Protocol title

Therapeutic efficacy surveillance of malaria treatment and drug resistance monitoring in Gia Lai and Phu Yen provinces of Central Vietnam

Protocol short title

Surveillance of antimalarial drug efficacy and drug resistance in Central Vietnam

Protocol No. VDCP01

Principal Investigator: Dr. Huynh Hong Quang

24 June 2021 - Version No. 2

Annex C

PARTICIPANT INFORMATION SHEET AND CONSENT FORM FOR ADULTS

Protocol title: Therapeutic efficacy surveillance of malaria treatment and drug resistance monitoring in Gia Lai and Phu Yen provinces of Central Vietnam

Principal Investigator: Dr. Huynh Hong Quang, IMPE, Quy Nhon, Vietnam.

Purpose of the study

Malaria is a deadly disease caused by a parasite transmitted by mosquitoes that can cause malaria symptoms such as fever, chills, headache, tiredness and nausea, and death without effective treatment. The Vietnam Ministry of Health (MoH)is aiming to eliminate malaria from the country by 2030.

You have been invited to take part in this malaria study because you have a malaria infection and you live in either Krong Padistrict, Gai Lai province or Song Hinh district, Phu Yen province. We plan to recruit up to 180 people with malaria infections into this research study from the two provinces between May 2021 and May 2022. To achieve this aim, information is required on how well the treatment drugs are working to cure people of malaria infections and whether the malaria parasite is becoming resistant to the drugs. We invite people from your commune who have malaria to participate in this study to determine how well does the drug treatment work to remove the malaria from their body.

The study is being carried out by the Vietnam MoH Institute of Malariology, Parasitology and Entomology (IMPE-QN, Quy Nhon) in collaboration with the Vietnam People's Army Military Institute of Preventive Medicine (MIPM, Hanoi), and the Australian Defence Force Malaria and Infectious Disease Institute (ADFMIDI, Brisbane, Australia).

Please take time to read this information carefully, ask any questions that you may have, so that you understand what will happen to you during the study. Then consider if you want to take part. If you need more time to read this information, tell the study team from IMPE-QN/MIPM. You will be given a copy of this form to take home with you.

Your taking part in this study is completely voluntary. You can decide not to be in the study without any reason. If you do not want to be in the study, you will still receive free treatment for your malaria infection. If you agree to be in the study, you may withdraw at any time by informing the IMPE-QN/MIPM doctor,without loss of benefits to which you have a right to receive.

Your involvement in the study

If on screening you have symptoms of malaria and found to be infected with malaria parasites in your finger prick blood sample (a few drops), you will be invited to participate in this study. After agreeing to be in the study, you will be asked to answer some questions about yourself, where you live and have travelled recently, your protection against malaria infections, and a physical examination to determine your general health.

If you are infected with *P. falciparum* malaria*,* you will be treated by the IMPE-QN/MIPM doctor with a 3-day course of pyronaridine-artesunate to treat malaria in your blood and a single dose of primaquine to stop malaria transmission. These drugs are recommended by the Vietnam MoH. You will also be invited to provide another finger prick blood sample to re-

check for malaria at about 12 hourly intervals on days 1, 2, and 3, and then once on days 7, 14, 21, 28, 35 and 42 after starting treatment to determine how well the treatment has gone.

Some people may be infected with another malaria infection, *P. vivax* that will require treatment with chloroquine plus primaquine to treat the infection in both their blood and liver. If you are infected with this malaria, you will be treated with a 3-day course of chloroquine plus primaquine daily for 14 days. The IMPE-QN/MIPM study doctor will observe you taking chloroquine plus primaquine daily for the first 3-days and for the next 11 days you will take primaquine daily without supervision. To assess how well you take primaquine daily for the 11 days without supervision by the IMPE-QN/MIPM study team, we will ask you to complete an eight item questionnaire on days 7 and 14 after starting primaquine dosing.

What your blood will be used for in this study

Your finger prick blood sample will be used to produce blood films to determine the presence and number of parasites in your blood, and the species of malaria by microscopy. We will test your blood sample collected from your arm or finger with a new device that measures malaria pigment produced by the parasite called hemozoin to determine whether you are infected with either drug sensitive or resistant parasites. If malaria parasites are present you will be treated by IMPE-QN/MIPM doctor in accordance with the Vietnam MoH guidelines. Your blood will be used to detect if drug resistant parasites are present and for the analysis of the genetic background of the malaria parasites. We will also measure your blood antimalarial drug concentrations to ensure that you had good drug exposure.

You will be invited to provide a blood sample (4 mL) from your arm to determine how well the parasites in your body are killed by standard antimalarial drugs grown in special containers in the laboratory. This will tell us the level of parasite resistance in your community. Also, with another 5 mL of your blood we will use a powerful molecular assay called whole genome sequencing that can potentially detect new resistant parasites.

We will keep your blood samples that cannot identify you for up to 15 years from the time of blood collection. If during this time new molecular assays or devices for malaria diagnosis and for studying drug resistance are developed, we may re-test your blood samples with these molecular assays or devices. Your blood will not be used for any other purpose.

If, however, you experience symptoms of malaria during the follow up period of 42 days, we will invite you to provide us with another finger prick blood sample, so we can check your blood for malaria and if parasites are present the IMPE-QN/MIPM doctor will retreat you with a different drug recommended by the Vietnam MoH. With your blood sample, we will measure your blood drug levels to see whether you had enough drug in your body to kill the malaria parasite. Also, with your blood we may be able to determine whether you were infected with drug resistant malaria. All information from you will help us identify high risk areas of malaria in your community.

Risks and discomforts

1) Failure of treatment. There is a small chance that the treatment drug might fail to cure your malaria, leaving you in danger of severe disease. For this reason we will check your blood frequently after treatment to make sure that your malaria has been cured. If we find that the drug does not clear your malaria infection or the malaria comes back we will retreat you with another drug combination recommended by the Vietnam MoH.

2) Side effects from the drugs. As with any drug, a small number of people may have side

effects that cannot be predicted. The most common side effects of the drugs that you may receive in this study are dizziness, muscle pains, fever, vomiting, headache, chills, diarrhea, skin rash, abdominal pain, fatigue, and loss of appetite. These side effects are usually mild, should not affect your daily activities and generally go away quickly once treatment is finished. You must always come quickly to see the IMPE-QN/MIPM doctor if you have any illness or injury. The IMPE-QN/MIPM doctor is available 24 hours a day, seven days a week to see you during the study. If you have a medical problem due to your involvement in the study, we will help you get medical care for it.

3) Risks and discomforts from blood sampling. Taking blood from the arm or finger causes a brief sharp pain. The well trained and experienced IMPE-QN/MIPM doctor or technician will collect the blood from your arm or finger. There is a very low risk of infection and/or bruising where the needle is stuck in your arm or finger. If you become dizzy with pain or at the sight of blood, please tell the doctor or technician to lie you down and they will look after you.

4) Risk of early withdrawal before completing treatment and/or before the 42 day follow-up period is completed. You are free to withdraw from the study at any time. You may also be withdrawn by the Principal Investigator or IMPE-QN/MIPM doctor. Possible reasons for withdrawal could include a serious side effect or failure by yourself to carry out the requirements of the study. If you select to withdraw before completing treatment you run the serious risk of developing life threatening malaria. So it is very important that you complete your treatment. If you withdraw before the Day42 of follow-up is completed you run the risk that the malaria may come back. So it is important that the follow-up is completed to make sure that you are cured.

Questionnaire

You will be asked to answer questions related to the study such as your movement during the last two weeks and did you use malaria prevention methods.

Benefits

If we find malaria parasites in your blood by looking down a microscope you will be treated at the commune health station in accordance with the Vietnam MoH antimalarial drug treatment guidelines. The main benefits to you for participating in the study is the IMPE-QN/MIPM doctor will closely monitor your health and wellbeing. By following you for 42 days after starting drug treatment the doctor will be able to determine how well the drug has performed in curing you of malaria. If, however, you are unlucky to be infected with a malaria parasite that the drug does not cure your infection, the IMPE-QN/MIPM doctor will re-treat you quickly with another drug that is expected to be effective in removing the parasite from your body.

Protection of personal details

The Principal Investigator (Dr. Huynh Hong Quang) and the IMPE-QN/MIPM doctor will make sure your personal details are kept private during and after the study. Your name will not appear on your blood films or blood sample vials. Only the IMPE/MIPM study team will know who are in the study. The consent form and information obtained from you will be stored at the field site (i.e. communal health station) for up to six months and at IMPE Quy Nhon for 15 years in a locked filing cabinet/drawer. After 15 years all your study documents will be destroyed by incineration. We will report the findings from this study, but your name will not appear on any reports or presentations. We will also seek your approval to check the Vietnam

MoH records of your malaria history 12 months before and 12months after your entry into this study.

Compensation

You will receive no money or other gifts for being in the study. However, if you live far away from the health station that the study team is unable to pick you up, we will give you enough money to pay for your transportation to and from the health station to your home. Also, we will cover any additional medical costs that may be due to you for being in the study. You will be provided with water and food for drug administration at the health station and you will receive food for your weekly return to the health station during the follow-up period.

Questions

If you have any questions, complaints or worries about being in the study, you can call or visit the IMPE/MIPM study team to discuss your concerns with them. Also, you may contact Dr. Huynh Hong Quang (Tel: 0905103496) at IMPE Quy Nhon to have your questions or worries answered. If you have questions about the study and your rights as a study participant, you may contact the Institutional Review Board at the Vietnam MoH (Tel. +84-243-384-6688) that approved the study. If you do not have phone access, the IMPE-QN/MIPM study team can help you contact the Institutional Review Board.

STATEMENT OF CONSENT FOR ADULTS (AGE ≥18 YEARS OLD)

Protocol title: Therapeutic efficacy surveillance of malaria treatment and drug resistance monitoring in Gia Lai and Phu Yen provinces of Central Vietnam

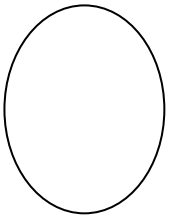
Principal Investigator: Dr. Huynh Hong Quang, IMPE Quy Nhon, Vietnam.

Your signature on this Consent Form shows that you have had this research study explained to you and you have had a chance to ask questions. You agree to voluntarily be in this study. Malaria patients like yourself will be recruited into the study between May 2021 and May 2022.

The information collected from you will be kept private and used for the purpose of this study. Your study results will be made available to you freely upon your request and any published reports of this study will preserve your personal details. You understand that you are not bound to be in this study and that you are free to withdraw from the study at any time with no loss of benefits or rights to your future health care.

You provide approval for your blood to be re-tested within the next 15 years with new molecular assays or devices and that you give permission for the Principal Investigator to check the Vietnam MoH records of your malaria history 12 months before and 12 months after your entry into the study.

You will be given a copy of the signed information/consent sheet for your records. Should you have any worries about how the study is being carried out, please come forward and contact the Principal Investigator or IMPE-QN/MIPM doctor in person. After you fully understand what will take place with you being in the study, you will need to sign your name or provide a thumb print on the consent form.

Participant's Name (Print)		___ ___ / ___ ___ / _____ DD MM YYYY
Participant's Signature	(THUMB PRINT)	

Witness signature: If the participant is illiterate, a literate witness must sign. The witness can be a friend, relative or Commune leader/representative. If possible, this person should be selected by you and should have no connection with the IMPE-QN/MIPM study team.

I have witnessed the accurate reading of the consent form to the participant, who has had the opportunity to ask questions. I confirm that the participant has given consent freely.

Print name of witness:	
Signature of witness:	
Date:	___ ___ / ___ ___ / _____ DD MM YYYY

IMPE-QN/MIPM doctor's signature for participant consent:

I have accurately read or witnessed the accurate reading of the consent form to the participant, who has had the opportunity to ask questions. I confirm that the participant has given consent freely.

	___ ___ / ___ ___ / _____ DD MM YYYY
Name of IMPE-QN/MIPM doctor taking Consent (Print)	
Signature of IMPE-QN/MIPM doctor taking Consent.	

Annex D

PARTICIPANT INFORMATION SHEET AND PARENT/GUARDIAN PERMISSION FORM FOR CHILDREN (≥5 YEARS AND ≥20 KG TO < 18 YEARS OLD) INFECTED WITH *P. FALCIPARUM* AND FOR CHILDREN (≥5 TO < 18 YEARS OLD) INFECTED WITH *P. VIVAX* MALARIA

Protocol title: Therapeutic efficacy surveillance of malaria treatment and drug resistance monitoring in Gia Lai and Phu Yen provinces of Central Vietnam

Principal Investigator: Dr. Huynh Hong Quang, IMPE, Quy Nhon, Vietnam.

Purpose of the study

Malaria is a deadly disease caused by a parasite transmitted by mosquitoes that can cause malaria symptoms such as fever, chills, headache, tiredness and nausea, and death without effective treatment. The Vietnam Ministry of Health (MoH) is aiming to eliminate malaria from the country by 2030.

Your child has been been invited to take part in thismalaria study because he/she has a malaria infection and lives in either Krong Pa district, Gai Lai province or Song Hinh district, Phu Yen province. We plan to recruit up to 180 people with malaria infections into this research study from the two provinces between May 2021 and May 2022. To achieve this aim, information is required on how well the treatment drugs are working to cure people of malaria infections and whether the malaria parasite is becoming resistant to the drugs. We invite people from your commune who have malaria to participate in this study to determine how well does the drug treatment work to remove the malaria from their body.

The study is being carried out by the Vietnam MoH Institute of Malariology, Parasitology and Entomology (IMPE-QN, Quy Nhon) in collaboration with the Vietnam People's Army Military Institute of Preventive Medicine (MIPM, Hanoi), and the Australian Defence Force Malaria and Infectious Disease Institute (ADFMIDI, Brisbane, Australia).

Please take time to read this information carefully, ask any questions that you may have, so that you understand what will happen to your child during the study. Then consider if you want your child to take part. If you need more time to read this information, tell the study team from IMPE-QN/MIPM. You will be given a copy of this form to take home with you.

Your child taking part in this study is completely voluntary. You can decide for your child not to be in the study without any reason. If you do not want your child to be in the study, he/she will still receive free treatment for their malaria infection. If you agree for your child to be in the study, he/she may withdraw at any time without loss of benefits to which your child has a right to receive. To withdraw your child you only need to inform the IMPE-QN/MIPM doctor.

Your child's involvement in the study

If on screening your child has symptoms of malaria and found to be infected with malaria parasites in his/her finger prick blood sample (a few drops), your child will be invited to participate in this study. After agreeing to be in the study, your child will be asked to answer some questions about themselves, where he/she lives and have travelled recently, his/her protection against malaria infections, and a physical examination to determine your child's general health.

If your child is infected with *P. falciparum* malaria*,* he/she will be treated by the IMPE-QN/MIPM doctor with a 3-day course of pyronaridine-artesunate to treat malaria in their

blood and a single dose of primaquine to stop malaria transmission. These drugs are recommended by the Vietnam MoH. Your child will also be invited to provide another finger prick blood sample to re-check for malaria at about 12 hourly intervals on days 1, 2, and 3, and then once on days 7, 14, 21, 28, 35 and 42 after starting treatment to determine how well the treatment has gone.

Some children may be infected with another malaria infection, *P. vivax* that will require treatment with chloroquine plus primaquine to treat the infection in both their blood and liver. If your child is infected with this malaria, he/she will be treated with a 3-day course of chloroquine plus primaquine daily for 14 days. The IMPE-QN/MIPM doctor will observe you child taking chloroquine plus primaquine daily for the first 3-days and for the next 11 days your child will take primaquine daily with supervision by the child's parent or guardian. To assess how well your child takes primaquine daily for the 11 days without supervision by the IMPE-QN/MIPM study team, we will ask the child's parent or guardian to complete an eight item questionnaire on days 7 and 14 after starting primaquine dosing.

What your child's blood will be used for in this study

Your child's finger prick blood sample will be used to produce blood films to determine the presence and number of parasites in his/her blood, and the species of malaria by microscopy. If malaria parasites are present your child will be treated by IMPE-QN/MIPM doctor in accordance with the Vietnam MoH guidelines. We will test your child's finger prick blood sample with a new device that measures malaria pigment produced by the parasite called hemozoin to determine whether your child is infected with either drug sensitive or resistant parasites. Your child's blood will be used to detect if drug resistant parasites are present and for the analysis of the genetic background of the malaria parasites. We will also measure your child's blood antimalarial drug concentrations to ensure that he/she had good drug exposure.

We will keep your child's blood samples that cannot identify him/her for up to 15 years from the time of blood collection. If during this time new molecular assays for malaria diagnosis and for studying drug resistance are developed, we may re-test your child's blood samples with these molecular assays. Your child's blood will not be used for any other purpose.

If, however, your child experience symptoms of malaria during the follow up period of 42 days, we will invite your child to provide us with another finger prick blood sample, so we can check his/her blood for malaria and if parasites are present the IMPE-QN/MIPM doctor will retreat you with a different drug recommended by the Vietnam MoH. With your child's blood sample, we will measure his/her blood drug levels to see whether he/she had enough drug in their body to kill the malaria parasite. Also, with your child's blood we may be able to determine whether he/she was infected with drug resistant malaria. All information from your child will help us identify high risk areas of malaria in your community.

Risks and discomforts

1) Failure of treatment. There is a small chance that the treatment drug might fail to cure your child's malaria, leaving him/her in danger of severe disease. For this reason we will check your child's blood frequently after treatment to make sure that his/her malaria has been cured. If we find that the drug does not clear your child's malaria infection or the malaria comes back we will retreat your child with another drug combination recommended by the Vietnam MoH.

2) Side effects from the drugs. As with any drug, a small number of people may have side

effects that cannot be predicted. The most common side effects of the drugs that you may receive in this study are dizziness, muscle pains, fever, vomiting, headache, chills, diarrhea, skin rash, abdominal pain, fatigue, and loss of appetite. These side effects are usually mild, should not affect your child's daily activities and generally go away quickly once treatment is finished. Your child must always come quickly to see the IMPE-QN/MIPM doctor if he/she has any illness or injury. The IMPE-QN/MIPM doctor is available 24 hours a day, seven days a week to see your child during the study. If your child has a medical problem due to his/her involvement in the study, we will help your child to get medical care for it.

3} Risks and discomforts from blood sampling. Taking blood from the finger causes a brief sharp pain. The well trained and experienced IMPE-QN/MIPM doctor or technician will collect the blood from your child's finger. There is a very low risk of infection and/or bruising where the needle is stuck in your child's finger. If your child becomes dizzy with pain or at the sight of blood, please tell the doctor or technician to lie him/her down and they will look after your child.

4) Risk of early withdrawal before completing treatment and/or before the 42 day follow-up period is completed. Your child is free to withdraw from the study at any time. Your child may also be withdrawn by the Principal Investigator or IMPE-QN/MIPM doctor. Possible reasons for withdrawal could include a serious side effect or failure by your child to carry out the requirements of the study. If your child selects to withdraw before completing treatment, he/she runs the serious risk of developing life threatening malaria. So it is very important that your child completes his/her treatment. If your child withdraws before the Day42 of follow-up is completed he/she runs the risk that the malaria may come back. So it is important that the follow-up is completed to make sure that you are cured.

Questionnaire

Your child will be asked to answer questions related to the study such as his/her movement during the last two weeks and did he/she use malaria prevention methods.

Benefits

If we find malaria parasites in your child's blood by looking down a microscope he/she will be treated at the commune health station in accordance with the Vietnam MoH antimalarial drug treatment guidelines. The main benefits to your child for participating in the study is the IMPE-QN/MIPM doctor will closely monitor his/her health and wellbeing. By following your child for 42 days after starting drug treatment the doctor will be able to determine how well the drug has performed in curing his/her malaria. If, however, your child is unlucky to be infected with a malaria parasite that the drug does not cure his/her infection, the IMPE-QN/MIPM doctor will re-treat your child quickly with another drug that is expected to be effective in removing the parasite from his/her body.

Protection of personal details

The Principal Investigator (Dr. Huynh Hong Quang) and the IMPE-QN/MIPM doctor will make sure your child's personal details are kept private during and after the study. Your child's name will not appear on his/her blood films or blood sample vials. Only the IMPE/MIPM study team will know who are in the study. The consent form and information obtained from you will be stored at the field site (i.e. communal health station) for up to six months and at IMPE Quy Nhon for 15 years in a locked filing cabinet/drawer. After 15 years all your child's study documents will be destroyed by incineration. We will report the findings from this study, but your child's name will not appear on any reports or presentations. We will also seek your

approval to check the Vietnam MoH records of your child's malaria history 12 months before and 12 months after your child entry into this study.

Compensation

Your child will receive no money or other gifts for being in the study. However, if your child lives far away from the health station that the study team is unable to pick him/her up, we will give you enough money to pay for your child's transportation to and from the health station to his/her home. Also, we will cover any additional medical costs that may be due to your child for being in the study. Your child will be provided with water and food for drug administration at the health station and he/she will receive food for your child's weekly return to the health station during the follow-up period.

Questions

If you have any questions, complaints or worries about your child being in the study, you can call or visit the IMPE/MIPM study team to discuss your concerns with them. Also, you may contact Dr. Huynh Hong Quang (Tel: 0905103496) at IMPE Quy Nhon to have your questions or worries answered. If you have questions about the study and your child's rights as a study participant, you may contact the Institutional Review Board at the Vietnam MoH (Tel. +84-243-384-6688) that approved the study. If you do not have phone access, the IMPE-QN/MIPM study team can help you contact the Institutional Review Board.

PARENT/GUARDIAN PERMISSION FOR CHILDREN (≥5 YEARS AND ≥20 KG TO <18 YEARS OLD) INFECTED WITH *P. FALCIPARUM* AND FOR CHILDREN (≥5 YEARS TO <18 YEARS OLD) INFECTED WITH *P. VIVAX* MALARIA

Protocol title: Therapeutic efficacy surveillance of malaria treatment and drug resistance monitoring in Gia Lai and Phu Yen provinces of Central Vietnam

Principal Investigator: Dr. Huynh Hong Quang, IMPE, Quy Nhon, Vietnam.

Your signature on this permission form shows that you have had this research study explained to you and you have had a chance to ask questions on behalf of your child. You are willing to have your child be in this study. Other children with malaria infections will be recruited into the study between May 2021 and May 2022.

The information collected from your child will be kept private and used for the purpose of this study. Your child's study results will be made available to you freely upon your request and any published reports of this study will not have your child's personal details. You understand that your child is not bound to be in this study and that you are free to withdraw your child from the study at any time with no loss of benefits or rights to his/her future health care.

You provide your approval for your child's blood to be re-tested within the next 15 years with new molecular assays or devices and that you give permission for the Principal Investigator to check the Vietnam MoH records of your child's malaria history 12 months before and 12 months after his/her entry into the study.

You will be given a copy of the signed information/consent sheet for your records. Should you have any worries about how the study is being carried out, please come forward and contact the Principal Investigator or IMPE-QN/MIPM doctor in person. After you fully understand what will take place with your child being in the study, you will need to sign your name or provide a thumb print on the consent form.

Child name (Print)

Child's parent/Guardian name (Print)		___ ___ / ___ ___ / _____ DD MM YYYY
Child's parent/Guardian signature	(THUMB PRINT)	

Witness signature: A witness' signature is required only if the child's parent/guardian is illiterate. In this case, a literate witness must sign. The witness can be a friend, relative or

Commune leader/representative. If possible, this person should be selected by the child's parent/guardian and should have no connection with the IMPE Quy Nhon /MIPM study team.

I have witnessed the accurate reading of the parental/guardian permission form to the parent/guardian, who has had the opportunity to ask questions. I confirm that the child's parent/guardian has given permission freely for their child to take part in the study.

Print name of witness:	
Signature of witness:	
Date	___ ___ / ___ ___ / _____ DD MM YYYY

IMPE-QN/MIPM doctor's signature for participant consent:
I have accurately read or witnessed the accurate reading of the parental/guardian permission form to the parent/guardian, who has had the opportunity to ask questions. I confirm that the parent/guardian has given permission freely for their child to be in the study.

	___ ___ / ___ ___ / _____ DD MM YYYY
Name of the IMPE-QN/MIPM doctor taking parental/guardian permission (Print)	
Signature of the IMPE-QN/MIPM doctor taking parental/guardian permission	

Annex E

PARTICIPANT INFORMATION SHEET AND STATEMENT OF ASSENT FOR CHILDREN (AGED 12 to<18 YEARS OLD)

Protocol title: Therapeutic efficacy surveillance of malaria treatment and drug resistance monitoring in Gia Lai and Phu Yen provinces of Central Vietnam

Principal Investigator: Dr. Huynh Hong Quang, IMP, Quy Nhon, Vietnam.

This informed assent form is for children aged 12 to <18 years old who have been invited to take part in thismalaria study because they have a malaria infection and they live in either Krong Pa district, Gai Lai province or Song Hinh district, Phu Yen province. We plan to recruit up to 180 people with malaria infections into this research study from the two provinces between May 2021 and May 2022.

This informed assent form has two parts:

I. Information sheet (to share information about the study with you)

II. Certificate of assent (for signatures or thumbprint if you agree to take part)

You will be given a copy of the full informed assent form.

Part I. Participant Information Sheet

You have been invited to take part in this research malaria study. Malaria is a deadly disease caused by a parasite transmitted by mosquitoes that can cause malaria symptoms and death without effective treatment. The Vietnam Ministry of Health (MoH)is aiming to eliminate malaria from the country by 2030. To achieve this aim, information is required on how well the treatment drugs are working to cure people of malaria infections and whether the malaria parasite is becoming resistant to the drugs. We invite people from your commune who have malaria to participate in this study to determine how well does the drug treatment work to remove the malaria from their body.

The study is being carried out by the Vietnam MoH Institute of Malariology, Parasitology and Entomology (IMPE-QN, Quy Nhon) in collaboration with the Vietnam People's Army Military Institute of Preventive Medicine (MIPM, Hanoi), and the Australian Defence Force Malaria and Infectious Disease Institute (ADFMIDI, Brisbane, Australia).

As the IMPE-QN/MIPM doctor I am going to give you information and invite you to be in this study. Please take time to read this information carefully, ask any questions that you may have, so that you understand what will happen to you during the study. Then consider if you want to take part. If you need more time to read this information, tell the study team from IMPE-QN/MIPM. Your taking part in this study is completely voluntary. You can decide not to be in the study without any reason. If you do not want to be in the study, you will still receive free treatment for your malaria infection.

We have discussed this study with your parent or guardian, and they know that we are also asking you for your agreement. If you decide to be in the study, your parent or guardian will also have to agree. If you do not wish to be in the study, you do not have to do so, even if your parent has agreed. It is your choice. If you decide not to be in the study, nothing will change; and if you have malaria you will receive the standard malaria treatment from the health station. Even if you say 'Yes' now, you can change your mind later and it will still be

okay. You may withdraw at any time without loss of benefits to which you have a right to receive. You can withdraw from the study by informing the IMPE-QN/MIPM doctor. You may discuss anything on this form with your parents or friends or anyone else you feel comfortable talking too. There may be some words you do not understand or things that you want me to explain more because you are interested or concerned. Please ask me to stop at any time, and I will take time to explain.You will be given a copy of this form to take home with you.

IMPE-QN/MIPM Doctor: I have checked with the child, and he/she understands that being in the study is voluntary. _____ (initials)

What will be asked of you in this study

If on screening you have symptoms of malaria and found to be infected with malaria parasites in your finger prick blood sample (a few drops), you will be invited to participate in this study. After agreeing to be in the study, you will be asked to answer some questions about yourself, where you live and have travelled recently, your protection against malaria infections, and a physical examination to determine your general health.

If you are infected with *P. falciparum* malaria*,* you will be treated by the IMPE-QN/MIPM doctor with a 3-day course of pyronaridine-artesunate to treat malaria in your blood and a single dose of primaquine to stop malaria transmission. These drugs are recommended by the Vietnam MoH. You will also be invited to provide another finger prick blood sample to re-check for malaria at about 12 hourly intervals on days 1, 2, and 3, and then once on days 7, 14, 21, 28, 35 and 42 after starting treatment to determine how well the treatment has gone.

Some people may be infected with another malaria infection, *P. vivax* that will require treatment with chloroquine plus primaquine to treat the infection in both their blood and liver. If you are infected with this malaria, you will be treated with a 3-day course of chloroquine plus primaquine daily for 14 days. The IMPE-QN/MIPM doctor will observe you taking chloroquine plus primaquine daily for 3-days and for the next 11 days you will take primaquine daily without supervision. To assess how well you take primaquine daily for the 11 days without supervision by the IMPE-QN/MIPM study team, we will ask you to complete an eight item questionnaire on days 7 and 14 after starting primaquine dosing.

IMPE-QN/MIPM Doctor: I have checked with the child, and he/she understands what is expected of them to participate in the study. _____ (initials)

What your blood will be used for in this study

Your finger prick blood sample will be used to produce blood films to determine the presence and number of parasites in your blood, and the species of malaria by microscopy. We will test your finger prick blood sample with a new device that measures malaria pigment produced by the parasite called hemozoin to determine whether you are infected with either drug sensitive or resistant parasites. If malaria parasites are present you will be treated by IMPE-QN/MIPM doctor in accordance with the Vietnam MoH guidelines. Your blood will be used to detect if drug resistant parasites are present and for the analysis of the genetic background of the malaria parasites. We will also measure your blood antimalarial drug concentrations to ensure that you had good drug exposure.

We will keep your blood samples that cannot identify you for up to 15 years from the time of blood collection. If during this time new molecular assays or devices for malaria diagnosis and for studying drug resistance are developed, we may re-test your blood samples with these molecular assays or devices. Your blood will not be used for any other purpose.

If, however, you experience symptoms of malaria during the follow up period of 42 days, we will invite you to provide us with another finger prick blood sample, so we can check your blood for malaria and if parasites are present the IMPE-QN/MIPM doctor will retreat you with a different drug recommended by the Vietnam MoH. With your blood sample, we will measure your blood drug levels to see whether you had enough drug in your body to kill the malaria parasite. Also, with your blood we may be able to determine whether you were infected with drug resistant malaria. All information from you will help us identify high risk areas of malaria in your community.

IMPE-QN/MIPM Doctor: I have checked with the child, and he/she understands what his/her blood will be used for in the study. _____ (initials)

Risks and discomforts

1) Failure of treatment. There is a small chance that the treatment drug might fail to cure your malaria, leaving you in danger of severe disease. For this reason we will check your blood frequently after treatment to make sure that your malaria has been cured. If we find that the drug does not clear your malaria infection or the malaria comes back we will retreat you with another drug combination recommended by the Vietnam MoH.

2) Side effects from the drugs. As with any drug, a small number of people may have side effects that cannot be predicted. The most common side effects of the drugs that you may receive in this study are dizziness, muscle pains, fever, vomiting, headache, chills, diarrhea, skin rash, abdominal pain, fatigue, and loss of appetite. These side effects are usually mild, should not affect your daily activities and generally go away quickly once treatment is finished. You must always come quickly to see the IMPE-QN/MIPM doctor if you have any illness or injury. The IMPE-QN/MIPM doctor is available 24 hours a day, seven days a week to see you during the study. If you have a medical problem due to your involvement in the study, we will help you get medical care for it.

3} Risks and discomforts from blood sampling. Taking blood from the arm or finger causes a brief sharp pain. The well trained and experienced IMPE-QN/MIPM doctor or technician will collect the blood from your arm or finger. There is a very low risk of infection and/or bruising where the needle is stuck in your arm or finger. If you become dizzy with pain or at the sight of blood, please tell the doctor or technician to lie you down and they will look after you.

4) Risk of early withdrawal before completing treatment and/or before the 42 day follow-up period is completed. You are free to withdraw from the study at any time. You may also be withdrawn by the Principal Investigator or IMPE-QN/MIPM doctor. Possible reasons for withdrawal could include a serious side effect or failure by yourself to carry out the requirements of the study. If you select to withdraw before completing treatment you run the serious risk of developing life threatening malaria. So it is very important that you complete your treatment. If you withdraw before the Day42 of follow-up is completed you run the risk that the malaria may come back. So it is important that the follow-up is completed to make sure that you are cured.

IMPE-QN/MIPM Doctor: I have checked with the child, and he/she understands the risks and discomforts which they may experience with their participation in the study. _____ (initials)

Questionnaire

You will be asked to answer questions related to the study such as your movement during the last two weeks and did you use malaria prevention methods.

IMPE-QN/MIPM Doctor: I have checked with the child, and he/she understands the questions. _____ (initials)

Benefits

If we find malaria parasites in your blood by looking down a microscope you will be treated at the commune health station in accordance with the Vietnam MoH antimalarial drug treatment guidelines. The main benefits to you for participating in the study is the IMPE-QN/MIPM doctor will closely monitor your health and wellbeing. By following you for 42 days after starting drug treatment the doctor will be able to determine how well the drug has performed in curing you of malaria. If, however, you are unlucky to be infected with a malaria parasite that the drug does not cure your infection, the IMPE-QN/MIPM doctor will re-treat you quickly with another drug that is expected to be effective in removing the parasite from your body.

IMPE-QN/MIPM Doctor: I have checked with the child, and he/she understands the benefits that they will receive by participating in the study. _____ (initials)

Protection of personal details

The Principal Investigator (Dr. Huynh Hong Quang) and the IMPE-QN/MIPM doctor will make sure your personal details are kept private during and after the study. Your name will not appear on your blood films or blood sample vials. Only the IMPE/MIPM study team will know who are in the study. The consent form and information obtained from you will be stored at the field site (i.e. communal health station) for up to six months and at IMPE Quy Nhon for 15 years in a locked filing cabinet/drawer. After 15 years all your study documents will be destroyed by incineration.We will report the findings from this study, but your name will not appear on any reports or presentations. We will also seek your approval to check the Vietnam MoH records of your malaria history 12 months before and 12 months after your entry into this study.

IMPE-QN/MIPM Doctor: I have checked with the child, and he/she understands how their personal details will be protected. _____ (initials)

Compensation

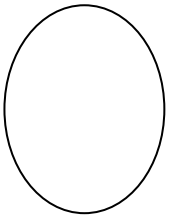
You will receive no money or other gifts for being in the study. However, if you live far away from the health station that the study team is unable to pick you up, we will give you enough money to pay for your transportation to and from the health station to your home. Also, we will cover any additional medical costs that may be due to you for being in the study. You will be provided with water and food for drug administration at the health station and you will receive food for your weekly return to the health station during the follow-up period.

IMPE-QN/MIPM Doctor: I have checked with the child, and he/she understands that they will not receive compensation for their participation in the study._____ (initials).

Part II: Certificate of assent for children (Aged 12 to <18 years old)

I have been invited to be in a malaria research study in my commune. I am aware that other children will be recruited into the study between May 2021 and May 2022. I understand that I will provide blood samples as required by the IMPE-QN/MIPM doctor. I have been informed that the risks are small and may include finger prick pain. I am aware that there will be no benefit to myself personally and that I will not be given a gift (example money). I have been provided with the name of the Principal Investigator who can be contacted easily with the telephone number that I was given.

- I know that I can choose to be in the study or not to be in the study. I know that I can stop whenever I want.
- I approve for my blood to be re-tested within the next 15 years with new molecular assayor devices.
- I give permission for the Principal Investigator to check the Vietnam MoH records of my malaria history 12 months before and 12 months after my entry into the study.
- I have read this information (or had the information read to me) and I understand it.
- I have had my questions answered and know that I can ask questions later if I have them.
- I understand that any changes to this study will be discussed with me.
- I agree to take part in the study.

Child's name (Print)		_____ YYYY Child's year of birth
Child's signature	**(thumbprint)**	

Witness signature: A witness signature and the child's are required only if the child is illiterate. In this case, a literate witness must sign. The witness can be a friend, relative or commune leader/representative. If possible, this person should be selected by the child's parent/guardian and should have no connection with the IMPE-QN/MIPM study team.

I have witnessed the accurate reading of the assent form to the child, who has had the opportunity to ask questions. I confirm that the child has given assent freely to be in the study.

Print name of witness:	
Signature of witness:	
Date:	___ ___ / ___ ___ / _____ DD MM YYYY

IMPE-QN/MIPM doctor's signature for participant assent:

I have accurately read or witnessed the accurate reading of the assent form to the child, who has had the opportunity to ask questions. I confirm that the child has given assent freely to be in the study.

	___ ___ / ___ ___ / _____ DD MM YYYY
Name of the IMPE-QN/MIPM doctor taking assent (Print)	
Signature of the IMPE-QN/MIPM doctor taking assent	