vaccines, some women who have received this vaccine have had a reaction at the injection site (such as pain, redness, bruising, swelling, or itching). These reactions were generally mild to moderate and lasted only a short time.

You may experience “flu like symptoms” (such as tiredness, pain in your muscles, or a general feeling of discomfort) after vaccination. These symptoms may be related to your body’s immune system responding to the vaccine.

Because this vaccine is made up of proteins from GBS, you may have a fever after vaccination. No fevers have been reported after this vaccine so far.

All vaccines have a very rare risk of a severe allergic reaction. Symptoms of this kind of allergic reaction may include difficulty in breathing, dizziness, itching, swelling of the lips, tongue or throat, coughing, or rash. Allergic reactions happen soon after vaccination and may be life threatening. This is why we keep you in the clinic for at least 30 minutes after vaccination. We are prepared to give you immediate treatment for an allergic reaction. No one who has received the vaccine so far has had any sign of an allergic reaction.

Because this is an experimental vaccine that is still being studied, there may be other side effects or risks that we do not know about.

Many procedures for this study are procedures that happen during a regular visit to your doctor during pregnancy or after a baby is born. If you take part in this study, you and your baby will have more blood draws than you would in your routine care. There may be pain or bruising at the site where the blood is drawn. You may feel faint. An infection at the site of the blood draw is possible. but this is very rare.

Pumping breast milk might cause brief pain (10 or 15 seconds) at the beginning while the collagen fibres in your nipples stretch. You may have slight tenderness of the nipple.

WHAT IF SOMETHING GOES WRONG?

The Sponsor (MinervaX) has taken out an insurance policy that meets the requirements of the Association of the British Pharmaceutical Industry (ABPI). The insurance covers any damages to your or your baby’s health or well-being that can reasonably be attributed to your taking part in the study. Any payment would be without admission of legal liability.

If needed by the insurer, you may have to cooperate in the investigation of the injury (for example, provide extra information or have medical tests, which the insurer will pay for).

WHAT HAPPENS IF I DON’T WANT TO CARRY ON IN THE STUDY?

You can withdraw from the study at any time, and you do not have to give a reason. We may ask you why you wish to withdraw to make sure that you do not have any side effects and to give you

the best care that we can, but you do not have to give a reason and if you choose not to, your decision will be respected. This decision will not affect the care you get from your doctors. We will ask you to attend a final study visit to check the health of you and your baby.

CAN MY PARTICIPATION IN THIS STUDY BE ENDED EARLY?

Yes. The study doctor may take you out of the study if you have a side effect or other medical condition that makes further participation potentially harmful for you or your unborn baby.

The study may also be stopped before completion.

WILL I BE INFORMED IF THERE IS NEW INFORMATION ABOUT THE VACCINE?

Yes. If there is any new information that may affect your or your baby's health or well-being or your choice to stay in this study, we will inform you in a timely manner. If that happens, we may ask you to sign a new Consent Form to confirm you are happy to continue in the study.

WILL IT COST ME MONEY TO TAKE PART IN THIS RESEARCH?

No. You will not be charged for GBS-NN/NN2 or any study-specific tests or procedures.

WILL I BE PAID FOR TAKING PART IN THIS RESEARCH?

We will reimburse you for travel expenses you incur for attending any extra visits required for the study.

WHAT WILL HAPPEN TO THE SAMPLES MY BABY AND I PROVIDE IN THIS STUDY?

The collection of blood, urine and breast milk samples is an important part of this study. The samples will be sent to laboratories for use in checking the effects of GBS-NN/NN2. Some samples will be sent to laboratories in your country, and some will be sent to laboratories in Europe. The samples will not be labelled with information which can be used to identify you or your baby.

The blood and urine samples taken for safety tests will be destroyed after testing.

For the samples taken for testing immune response (blood and breast milk), any sample remaining after testing will be transferred to a biobank. The samples kept in the biobank will be used for future research involving infectious diseases and vaccines. No genetic tests will be done. The biobank will keep these samples under conditions that comply with national law, including data protection regulation. These samples may be analysed and stored for up to 14 years after we have analysed the data from this study and any left will then be destroyed. Future exploratory research is not mandatory, however you are encouraged to provide your consent to permit the storage of samples from you and your baby. If you have any concern about the provision of blood and breast milk samples for such purposes, please discuss this with us. You are under no obligation to provide breast milk to participate in this study.

WILL ANY OF MY OTHER HEALTH CARE PROVIDERS NEED TO SHARE MY HEALTH INFORMATION WITH THE RESEARCHERS OF THIS STUDY?

Yes. With your consent, your GP, obstetrician, and other doctors treating you or your baby will be told that you are taking part in this study along with details about the study vaccine and tests

performed. In addition, your GP will be asked to tell the study team if you or your baby have any unexpected illnesses or issues and may be asked for additional information if this occurs.

WILL MY TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL?

Yes. We will not tell anyone that you are participating in this study except for your GP, obstetrician and other doctors who may be treating you or your baby.

WHO WILL HAVE ACCESS TO MY PERSONAL DATA AND DATA CONCERNING MY HEALTH?

Your and your baby's personal data and data concerning your health will be kept confidential according to UKdata privacy laws. The Sponsor (MinervaX) and companies helping MinervaX conduct the study will have access to these data to ensure we are performing the study properly. Representatives of government regulatory authorities and members of ethics committees may also access these data for the same reason.

HOW WILL MY PERSONAL DATA AND DATA CONCERNING MY HEALTH BE USED AND PROCESSED?

We will provide the data we collect about you and your baby in this study to the Sponsor (MinervaX) or to another company helping MinervaX run the study for analysis and to health authorities, e.g., age, ethnicity, and data concerning health.

The Sponsor (MinervaX) controls the data for this study and is responsible for their processing. Every person who has access to your data is subject to national data protection laws and to the General Data Protection Regulation (GDPR).

The data we collect may be used to support other research in the future and may be shared anonymously with other researchers. Your and your baby's identities will not appear on any of the study data collected and kept by the Sponsor for their analyses. Your data will be connected only to a unique ID number, and the link from this ID number to your and your baby's identities will be known to only your study doctor and his/her team.

To interpret the results of this study, the data collected will be entered into a computer and may be transferred to third parties in other countries for processing and storage. This means that your data may be transferred to countries which do not have the same level of data protection as the UK. All parties have in place the appropriate safeguards to ensure your information remains confidential. The data protection laws in these countries vary; however, everyone involved in this process has a duty to protect your identity and use the data for legitimate healthcare purposes only. If the data are disclosed to third parties, all appropriate measures will be taken to protect the data.

Your and your baby's personal data and data concerning your health cannot be used without your consent. You will not be able to participate in the study if you do not provide this consent.

If you withdraw consent to taking part in the study, your consent to analysis of your and your baby's data remains in place. If you withdraw from the study, no new information about you or your baby will be collected.

Under data protection laws, you have a right to access, correct, update, restrict, object to the processing of, or delete the personal data and data concerning your health that is processed. You can also ask for a copy of the data in a structured, commonly used, and machine-readable format. We may ask to verify your identity before the data are provided. We will respond to your request in accordance with data privacy laws and regulations on clinical trials. If needed, you have the right to correct your personal data and data concerning your health but not study data, for which your rights

may be limited to ensure the scientific integrity of the study and the safety of other people in the study.

If you have any questions or concerns about the processing of your personal data or data concerning your health, ask your study doctor. You also have the right to contact or make complaint to the Sponsor (MinervaX) Data Protection Officer or to your local Data Protection Authority about the processing of your or your baby's personal data and data concerning your or your baby's health:

Sponsor Data Protection Officer:
Per Fischer
MinervaX ApS
Ole Maaløes Vej 3
DK-2200 Copenhagen N
Denmark
E-mail: pbf@minervax.com

Data Protection Authority:
The Information Commissioner's office
Water lane, Wycliffe House, Wilmslow, Cheshire SK9 5AF
E-mail: casework@ico.org.uk
Tel: 01625 545 700

WHAT WILL HAPPEN TO THE RESULTS OF THIS STUDY?

No matter what the outcome of this study is, the results will be published on the internet on the European Union Clinical Trials Register (www.clinicaltrialsregister.eu/) or on the U.S. National Library of Medicine website (www.ClinicalTrials.gov). They may also be published in an article in a medical journal or presented at a scientific meeting. In any case, the data will be grouped, and no data which can be used to identify you or your baby will be made public.

WHO IS ORGANISING AND PAYING FOR THIS STUDY?

The Sponsor (MinervaX) is organising and paying for this study. The Sponsor is paying the study site for performing this study.

WHO HAS REVIEWED THE STUDY?

A Research Ethics Committee has reviewed this study. A Research Ethics Committee is a group of scientific and non-scientific individuals independent of the Sponsor and the study site who perform the initial and ongoing ethical review of the study with the participant's rights, safety and well-being in mind. If you have questions about your rights as a research study participant, you may contact NHS Patient Advice and Liaison Service (PALS) on 0208 725 3887.

WHO DO I CONTACT IF I WOULD LIKE FURTHER INFORMATION ABOUT THE STUDY?

Research Midwives at St George's University Hospitals NHS Foundation Trust
Phone number: 0208 725 3887
Email: MVX0004trial@sgul.ac.uk

WHO DO I CONTACT IN THE EVENT OF AN EMERGENCY?

In the case of a medical emergency you can contact the on-call doctor on 07920 158212, please have your participant number to hand when calling.

WHO DO I CONTACT IF I WISH TO MAKE A COMPLAINT?

Any complaint you have will be addressed. Please speak to a member of the research team during your study visits or by phone using the contact numbers provided.

You may also contact the NHS Patient Advice and Liaison Service (PALS) which offers confidential support and advice. It is independent from the study team and may help to resolve problems. Your local PALS is:

Phone Number: 020 8725 2453
Email address: pals@stgeorges.nhs.uk

THANK YOU FOR READING THIS INFORMATION SHEET

You will receive a copy of it and of your signed Consent Form to keep.

Consent Form

EudraCT number: **IRAS ID:**	2021-003214-40 301103
Participant Screening ID:	
Study Number:	MVX0004
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Short Title:	Study of 4 regimens of Group B Streptococcus vaccine (GBS-NN/NN2) in pregnant women
Sponsor:	MinervaX Aps Ole Maaløes Vej 3 DK-2100 Copenhagen N. Denmark
Study Doctor:	**Professor Paul Heath**

Please initial each box.

1. I confirm that I have read the information sheet dated..... (version.....) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that relevant sections of my and my baby's medical notes and data collected during the study, may be looked at by individuals from MinervaX, from regulatory authorities or from St Georges University Hospital Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐
4. I agree that personal data about me and my baby may be sent to countries outside of the UK and EU. ☐

5. I agree to my GP and obstetrician being informed of my participation in the study. I agree to my GP and obstetrician being involved in the study, including any necessary exchange of information about me between my GP and the research team. ☐

6. I understand that the information held and maintained by St Georges University Hospital Trust, may be used to help contact me or provide information about my health status. ☐

7. I agree to the collection of samples of colostrum and breastmilk (OPTIONAL) ☐

8. I agree that my samples (breast milk, blood) and my baby's samples (blood) may be stored for up to 14 years after data from this study have been analysed and they will then be destroyed. (OPTIONAL) ☐

9. I agree to take part in the above study ☐

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Name of Participant	Date	Signature
Name of Person Seeking Consent	Date	Signature

Copies: Original in site file, copy to participant, copy to medical notes