KINSHASA SCHOOL OF PUBLIC HEALTH, UNIVERSITY OF KINSHASA (DRC)

and

UNIVERSITY OF OXFORD (UK)

STUDY TITLE

Assessing the safety of low dose primaquine in *Plasmodium falciparum* infected African children with glucose 6 phosphate dehydrogenase deficiency

Short Study Title: Primaquine in Africa children (PAC)

Principal Investigator:
Prof. Marie Onyamboko
Kinshasa School of Public Health, University of Kinshasa, DRC
Contact number: 0990024201*;* e-mail: akatshimarie@yahoo.fr

Independent Person that can be contacted by the patient
Prof. Patrick Kayembe Kalambayi
President of Kinshasa School of Public Health Institutional Review Board
Contact number: 081-811-1182; e-mail: patkayembe@yahoo.fr

PATIENT INFORMATION SHEET *and*
INFORMED CONSENT FORM

Please read this document carefully, it explains the study, your child rights and our responsibilities to him/her. If you have any questions concerning the study please do not hesitate to ask any of the doctors. If you wish to talk to a person independent from the study, ask to the staff, they will direct you to him/her. Before you decide, it is important for you to understand why the research is being done and what it will involve. Take your time to decide.

PLEASE KEEP THIS DOCUMENT WITH YOU

PATIENT INFORMATION SHEET

Today you are being asked to allow your child (child under your care in the case of a legal guardian) to participate in a research study because he/she has been diagnosed with uncomplicated malaria. This malaria is called falciparum malaria. It is a potentially lethal disease transmitted by mosquitoes. In this leaflet, we will give you information about the study to help you decide whether or not you wish your child to participate.

What is the study about?

- Your child will be treated with ARTEMETHER-LUMEFANTRINE or DHA-PIPERAQUINE. These medicines are used in many countries as standard treatment for uncomplicated malaria.
- In addition, we will also give him/her one dose of a medicine called PRIMAQUINE. A small dose of PRIMAQUINE helps in eliminating the parasites from the body and prevents the spread of malaria from one person to another.
- PRIMAQUINE at this dose is generally very safe to use; however, in some people with a genetic disorder of the red blood cells called G6PD deficiency, it might cause a medical condition called anaemia
- Anaemia is a treatable disorder of the blood that is due to many causes. Anaemia can be mild and people are not even aware they have this condition or it can be severe and people might need a blood transfusion
- With this study we want to find out if this dose of PRIMAQUINE causes anaemia in African children with this genetic condition
- PRIMAQUINE, at higher dose, is an approved medicine in many countries for curing another type of malaria, called vivax malaria.

What will happen if my child takes part to the study?

- The study doctors will examine your child today and if eligible he/she will be hospitalised for 4 days or longer according to his/her medical condition
- There will be four groups of children; each group will receive one of the following combinations of medicines:

    1. ARTEMETHER-LUMEFANTRINE and PRIMAQUINE
    2. ARTEMETHER-LUMEFANTRINE and PLACEBO
    3. DHA-PIPERAQUINE and PRIMAQUINE
    4. DHA-PIPERAQUINE and PLACEBO

- PLACEBO is a tablet which looks like PRIMAQUINE but has no medicine in it so it has no effect. The doctors and nurses in the ward will not know if your child receives PRIMAQUINE or PLACEBO, because the tablets look alike. This will help us assess the efficacy of the drug without being biased
- The doctors and nurses will not decide which group your child will be assigned to. In fact, your child will be assigned to one of the four treatment groups by chance (like flipping a coin)
- During the hospitalisation a small cannula will be inserted in the forearm of your child while he/she is hospitalised for blood tests. These tests will allow us to monitor your child's health and if the treatment is successful
- In some children, we will also collect a few drops of blood more frequently from the cannula in the first 24 hours to assess how the drug is absorbed in their bodies.
- In all cases, the amount of blood removed will be too small to affect your child's health - 30 mL, less than 2 tablespoons in a period of 6 weeks.
- These drugs will be given by mouth

- All children will receive the necessary therapies for curing malaria, including a blood transfusion if necessary.

What will happen if my child leaves the hospital?

After 4 days, if your child is well he/she will be sent home.

You will be asked to return to the clinic 7 more times (at day 5, 7, 14, 21, 28, 35, 42) with your child. At each visit your child will be examined by the study doctors and a few drops of blood will be taken to check his/her health. The visit will take about 1 hour.

If at any time your child is unwell during the next 42 days you are requested to come directly to the research centre or to contact us by phone. There will be someone at the study clinic every day and also at night and you can call and or come anytime.

If at any time your child is not completely cured, the doctor will treat him/her with the appropriate medical care. The doctor, throughout the study, will always do what is best for your child.

In case you miss an appointment, the medical staff will contact you to find out why you missed the appointment and bring you and your child to the clinic for assessment.

If you agree, your child will be one of the 1600 patients who will participate to this study in DRC and in Uganda.

Does my child have to take part?

No. Your child should only take part if you decide you want to. We want to give you enough information to help you make an informed decision. You have the right to refuse your child's participation for any reason without any negative consequences. Your child's malaria will still be treated properly.

If you decide that you do not want your child to participate in the study or decide to withdraw your child from the study after enrolment, this will not affect your child's care. You will be referred to the hospital outpatient department, where standard care is available.

What are the advantages of taking part?

Your child will receive clinical care from the medical officers and nurses of the project staff in the study clinic. This will include care for unscheduled sick visits.

We will test your child for G6PD deficiency and Sickle Cell Anaemia (SS) blood disorders that can affect his/her health. Your child will benefit from knowing if they have these blood disorders and we will communicate you the results of the tests as soon as we have them. This knowledge will also help us, other doctors and researchers to understand how the medicines work.

The knowledge gained from this study will contribute to the effort of eliminating malaria.

What are the disadvantages of taking part?

Side effects, like nausea, headache or dizziness, could occur after using antimalarial medicines but they are generally mild and short-lived.

Anaemia could develop following the use of PRIMAQUINE and in a severe case a blood transfusion might be required.

The risk of drawing blood includes temporary discomfort from the needle stick and bruising. Your blood will be taken by an experienced laboratory technician to prevent and/or limit these problems. The amount of blood removed will be too small to affect your child's health.

If your child has any side effects from the drugs or develops any unexpected medical problems during the study, we will your child fully and with no charge to you or your family. In the unlikely event that your child is harmed as a direct result of participation in the study and compensation will be available.

Do I have to pay for medical care received in the study?

No. If your child participates you will not have to pay for treatment, medical tests or clinic visits. We will reimburse any transport costs incurred for the clinic visits. Meals and soap for personal hygiene will be provided while your child is admitted in our clinic.

Who will have access to my child's information?

All information collected in this study will be treated confidentially by the medical staff. To help this process, your child will be assigned an identification number to be used instead of his/her name on the medical files, on all study forms, blood tubes, and computer databases.

Some samples will be transferred to a specialised laboratory overseas for the medical tests that we cannot perform here.

The information collected will be reviewed only by authorised staff to ensure that your child's safety and rights are protected while participating in the study. They will also treat the data confidentially.

The findings might be published in a medical journal. The study participants will never be identified by name.

The researchers and doctors who carry out this study guarantee that the study conduct and the results will not be influenced at any time by the study funder and they will always act in the best interest's of your child. After the study is completed, you may request an explanation of the study results.

Who is conducting this study and who has approved it?

The study is conducted by a group of doctors and scientists from the Kinshasa School of Public Health and the University of Oxford, England. The study is sponsored by and insured via the University of Oxford and funded by the Medical Research Council of England. This research has been reviewed by a committee of experts, known as the Research Ethics Committee, to protect your child's rights and welfare.

Implication of your signature or thumbprint

If you give consent for your child to participate in this study you should sign the consent form (or you should place your thumbprint in case you cannot read and/or write). Your signature or thumbprint below means that you have understood the information given to you about your child's participation in the study. You will be given a copy of this consent form for you to keep.

What if I have questions?

If you have questions or if a research-related injury occurs, please contact Dr. Marie Onyamboko (Contact Number 099- 002-4201).

You may also come to the project office located at Hôpital General de Kinshasa, Pavillon 27, Avenue Tombalbaye 68-78, Kinshasa I-Gombe, DRC

If you have any questions about your child's rights as a study participant, please contact Prof. Patrick Kayembe Kalambayi (Contact Number: 081-8111-182).

WE THANK YOU FOR YOUR TIME

INFORMED CONSENT FORM FOR PARTICIPATION IN A RESEARCH PROJECT

STUDY NUMBER |__|__|__|__|-|__|__|__|

Study Title: Assessing the safety of low dose primaquine in *Plasmodium falciparum* infected African children with glucose 6 phosphate dehydrogenase deficiency, Primaquine in African children (PAC)

Principal Investigator: Prof. Marie Onyamboko (tel. 0990024201)

Principal Investigator:

I, _____ mother / father / legal representative (aged 18 or above) declare that I have understood the objectives and purposes of this study.

I agree that my child _____, aged _____ years _____months, participates in this study. I am aware that I can withdraw my child from the study at any time without any consequence to my child or to me.

I allow ☐ / do not allow the blood of my child to be stored for future study ☐

I allow ☐ / do not allow the clinical data and results from blood analyses that is stored in the database to be shared with other researchers to use in the future ☐

I allow ☐ / do not allow the study to use the clinical data that has been collected if I take my child out of the study ☐

☐ I have read the document and hereby agree to participate in this research study

☐ The participant cannot read/write, but the researcher has read the document to him/her. He/she has listened and clearly understood. He/she hereby agrees to participate in this research study

Parent / Legal representative

Name_____ **Signature or Thumbprint** _____

Date |__|__|__|__|__|__|__|__| **Time** |__|__:__|__|

Impartial Witness (if participant cannot read/write)

Name_____ **Signature** _____

Date |__|__|__|__|__|__|__|__| **Time** |__|__:__|__|

Person Taking Consent

Name_____ **Signature** _____

Date |__|__|__|__|__|__|__|__| **Time** |__|__:__|__|