Informed Consent Form

Title: A Phase 3 Trial to Evaluate the Safety, Immunogenicity, and Non-Interference with Concomitant Routine Vaccines, of a Meningococcal Serogroup ACYWX Conjugate Vaccine (NmCV-5) in Comparison with MenACWY-TT Conjugate Vaccine in Healthy Malian Infants

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INFORMED CONSENT FORM
AND
AUTHORIZATION TO DISCLOSE HEALTH INFORMATION

Sponsor / Study Title:	**A Phase 3 Trial to Evaluate the Safety, Immunogenicity, and Non-Interference with Concomitant Routine Vaccines, of a Meningococcal Serogroup ACYWX Conjugate Vaccine (NmCV-5) in Comparison with MenACWY-TT Conjugate Vaccine in Healthy Malian Infants**
Protocol Number:	**20-0024**
Site Principal Investigator: (Study Doctor)	Samba Sow, MD [redacted] ; [redacted]
Co-Investigators:	Wilbur Chen, MD [redacted] Karen Kotloff, MD [redacted] Milagritos Tapia-Sow, MD [redacted] Fadima Cheick Haidara, MD [redacted] Fatoumata Diallo, MD [redacted] Youssouf Traoré, MD [redacted]
Telephone:	+223 20236031
Address:	Centre pour le Développement des Vaccins, Mali (CVD-Mali) Bamako, Mali, Ex-Institut Marchoux Ministère de la Santé et du Dévéloppement Social Bamako, Mali, West Africa

Concise Summary

The information in this form will help you decide whether to provide permission for your infant to be in the meningitis vaccine research study. Being in the study is voluntary. You can choose for your infant not to be in the study, and he/she will receive their standard vaccines for meningitis (MenAfrivac), yellow fever and measles instead of the study vaccines. You may decide not to participate, or you may decide that you no longer want your infant to be in the study. Please contact the study staff if you decide today or in the future to stop taking part in this study. Your decision will not result in loss of medical care for your infant. Please let the study team know if you have any questions.

This study is funded by the National Institute of Health (NIH) and is being conducted by the University of Maryland (UMB) and the Centre pour le Developpement des Vaccins – Mali.

This study is to learn more about the safety and the immune response to an experimental vaccine to protect against the germ called meningococcus. This germ can cause infection of the fluid around the brain. Infants in Mali are presently vaccinated against one type of this germ, type A, at 9 months of age. There is another vaccine, MenACYW-TT, that protects against 4 types. The experimental vaccine, NmCV-5 we are studying may protect against 5 types. In this first visit, we will see if your infant is able to participate in this study. If your infant is eligible then he/she will be assigned to one of 2 groups. If your infant is in Group 1, he/she will receive NmCV-5 or MenACYW-TT today. If your infant is in group 2, then he/she will receive it at 15 months of age. Participants will have 5 to 6 clinic visits during the study and will have blood collected 4 times over the 2 years after receiving the meningitis vaccine. There are no major safety concerns, however there are known safety risks listed below in the main consent document. There have been no safety concerns with the experimental vaccine but it's possible that there are effects that are unknown.

If you would like to learn more about this study, please continue to read or listen to this document.

What is the purpose for the vaccine study?

The purpose of this study is to learn about how a new experimental meningitis vaccine, NmCV-5 (made by Serum Institute of India Pvt. Ltd.), may protect against the bacteria, meningococcus, that causes meningitis. Vaccines teach your body how to fight the bacteria that causes meningitis. Infants in Mali are presently vaccinated against one type of this germ, type A, at 9 months of age. Another meningitis vaccine currently approved in Mali (MenACYW-TT, made by Pfizer) protects against four types of this germ. NmCV-5 may protect against 5 types. The study will compare the two vaccines, NmCV-5 and MenACYW-TT, to see if the new vaccine may protect as well as the approved one. We will also determine if NmCV-5 has an effect on the other vaccines that your infant receives as part of their regular vaccines.

Your infant will receive their vaccines for measles, yellow fever and meningitis as part of their participation in this study. The measles vaccine will also contain the rubella vaccine. Rubella is an infection that can occur to infants before they are born and can cause problems in the eyes, brain and heart. The vaccine can help to decrease the number of infections that a pregnant women may be exposed to. The World Health Organization recommends vaccination against rubella. All infants who participate in this study will receive rubella vaccine.

The study will enroll up to 1320 infants around 9 months of age. The infants will be assigned to one of two groups, Group 1 and Group 2. Assignment to these groups will be by chance (like taking a grain of rice from a bag). You and your study doctor will not know which meningitis vaccine your infant will receive. Infants who are in Group 1 will receive one of the meningitis vaccines (NmCV-5 or MenACYW-TT) at 9 months of age. There will be 400 infants who receive NmCV-5 and 200 infants who will receive MenACYW-TT at 9 months of age. Infants in Group 2 will receive the meningitis vaccine at 15 months of age. There will be 400 infants who receive NmCV-5 and 200 infants who will receive MenACYW-TT at 15 months of age.

In addition, at 9 months of age, all participants will receive the routine yellow fever vaccine and the measles rubella vaccine. At 15 months of age, all infants will receive a second measles rubella vaccine, this is an extra vaccine that is not part of the routine in Mali.

Procedures

If you agree for your infant to take part in this study, your infant will have 5 or 6 clinic visits over a period of up to 2.5 years.

If your infant is eligible and you agree to have your infant participate in the study, your infant will have a few things done today and at future visits.

Screening Visit

If you consent for your infant to be screened for the vaccine study, your infant will have a visit to check if he/she can be enrolled in the study. **The visit will include a physical exam including pulse, respiratory rate, temperature, height and weight. We will also ask about your infant's medical history including medications, vaccinations, and demographic information.**

Enrollment/Visit 1

If your infant was assigned to Group 1, then at 9 months of age, the following will occur:

- The study staff will collect blood (5 ml) from your infant and also test your infant's blood for malaria.
- The study staff will give your infant the yellow fever, measles-rubella, and the study meningitis vaccine. Your infant will be observed for 30 minutes in the clinic after vaccination.
- A picture of you and your infant will be taken to make an identification card for you as a participant of the study.
- A field worker will come to your home for the next 4 to 7 days to check on your infant.
- A field worker will also occasionally come to your home to remind you of the upcoming study visit.
- Your infant should not receive any other meningitis vaccine while he/she is participating in this study.

If your infant was assigned to Group 2 then he/she will receive the meningitis vaccine at 15 months of age and at 9 months of age the following will occur:

- The study staff will give your infant the yellow fever and measles-rubella vaccines.
- A picture of you and your infant will be taken to make an identification card for you as a participant of the study.
- A field worker will come to your home occasionally to remind you of the upcoming study visit.
- You will be asked to return in 6 months, when your infant is 15 months old, for a clinic visit. At that visit:
    - Your infant will have a physical exam including height and weight.
    - Review your infant's medical history including medications and vaccinations.
    - The study staff will collect blood (5 ml) from your infant and also test your

infant's blood for malaria.
    - The study meningitis vaccine and a second measles-rubella vaccine will be given to your infant. Your infant will be observed for 30 minutes in the clinic after vaccination.
    - A field worker will come to your home for the next 4 to 7 days to check on your infant.
    - Your infant should not receive any other meningitis vaccine until he/she returns to the clinic for vaccination and while he/she is part of this study.
- If you return in 6 months when your infant is 15 months of age and your infant is not eligible to continue in the study or we have already enrolled the maximum number of participants, your infant will be given the measles-rubella vaccine and an approved meningitis vaccine instead of the experimental one being used in this study. No further visits will occur for you and your infant.

Home Visit after your infant receives the study meningitis vaccine

A field worker will visit you and your infant at your home each day for 4 to 7 days after the meningitis vaccination to collect information about any reaction your infant may have after vaccination. If a bad reaction occurs or continues past the fourth day, the field worker or a study doctor may visit your home to check on your infant until the reaction gets better. You may also be asked to bring your infant back to the study clinic at other times if your infant is sick or needs care. The study doctor will determine what activities will be needed after going over any symptoms that your infant is having.

The field worker will remind you of any upcoming study visits and answer any questions that you have.

Clinic Visit 2 – Day 8 after meningitis vaccination

- Reviewing your infant's recent medical history
- Reviewing medications and vaccinations taken since the last visit
- Reviewing your home visit worksheets
- A physical exam including pulse, respiratory rate, temperature
- A field worker will also occasionally come to your home to remind you of the upcoming study visit.

Then you and your infant will return for the following visits: Clinic Visit 3 which will occur 28 days after meningitis vaccination, Clinic Visit 4 which will occur 6 months after meningitis vaccination and Clinic Visit 5 which will occur 2 years after meningitis vaccination. At each of these visits, the following will occur:

- If your infant was in Group 1 and was randomized to receive the meningitis vaccine at 9 months of age, your infant will receive another measles-rubella vaccine at Clinic Visit 4, at 15 months of age
- Reviewing your infant's recent medical history
- Reviewing medications and vaccinations taken since the last visit
- A physical exam for your infant including pulse, respiratory rate, temperature
- Collection of blood samples (10 ml or 2 teaspoons at Clinic Visit 3 and 5ml or 1 teaspoon

at Clinic Visits 4 and 5)
- A field worker will also occasionally come to your home to remind you of the upcoming study visit.

Your infant's medical record will be updated to note your infant received the meningitis, measles-rubella and yellow fever vaccines.

Laboratory Testing of Blood Specimens

The blood samples collected from your infant will be tested to look at your infant's immune response to the study vaccine. Genetic testing will not be done on the samples.

The results of these tests are useful only for research purposes. **Your infant's individual results will not be available to you or your infant's regular doctor and will not be placed in your medical record.**

Blood samples for these research tests may be sent to a central storage facility in Mali or the United States or sent directly to the research testing laboratories in England and the United States. These blood samples will not be labeled with your infant's name or initials, or any other information that could easily identify your infant. These blood samples will be labelled only with a code to help protect your confidentiality. Staff at the central storage facility and research testing laboratories will not know your identity, or even the study identifier you were assigned. However, the study staff will keep a list in a secure area with your name, contact information and the code that can link the blood samples to you, if needed.

What happens to the blood specimens after testing?

After all tests required for this study are done, we will save your infant's leftover blood samples for possible future research instead of throwing them away. We may share these samples and the information we collect about your infant with the study researchers or other researchers, but we will not share your name or contact information with other researchers. These samples could be tested in the future to look at your infant's response to other vaccines or germs. There is no time limit on how long these samples will be stored. Before any testing is done on stored samples, the tests must be reviewed and approved by the Sponsors and the local IRB/Ethics Committee of the researcher requesting the specimens.

You do not have to agree to let us to save your infant's blood samples for future research. If you choose not to let us to save these samples for future research, they will be destroyed when the study is over. Your infant's medical care at this clinic will not be affected if you do not agree to save your infant's samples for future research.

If you decide at any time that you do not want the blood samples stored for future research, you must contact the study staff who will then notify the laboratory/specimen archive so they may be destroyed.

Potential Risks and Discomforts

There may be some risks to being in this study. Your infant may experience one or more of the risks or side effects explained below. You should discuss these with the study doctor or study staff. Many side effects go away shortly if treated, but in some cases, side effects can be serious, long lasting, or permanent.

Infants may experience side effects after vaccination with the NmCV-5 vaccine. This is an experimental meningococcal vaccine which is not locally approved. Side effects may include:

- Pain, redness, swelling, or bruising at injection site
- Fever, irritability, or fatigue (feeling tired or drowsy)
- Loss of appetite, nausea, or vomiting

After vaccination with the MenACYW-TT, Measles-Rubella, and Yellow Fever vaccines, a person might experience:

- Pain, dizziness, aching, itching, or a general feeling of illness
- Redness, swelling, or bruising at injection site
- Fever, chills, headache, loss of appetite, irritability, or fatigue (feeling tired or drowsy)
- Diarrhea, nausea, or vomiting
- Lump at injection site, skin rash, or limb swelling

After receiving any vaccine or medication, an infant may rarely experience an immediate allergic reaction called anaphylaxis (also known as allergic shock). This type of reaction may include symptoms such as skin rash (hives), sweating, swelling around the mouth, throat, and eyes, and difficulty breathing.
If a participant has a severe allergic reaction, CVD-Mali personnel will be present to provide any immediate care that is required.

<u>Risk with blood collection</u>
Having your blood taken can cause pain, a bruise or an infection. To reduce the risk of these side effects, this procedure is performed by qualified personnel who will wipe the area clean with alcohol and will only use clean equipment.

The information that is collected for the study will have identifiers removed, such as name, address, and identification numbers.

There is a risk of loss of confidentiality of your information. You will read more about the protection of your information later in this consent form.

There may be risks and discomforts we do not know about right now. It is possible that we will learn new information on the risks and discomforts of being in this study. If this happens, the study doctor will tell you about them. Then you can decide if you want to continue to be in this study or not.

The WHO recommends vaccination against the meningococcus germ by 18 months of age. Usually, infants in Mali are vaccinated at 9 months of age with MenAfriVac but infants in Group 2 will receive the MenACYW-TT or NmCV-5 at 15 months of age. Since MenAfriVac vaccination became routine several years ago, infections with meningococcus type A are rare and therefore there is little risk with delaying vaccination against meningococcus.

Benefits of Being in The Study

All study participants will be given the opportunity to receive two doses of a measles-rubella-containing vaccine to improve protection against measles and will also benefit the infant through protection from rubella. Instead of the meningitis vaccine that protects against one kind of meningitis-causing bacteria (MenAfriVac), participants will receive either NmCV-5 vaccine or MenACWY-TT vaccine. There is the possible benefit of being protected against more types of meningitis bacteria which are known to cause diseases. The health of all study participants will be followed carefully with scheduled follow-up visits with the research clinic and this close follow-up may also provide a benefit to the infant through improved access to medical care. We will provide you with an identification card that indicates that your infant is in this study.

Alternatives to Participating in This Study

You can choose for your infant to not participate in this study. If you wish for your infant to receive the standard vaccine for meningitis (MenAfrivac), yellow fever and measles instead of the study vaccines or do not want to take part in research, then you can choose to not enroll your infant in this study.

Early Withdrawal from the Study and Follow-Up

Your infant's participation in this study is completely voluntary. You can decide to stop your infant's participation at any time. There is no penalty or loss of any benefits that he/she normally have if you choose not to enroll him/her, stop, or change your mind. Always tell the study staff if you wish to stop. They will discuss any concerns about your infant safety, and whether he/she needs any follow up or medical care.

Also, the study doctor may take you out of the study if this research is not in your infant's best interest. You could be removed from the study for any of the following reasons:

- If your infant is randomized to receive the study meningitis vaccine at 15 months of age and your infant is not eligible to continue in the study at that visit or we have already included the maximum number of children, your infant will be given the measles-rubella vaccine and an approved meningitis vaccine instead of the experimental one being used in this study. No further visits will occur for you and your infant.
- Reasons related to you (for example, if you move to another city or if you do not agree for your infant to receive the study vaccination)
- Reasons related to your infant's health (for example, if your infant has a serious reaction to the study vaccine)
- Because the study is stopped
- Any other reason

If you decide to stop or the study doctor withdraws your infant, we may ask you to come for a

final visit. This visit may include activities listed in the general study visits.

We will stop collecting your infant information and specimens for research when you withdraw your consent for the research or are withdrawn by the study doctor. However, any information and specimens collected prior to withdrawal may continue to be used for this study.

The Institutional Review Board (IRB), CVD-Mali ethics committee**,** other regulatory agencies, or the sponsors (NIH, UMB) who oversee the conduct of this study can stop the study at any time for safety concerns or other issues.

Compensation for Participation

You will receive the following compensation. On the vaccination visit and each clinic visit, you will receive 5 kg of sugar and reimbursement for transportation to the health center (1000fcfa).

Cost to the Participant

You will not have to pay to receive the study vaccines. There are no costs for the study visits, tests or procedures performed as part of this study.

Research-Related Injury

If your infant becomes sick or is injured while in the study, you should notify the study doctor as soon as possible. The study team will provide the appropriate care or refer your infant to another doctor for care. You should inform the healthcare professional treating you that you are participating in this study. In the case of an emergency, please go to the nearest health facility and please inform us of the illness.

The study site will ensure that your infant receives care for any illness or injury resulting from your participation in this study without any cost to you. Long term care will not be provided. The NIH will not provide any long-term medical care or any other payment for research related injuries.

Confidentiality

You and your infant's personal information will be maintained in locked file cabinets or on password protected computer files. Only people who are involved in this study will be allowed access.

To help protect your privacy, NIAID has a Certificate of Confidentiality for the study. Study staff cannot provide to any person not connected with the research your name, or any materials that contain identifiable, sensitive information about you, unless permitted by a law.

What information may be used and given to others?

If you choose to have your infant in this study, the study doctor and study staff will get personal information about him/her. This will include information that might identify your infant, such as name and address.

Information about your infant's reaction to the vaccines collected during the study visits and his/her specimen results will be analyzed by an NIH contractor in the United States. Personal information will not be provided for the study analysis.

Identifiers will be removed from the information or biospecimens. After removal, the information or biospecimens could be used for future research studies or provided to another investigator for future research studies without your additional informed consent.

Why will this information be used and/or given to others?

The sponsor (NIH) will analyze the study data including your infant's information. The NIH, UMB or their contractors may visit the clinic. They will review how the study is done. They will review your infant's information for this purpose. The information may be given to other governmental and regulatory agencies to support the review and monitoring of the study and regulatory requirements.

By signing and dating this consent form you are giving permission for representatives of the NIH, UMB, CVD-Mali, regulatory authorities, and study team to inspect sections of your medical and research records related to this study.

The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

Your study records will be kept at the study site for at least 2 years after licensing (if granted) of the investigational vaccine or for at least 2 years after the end of research with this study vaccine.

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Whom To Contact About This Study

During the study, if your infant experiences any medical problems, or you have questions or concerns about the study, please contact the study doctor. If your infant needs emergency care or is hospitalized, tell the treating doctor that you are participating in this research study.
If you have questions about the study call Dr Fatoumata Diallo at [redacted] Dr Youssouf Traoré at [redacted] Dr Fadima Cheick Haidara at [redacted] or Prof Samba Sow at [redacted]

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. To learn more about the ethical approval of this study or your rights as a research subject, you can contact the Ethics Committee at USTTB, Faculty of Medicine, Pharmacy and Odonto-Stomatology (FMPOS) at +223 2022 5277 or Prof. Mamadou

Marouf Keita at +223 6672 2022 (chairman) or Pr Mahamadou Diakité at +223 6623 1191 (permanent secretary).

CONSENT

Information about this study has been explained to me. I have read this consent form or had it read to me. My questions were answered by the study staff.

Check the applicable box (Yes or No) to document your decision:

My infant's blood samples may be kept for use in future research (please check one)?

☐ Yes ☐ No

I agree for my infant to participate in this study.

By signing this consent form, I have not given up any of my legal rights. I will get a copy of this consent to keep

_____
Printed Name of Participant

_____
Printed Name of Participant's Parent/Guardian

_____ _____
Signature/Thumbprint of Participant's Parent/Guardian Date

I attest that the parent of participant named above had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to be in this study.

_____
Printed Name of Person Explaining Consent

_____ _____
Signature of Person Explaining Consent Date

_____ _____
Signature of Witness Date

_____
Printed Name of Witness