

Supporting Guidelines for Informed Consent

MalariaGEN Project Team

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These guidelines are intended to help investigators in preparing the informed consent procedure for sample collection for MalariaGEN studies. They set out some general principles on informed consent in medical research, and also include specific information relating to MalariaGEN studies. The informed consent process in any research centre will need to be in accordance with the local setting. However, many of the important ethical principles and practicalities of obtaining informed consent will be common to all sites involved in MalariaGEN. For this reason, these guidelines are accompanied by an **informed consent template** which sets out a number of core elements required in any MalariaGEN informed consent form.

These guidelines are set out in two sections. Firstly some practical ethical considerations are introduced, these include: the layout of the information sheet, methods for recording consent, the question of when consent should be obtained, and finally, some additional practical considerations. Secondly, the guidelines introduce a number of considerations relating to the content of the information sheet.

A. Practical Aspects

1. Layout of the information sheet: for clarity and comprehensibility, it is recommendable to divide the information sheet into sections dealing with different topics, with a clear heading for each topic (see the template for suggestions). Local ethics committees might have their own guidelines on how to structure the informed consent form, and where this is the case you should follow these as much as possible. However, you might find it useful to follow the headings suggested in the template, if your ethics committee does not offer any guidance.

Developing a clear layout for the information sheet does take up much more space, but it improves clarity of the form.

2. Recording consent: the informed consent package should consist of an information sheet, read to participants prior to asking their consent, and preferably handed to them to take home, and a separate sheet on which to record consent. Developing a separate sheet for recording the signature of the prospective participant reduces the amount of paper you will need to archive.

It is good practice to repeat some basic information about the project on the consent form as well, either in bullet points or as condensed text (see point 11.1 of the template). You should also record the name and signature of the person who took the participants through the consent procedure, i.e. the nurse or health worker. Ethics committees do not always allow the recording of personal information other than the name of the person who is consenting, and you should keep this in mind when you are drafting the form.

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You should also consider whether it is standard practice in your country/setting to keep records of people who do not consent to participation. If you have no intention to keep such records, then there is no use in giving options (I do/ I do not consent) in the consent sheet, because this might create extra worry for the people who do not want to participate.

Last but not least, for obvious reasons, make sure that consent forms can be linked to samples.

3. When to go through consent: it is important to ensure that information is accessible and conducive to voluntary, informed and competent consent. In an ideal situation, the information should be communicated verbally in the participant's native language some time before sampling starts, allowing sufficient time for reflection and consultation with family and friends, after which the information may be repeated before asking a participant to sign the form.

However the practicalities of carrying out research on very sick children (when collecting samples from children with severe malaria, for instance) can make this difficult. There are time constraints; the parents are likely to be distressed; and genetic studies may be embedded in other research protocols. All these are likely to affect the validity of the consent procedure, and the consent procedure should aim to minimise disturbance caused by such factors. Some strategies to do this include:

- having at least one team member with dedicated responsibility for obtaining informed consent, to reduce time pressure and ensure good practice (see also point 5 below);
- having a closed space away from the ward and doctors where people can be taken through the consent form;
- developing protocols that prevent attempts to obtain consent in inappropriate circumstances, e.g. when there is extreme emotional distress;
- treating the initial consent process (e.g. on hospital entry) as preliminary, and following up with a second confirmatory consent process after the sample has been taken, when the parents are not emotionally distressed and have had a chance to reflect and consult.

In the case of collecting cord blood controls, you should not take women through the consent process when they are in labour. But in some cases this might be the only point of contact between researchers and pregnant women, and you will need to think about ways to obtain valid consent in these circumstances (although you should ensure there really are no alternatives!). One way to go about this might be to develop, in collaboration with other doctors, nurses and midwives, very strict entry criteria based on clinical signs e.g. those of foetal distress. This is one area in which we expect it to be possible for members of the MalariaGEN consortium to share from the experiences gained in other centres. We are, for example, currently working on these issues in the Gambia, and expect to report on different possibilities later.

4. Language: When drafting the informed consent sheet, it is important to avoid the use of language with powerful connotations. For instance, instead of writing 'we are *requesting* your help', write 'we are *asking for* your help'.

It is also important to avoid the use of scary language that might deter people from participation, or cause them unnecessary distress. For instance, instead of writing

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'many children become ill with malaria and *die*', you could use a metaphor that is sensitive to your local setting. (However, you should consider whether it is appropriate to make any reference to potential death of children when talking to parents whose child has just been admitted in the hospital with severe malaria). Similar considerations apply to other terms related to the research. For example, rather than including a phrase such as 'we *bleed* the child', it is better to describe how you obtain the sample in everyday language.

5. Other comments: It is important to remember that the information sheet is part of an *informed consent process* and it will be important to think carefully about the various elements of the process necessary to obtain genuinely valid consent. One common element of any process is likely to be the *involvement of a qualified person specifically trained for this particular task*, sitting down with prospective participants and discussing all aspect of the study. Although time consuming, this element of the procedure can be very important and helpful in ensuring that those who participate do so as a result of a good understanding. For obvious reasons, it is important that those people trained to take prospective participants through the informed consent procedure, know the details of this research project, and understand some of the science behind it. They should be able to answer any questions prospective participants might have. If you train people to take informed consent, be sure to sit in with the consent process regularly to ensure that they understand the project and explain it in the right terms.

B. Content of the information sheet

1. Introduction: Participants should be informed why they have been selected for this particular study, rather than other individuals, communities or ethnic groups. It is of particular importance to provide information on this for the collection of cord blood controls, or of samples from healthy children in for instance schools, since worries might easily arise about why researchers want blood from healthy children.

- it is important to address why people are asked to participate in the study

It is also important to provide a few sentences of background information on the project. In relation to MalariaGEN, you might want to consider including something like the following: MalariaGEN is a research network that comprises more than twenty research institutes in twenty countries. It aims at unravelling the genetic factors that contribute to resistance against severe malaria by comparing the genetic material from affected and non-affected children. Sampling is taking place in 14 malaria-endemic countries in Africa and Asia. In total, MalariaGEN studies will analyse over 60.000 samples, 25.000 of which will be collected specifically for MalariaGEN studies. Sample collection and DNA extraction will mainly be done in the local research institutions, but the genotyping of samples will be done in the UK, although data will be returned to local institutions as soon as it is produced.

- It is important to stress somewhere in the information sheet that samples will be shared with researchers from other countries

2. Procedure: It is important to be as clear as possible about the procedure of blood collection and data analysis, and make sure that the actual practice does not deviate

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from what has been said in the information sheet. It is good, as part of the explanation, to compare the quantity of blood that will be extracted with some well-known reference quantity that will be meaningful to the person from whom consent is being obtained, such as for instance tablespoons and teaspoons.

It is also important to be explicit about where the blood will be taken once it is collected, and what will be done with it. You might think about using this specific section of the information sheet to stress that there will be no benefits arising from participation: the tests done on the sample will not provide the researchers with any information about the health of the individual.

3. Risks and Benefits: Even though there are only minor risks associated with collecting a blood sample, it is very important that you insert a special section in the informed consent sheet that discusses these risks. Inserting such a section might prevent the development of misunderstandings about the project e.g. about its role in aggravating disease.

With regard to benefits, it is very important not to make promises that cannot be kept. The most important outcome of MalariaGEN studies will be 'knowledge', and even though a cure for malaria might *on the long term* be of benefit to the community, it is unrealistic to make any promises about how the community will practically benefit from participation in a MalariaGEN study.

- 'risks' should be mentioned before 'benefits', potentially in separate sections of the information sheet
- don't make promises you cannot keep
- if you offer something in return for participation, such as nutritional supplements or food, then be brief about this. Focussing too much on such benefits might lead to false inducement.

4. Privacy and Confidentiality: As is standard practice for research on human subjects, it is important to stress that the identity of study participants will be protected at all times, and that data will be kept secure in locked cabinets in a locked room. However, before making promises that cannot be kept, it is important to think about the practicalities of ensuring privacy in your own laboratory. Also, think through the practicalities of assigning code numbers to samples as they are collected/ arrive in the laboratory.

5. Voluntary: Informed consent should be absolutely voluntary, and it is important that this is clear both in the information sheet and when asking prospective participants for their consent. It should also be very clear that there are no consequences of refusal to participate for the individual.

- in the information sheet, insert a special heading on voluntary nature of participation
- the people trained to take prospective participants through the consent procedure should be very aware of these aspects

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6. Withdrawing from the study: Related to the above, both in the information sheet and in the process, it should be made clear to the participant that he or she can withdraw from the study at any time in the future, meaning that any samples obtained from that person (or from his or her child) will be destroyed. However, it should also be made clear that once samples have been genotyped, it will be no longer possible to withdraw the data derived from that sample. This is to say that although the original sample will be destroyed, it will not be possible to destroy or withdraw data that has already been used for analysis and publication.

- somewhere on the information sheet, the name of a person to contact if a participant wants to withdraw from the study should appear

7. Data: Because of the particular nature of genomic studies, it has been suggested that researchers should explore the possibilities of including a short section (perhaps even a few sentences) on the difference between the physical sample, and the data generated from it. It might be worthwhile to consider this when you are drafting your information sheets.

8. Storing blood: The objective of MalariaGEN studies is to better understand the genetic basis of resistance against malaria, hoping that such knowledge will eventually lead to the development of better means of preventing or curing the disease. At the moment, the technology to analyse genetic information is still very expensive and inefficient. However, the speed with which the technology is currently improved leads us to believe that we will be better able to reach our objective in the (near) future, which is why we intend to store the samples analysed in MalariaGEN studies for future analyses. It should therefore be made very clear to prospective participants that their samples will be stored for future use.