

H3Africa Guidelines for Informed Consent

Developed by the H3Africa Working Group on Ethics and
Regulatory Issues for the Human Heredity and Health (H3Africa)
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Preface

The H3Africa programme seeks to foster genomic research expertise on the African continent with the goal of using genomic methods to address health inequities in both communicable and non-communicable diseases. Under the H3Africa banner, genomic research on conditions such as cardiovascular disease, rheumatic heart disease and diabetes is supported. Genomics research in Africa raises a host of ethical issues, some of which are unique to the continent and its people, and others of which are similar to issues raised elsewhere in the world. In order to address these, the H3Africa consortium established a Working Group on Ethics, which is composed from representatives of each of the H3Africa funded research projects.

One of the challenges facing H3Africa investigators relates to informed consent. Obtaining informed consent for genomic research is challenging for many reasons, regardless of whether the research is conducted in Africa or elsewhere. Challenges are for instance how to explain complex concepts like 'genomics', but also that genomic data and, increasingly, genomic material) can be used for secondary analyses by investigators who were not involved in the original project. Furthermore, such uses may mean that it is in principle not possible to withdraw consent once the sample or data have gone beyond a certain point. For instance, once data has been used in a publication then that data cannot be withdrawn from that publication. In the context of sample and data sharing, it may therefore no longer be appropriate to seek consent for specific projects only. As sample and data sharing are foundational principles of the H3Africa initiative, we have elected to adopt broad consent for genomic studies as a starting point for the guidelines presented in this document.

Specific challenges in the African context are that a considerable proportion of the potential research participants may have received only basic education, have limited access to healthcare, or be poor. In addition, for some cultures and communities, the Western focus on autonomy (and individual informed consent therefore) may not resonate with a more communitarian worldview, in which case a different interpretation of autonomy might be relevant. Lastly, in many cultures across the African continent oral communication remains a very important means to share and transfer information. The requirement for a written form for consent to genomic research may in those cases simply be inappropriate. Whether and which alternative means of recording consent are acceptable in such settings remains a topic of academic debate. For this reason, it is important that the development of a consent process is informed by a wider community engagement effort aiming to meaningfully engage with prospective research participants and their communities to identify and discuss the ethical aspects of the research.

The H3Africa Working Group on Ethics convened (via skype and telephone) several times in the first few months of 2013 to discuss these issues, and to define a set of guidelines to help H3Africa investigators develop their consent documents. The purpose of these guidelines is not to be

prescriptive but to be a resource that can be adapted to different situations. Africa, after all, is a continent that houses thousands of different population groups with widely varying customs, languages and beliefs.

In developing these guidelines, we relied on work done previously by other genomic research projects in Africa. Specifically, we would like to acknowledge the efforts of the International HapMap Consortium, MalariaGEN and 1000Genomes.

Currently, there is a scarcity of published research on the perspectives and views of African research participants on issues relating to sample and data sharing and the creation and distribution of cell lines. As and when new insights are generated, these guidelines may evolve to incorporate the lessons learned. For the time being, we hope that these guidelines will be useful as a resource to all those conducting or planning to conduct genomic research in Africa.

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1. Introduction

The Human Heredity and Health in Africa (H3Africa) Consortium is a collection of cutting-edge research studies and infrastructure projects that will generate insight into the contribution of genomics to communicable and non-communicable diseases, train African investigators in genomic science and create or expand existing genomic infrastructure in Africa. Of key importance in this project is the need to obtain valid consent from participants. Drawing on existing national and international guidelines as well as experiences of the members of the H3Africa Working Group on Ethics, this document is intended to help H3Africa investigators in the preparation of consent processes and associated documents for H3Africa genomic studies. In this document, we suggest what kinds of information should be covered in the consent process, give examples for how to explain key concepts of genomic research, and discuss how consent documentation relates to the process of obtaining valid consent.

H3Africa studies will take place in many different research settings, including but not limited to rural settlements and village clinics and secondary or tertiary hospitals in more urbanized settings. Prospective participants may be educated and well-informed – for instance where research takes place in large urban hospitals – or they may have only received very basic or no education and have limited access to healthcare or modern media. Genomic studies also require the collection of samples from healthy people as controls. This can be a challenge especially when the collection of a blood sample is associated with disease and treatment. H3Africa investigators will need to design consent processes that are appropriate for each of these settings and target populations. The aim of this document is to outline important core elements and to provide template language that can be used by investigators in the development of their own consent materials. The guidelines are not meant to be prescriptive.

These guidelines were developed by the H3Africa Working Group on Ethics. The Working Group was established after some of the initial H3Africa investigators had already submitted their consent documents for ethics approval. These investigators are not required to redesign and resubmit their consent documents unless there is information that is deemed necessary to be included in consent documents for all H3Africa projects. The current guidelines will primarily inform H3Africa investigators that are yet to design their consent documents and processes.

2. Key characteristics of H3Africa studies relevant for consent

All the H3Africa studies share some characteristics that are relevant to the consent process. These are:

- I. The projects are primarily genomic research studies. Although the various studies may also involve other research components – for instance, some studies may integrate genomic methods with an epidemiological study design – H3Africa focuses specifically on genomic research. This means that, typically, participants are not enrolled in the studies for a long time. Usually, their involvement with the genomic study lasts only as long as it takes to take a blood or saliva sample, and collect clinical and demographic data. This means that the main risks for genomic studies tend not to be related to study participation per se, but more to issues like privacy and confidentiality of the personal information collected or generated. Genomic information is unique to individuals and it is therefore theoretically possible that a study participant might be identified from their data, but only if another sample of their DNA was taken, analysed and published elsewhere. The likelihood of this happening can be reduced if safeguards are in place, but even so, absolute guarantees of confidentiality cannot be made;
- II. In addition to samples from people who are suffering from the disease under investigation, the projects need to also collect samples from healthy volunteers as controls. Because in many settings across Africa, the collection of a blood sample is associated with disease and treatment, this could raise concern – especially if the consent documents speak of a disease that the person does not currently have;
- III. As is true for all genomic and genetic studies, genetic information is shared by genetically related persons and so information from one individual may also identify or be relevant to close relatives. Consent is usually obtained only from the individual, however;
- IV. H3Africa research studies will share phenotypic and genomic data for secondary analysis. This means that although samples may be collected for a study on a particular disease, the genomic data may be analyzed for many different diseases. Also, the data may be analyzed to look at population differences or to test new tools for analyzing genomic information. The consent information and processes need to make this very clear to potential participants;
- V. Samples from many of the H3Africa research studies will be deposited in H3Africa biorepositories for secondary use. These repositories will be located on the African continent. When samples are deposited in the biorepository, they can be used for other research in the future, including research on other diseases. NIH-funded studies are required to deposit study samples in an H3Africa biorepository and consent therefore needs to be obtained for this. Although this is not a requirement of funding for the Wellcome Trust, the Wellcome Trust is supportive of this policy as it will facilitate research in Africa in

the future. WT funded investigators should consider seeking consent for sample sharing and deposition in an H3Africa biorepository (subject to national legal requirements) as well;

- VI. In the longer term, the H3Africa ambition is that immortalized white blood cell lines will be generated from samples collected under the H3Africa umbrella to secure the availability of genomic material for the future, and to enable functional studies. Cell lines can be created from blood samples and can live in a laboratory indefinitely. Some investigators may consider seeking consent for the creation of cell lines so that participants will not need to be re-consented if the creation of cell lines is implemented in the future.

3. Designing consent documents

Consent documentation¹ normally consists of a) an information leaflet or sheet, and b) a signature sheet. In these guidelines, we refer to these together as ‘informed consent documents’. Consent document should be written in clear, simple language that can be understood by the research participants. When developing the consent documents, it is important to think about the likely literacy levels of the research participants, and try to tailor the consent document appropriately. Ideally consent forms should be piloted for comprehension and adjustments made as necessary.

Consent documents should be translated into a language that the research participants understand. In Africa, this may sometimes be a challenge, for instance when the vernacular language is spoken rather than read. In some cases people may prefer to read the English language consent document but to have the study explained in their own language because their own language is not normally put in writing. Also, some African languages may not have words for concepts like ‘privacy’, ‘confidentiality’, ‘data’, ‘research’ or ‘genomics’ but they could be explained using analogies. Most if not all cultures will have some understanding of inheritance and genomic scientists should explore how communities or population groups refer to the heritability of traits. In some cases, investigators might like to explore alternative means of communicating with participants about the study. Examples are developing a video or film about the project that participants can watch prior to the consent process, or developing a cartoon about the study. Both of these have been used for medical and genomic research in a variety of African settings.

Usually, field workers and study nurses understand a lot about what participants prefer, what they already know, what they are likely to understand and so forth. It is very important to involve field staff in the development of consent documents. Others, like community gatekeepers and representatives, could also be asked for input at this stage. You can ask these people for instance,

¹ In this document, we refer to ‘consent documents’ to describe all and any documents developed for use during the process of seeking consent. This normally includes a participant information sheet (sometimes also called an information brochure or leaflet) and a signature sheet (also called the consent record form, consent form or something similar).

whether people are likely to be able to read a form written in the vernacular, whether they are already familiar with concepts like inheritance, what challenges they usually encounter when seeking consent, what analogies can be used to explain scientific concepts and so forth. This information can be used in developing the consent forms for your study.

Lastly, it is important that the layout of consent document(s) is clear. A confusing layout (for instance, small font and/or margins or many titles that are underlined) can make it difficult to read and follow the information in it. Local and national ethics committees may have their own guidelines as to how to structure the consent documents and these should be followed as much as possible.

Once the consent documents have been developed and approved, it is important that those who are going to seek consent (such as nurses and fieldworkers) are provided with adequate training. Training should focus both on how to obtain valid consent (why is it important, what are the challenges and so forth), and on key scientific aspects of the project to enable them to explain the project to participants or respond to questions.

A few things to avoid if possible in the consent documents:

- Professional jargon
- Underlining or Italicizing large blocks of print
- Capital letters for titles or long pieces of text
- Use of acronyms
- Confusing layout.

4. Information for inclusion in H3Africa consent documents

There are many international guidelines available that detail the content of consent documents. Examples of such guidelines are those provided by the Council for International Organizations of Medical Sciences (2002), the World Medical Association (2008) and the International Council on Harmonisation (1996). A good description of the challenges relating to informed consent can be found in the Nuffield Council's 2002 report on the ethics of research in low income countries (Nuffield Council on Bioethics 2002) (2002). Some consent elements are required by local laws, regulations, or other guidance in the country where the research will be conducted. Where this is the case, then H3Africa projects need to include these elements in their forms.

All H3Africa consent documents need to make mention of data sharing. All consent documents for studies that are funded by the NIH need to seek consent for sample sharing, and this is also recommended for studies funded by the Wellcome Trust.

Consistent with other guidance, we strongly recommend that the following elements should be included in consent documents:

- A statement that the study involves *research*, an explanation of the *purposes* of the research and the *expected duration* of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
- A description of any reasonably foreseeable *risks* or discomforts to the subject;
- A description of any *benefits* to the subject or to others which may reasonably be expected from the research; A statement describing the extent, if any, to which *confidentiality* of records identifying the subject will be maintained;
- An explanation of whom to *contact* for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject;
- A statement that participation is *voluntary*, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled and the subject may *withdraw* from the study at any time without penalty or loss of benefits to which the subject is otherwise entitled. Procedures for withdrawing should be given. It should be clarified that whilst *the subject* has the right to withdraw, samples and data that have already been distributed or analysed cannot be rescinded;
- A statement about *the broad nature of the project* and the fact there will be *data* (and/or) *sample sharing*.

Where appropriate, the following elements should also be included:

- Anticipated circumstances under which the subject's participation may be terminated by the investigator (but this may only be relevant where the genomic study is integrated in another study such as a clinical trial);
- An explanation of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject (only relevant where the genomic study is integrated in another study that involves an intervention for health purposes);
- The approximate number of subjects involved in the study;
- For research involving more than minimal risk, an explanation as to whether any compensation or any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
- If relevant, any particular risks to groups that may arise as a result of a person's individual participation;
- A statement on the possibility that commercial products may be developed by others who use H3Africa samples or data.

Not all of the above elements may be relevant to all studies, and some studies may need to add additional elements to their consent documents. Any other information that pertains to the study and will be useful for the individual as he or she decides whether or not to take part in the study should be added to the consent document or provided orally at the time of consent if requested by the potential participant. Furthermore, an institution's Research Ethics Committee (REC) or Institutional Review Board (IRB) may require additional elements that are not specifically listed in guidelines or regulations to ensure that adequate information is presented in accordance with institutional policy and law.

5. Discussion of suggested elements for H3Africa research studies and sample language.

The excerpts with sample language provided here are relevant to H3Africa and genomic studies and are merely suggestions.

A. Study title

Try to come up with a short simple study title – avoid any words, acronyms or phrases that might be misconstrued. The study title needs to be broad in order to address not only the primary study but that the data and samples will be shared with the research community. Alternatively, you could have a lay title under the official title of your project. For instance, “Genomics of Disease X”.

B. Who are the investigators?

For example: *“This study will be carried out by investigators from institution XX. We are working with other investigators in XX different countries in Africa to study [Disease ABC]. Our study is part of the Human Heredity and Health in Africa (“H3Africa”) project.”*

Note: it is important to mention the H3Africa Consortium in the consent documents, because most of the policies concerning data release, sample sharing and so forth will be developed at the level of the Consortium, not for individual projects.

C. Purpose and scope of the research

Describe the problem that this research project is trying to solve, and how it may benefit others in the future. Also, describe the types of diseases or conditions being studied for which the samples and data may be used (including not only the initial study, but any possible future studies that may use the samples). Consider whether to specify a certain group of disease (for instance, cardiovascular disease or cancers) or to just say ‘other diseases’.

Sample language:

“This consent form will tell you why we want to do this study.

As you may know, many people have [Disease ABC]. We hope to discover how some people get sick with this disease. We hope that one day we could make a medicine that may help us treat this disease. There is some information about [Disease ABC] among people who live in Europe and America. This study is first time we will study Disease ABC] in Africa.

In the future, the information and samples that you provide for this study may be used to study other diseases by other investigators. You will not get any benefit directly from this study. But we hope that the information we get may benefit others who have [Disease ABC] in the future.

Please ask us questions about anything you do not understand or if you would like more information. We are happy to explain this to you more than once.

Please take whatever time you need to talk about the study with your doctor or nurse, the study staff, your family and friends.”

D. What will the study involve?

For example, will the participants be requested to provide a blood sample or provide medical information? You should also give an indication of how long it will take to participate in the study. In the informed consent document, it is important to not deviate too far from the topic of study with unrelated examples to explain difficult concepts such as genetics or genomics. But on the other hand, you should also seek to make sure that all the necessary information a person might want to evaluate to make an appropriately informed choice, is present in the informed consent document.

Sample language:

“We are asking to take XX ml of your blood – this is the same as XX tea/tablespoons. We will use your blood to study something called “genes”. These “genes” are present in all of us and are responsible for why people in families look like each other, but different from others. For example, some families are taller or shorter than others. This kind of information is passed from both the father and the mother to their children and on to their grandchildren, in other words, from one generation to the next. Some of these genes may prevent us from getting sick from condition XX in the first place. Some other genes may be one of the reasons we get sick when others do not.”

E. What will happen to the samples?

This section should describe the procedures that will happen to the samples – in as far as it is relevant for the participants to know. Where sample sharing is required, this section should also explain the plans to send the samples to a biorepository in Africa established for the H3Africa Program. You could also mention the existence of Material Transfer Agreement in this section. Note that it is currently not possible to include in the consent materials a complete description of the plans regarding the handling and access to samples as these are still under development.

One of the goals of the H3Africa biobank is to make samples as widely available as possible to facilitate future research. Investigators should therefore consider seeking consent that is sufficiently broad to allow this, in as far as that is acceptable to research participants and research ethics committees or institutional review boards.

It may be possible to seek specific consent for sample sharing, for instance through a layered consent approach (first seeking consent for the primary study, and then for sample sharing). One approach might be to develop two separate consent documents. Another might be to add a tick box to the consent documents to indicate whether people would/would not like their samples stored for future research. If investigators decide to follow this option, however, they need to develop a good management plan to ensure that the participant's choices are respected. This may be technologically or practically difficult, and people need to carefully consider the implications before deciding to use a layered consent approach. Another option would be to seek broad consent with permission to recontact a participant if there is ambiguity about an intended use. At all times, it is important that participants know how to contact the investigators should participants reconsider their decision.

The type of information that should be included is:

- That the samples will be coded so that all efforts will be made to protect the participants' privacy;
- Who will be the primary custodian(s) of the samples?;
- Who will have access to the samples (e.g., qualified investigators in universities, hospitals, government agencies, companies);
- How the biorepository will control and monitor access to the samples;
- The type of research that will be conducted. Broad or limited to the condition that they have given consent for;
- That the samples will not be sold, but that investigators may develop commercially valuable products based on studying the samples, and that if they do, participants will not be able to share in any profits (http://h3africa.org/ethics_governance_resource-sharing.cfm);

- What will happen with samples and data after patients die, and the effect of death on the right to withdraw. Options are for instance that this right is transferred to family members, or that it dissolves (meaning that samples can no longer be withdrawn when the participant dies).

However, since the governance mechanism of the biobanks is still under development it may not at this stage be possible to give accurate information for each of the above. Investigators must also carefully consider how (much) they will or need to explain about any possibly commercialization, as this may deter participants from participating.

Sample language:

“In order to do the research we have discussed, we must collect and store blood and health information from people like you with [X disease]. We will do some of the tests right away. Other tests may be done in the future. Once we have done the research that we are planning for this project, we would like to store your blood and information. We will store it together with the other samples that people have given from all over Africa as part of a big collection that is called a “biobank”. This “biobank” will be somewhere on the African continent. Investigators from all over the world can ask to use these samples for their research. Although the study you are being asked to participate in involves “Diseases ABC”, other scientists may like to use your sample to study other diseases. The samples will not be sold, but investigators may develop products based on studying your samples. If this happens, you will not be able to share in any profits.”

An example of a tiered or layered consent option is the following:

“Tick the option you choose:

I do not want my sample to be shared with other investigators.

OR

My sample can be shared with other investigators for research in a field related to [describe the field of your study, e.g. cardiovascular research].

OR

My sample can be shared with other investigators for research in any field.”

F. Cell line creation

The long term goal of the H3Africa project is to build capacity for the creation of cell lines from white blood cells. Cell lines can live in the laboratory indefinitely and will provide a resource for

research in the future. Because cell lines replicate indefinitely, they provide a renewable resource of DNA, RNA and other cell products. It is not currently clear how the creation of cell lines will be perceived by African research participants, investigators and ethics committees, how best to explain this concept to research participants, and if people are likely to consent to this procedure. It is also not clear what kinds of concerns participants may have with the creation of cell lines. Further research will be required to investigate this. The creation of cell lines is not planned for the current H3A projects and seeking consent for this procedure is entirely optional at this stage.

If investigators ask participants for consent for the creation of cell lines from their white blood cells, the following is suggested language:

“Your blood is built up of different things, including little things that are called cells. We would like to take some of these cells out of your blood. We will do something to your cells that makes them grow in the laboratory. We call this a “cell line”. With the cell line, we can always have access to some of your cells in the future, without asking for more samples from you. The kind of experiments we do may be related to [Disease ABC] but it is also possible that your sample will be used to study other diseases that affect people all over the world.”

G. What will happen to the data?

Genomic data generated in the context of H3Africa will be shared widely for secondary analysis and research, and investigators need to specifically seek consent for this. When data are shared with other investigators, they may for instance be analyzed for other diseases, for population ancestry or to test new statistical tools for analysis. The current proposal is for data to be shared through the European Genome-Phenome Archive, together with accompanying phenotypic and demographic information. When data are shared, they will be coded so that the participants’ privacy is protected as much as possible. However, because genomic information is unique to individuals, there is always a theoretical risk that participants could be identified if additional genetic information for the person is also available in the public domain. Investigators should also consider whether the risk that participants could be identified should be highlighted in the consent document.

Sample language for how the data will be maintained (e.g., in accordance with H3Africa policy, in a database available to qualified investigators over the Internet):

“To protect your privacy, we will replace your name with a code. We will only use this code on your sample and information about you. We will do our best to keep the code private. It is however always possible that someone could find out your name but this is very unlikely to happen.”

Sample language for who will have access to the data (e.g., qualified investigators in universities, hospitals, government agencies, companies) and how access to the data will be controlled.

“A goal of H3Africa is to create a way for investigators to share and learn from each other, especially within Africa. One of the best ways to do this is for scientists to share research data. We would like permission from you to share your data with other investigators across the world. We would like your permission to share your health history, laboratory test results and your genomic information. When we share this information, people will not know your name. Other investigators who want to use your data (without your name) will need to first ask for permission from the central repository. They will need to agree only to use the data for scientific research. The data could for example be used by investigators from universities, hospitals or from companies that make and sell medicines. The information from this study will be given free of charge. There is a small chance that your data, together with the data of many other people, could be used to develop new drugs. If this happens, there are no plans to share any profit with you.”

H. Voluntary nature of participation and right to withdrawal

Valid consent for H3Africa should be voluntary. The consent documents should include a special heading on the voluntary nature of participation. The people trained to take prospective participants through the consent procedure should be trained to ensure participants are not pressurized into participating. . They should also be made aware of other sources of pressure such as community leaders and family members.

Participants should be made aware that they 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 may no longer be possible to withdraw the data derived from that sample and it may not be possible to destroy samples sent to other investigators. This is to say that although the original sample can be destroyed if requested, it may not be possible to recover data or samples that have already been used for analysis and publication by investigators. However, the data can be taken out of the data repository so that no additional investigators are able to download and work on the data. The name of a person to contact if a participant wants to withdraw from the study should appear in the consent document.

Sample Language:

“It is a personal decision whether you take part in the study. In other words, it is up to you whether you want to participate in the study.”

“You can say “yes” and join the study; or you can also say “No,” you don’t want to join. If you participate in the study, you can change your mind later and decide that you don’t want to participate anymore and you do not want your blood to be used in this study. Please let us know and we will destroy the sample. If your sample has already been tested at the time you change your mind, your results and other data may have already been shared with other investigators. In that case, we will not be able to destroy this data. Your data can be removed from the central repository, however. That means that no additional researchers can get your data.”

“Whether you decide to join or not to join the study, the way we look after you in this clinic will be the same. It is your decision whether to be in the study or not.”

I. Potential risks associated with the research

Even though there are only minor risks associated with collecting a blood sample, it is important that you insert a special section in the informed consent document that discusses these risks. Inserting such a section might prevent the development of misunderstandings about the project (e.g. about its role in aggravating a disease). In genomic studies, there is a theoretical possibility that people could be identified even when data is anonymised, and this might also be discussed as a risk to the study. The types of risk you may want to mention in the informed consent are:

- Risks to the individual (e.g. breach of confidentiality);
- Physical risks (e.g., risks associated with blood draw) and non-physical risks (loss of privacy).

Sample language:

“We want to tell you that there are some risks with this study. For example, there is a small chance that things might not go well with taking your blood or the information we are collecting. Most of the time when we take blood it is safe, but sometimes, when we take the blood, people feel a bit faint or may get an infection. You may also get a bruise where we took the blood. If this happens please let us know and you will be treated. One potential risk of participating in this study is that information about you may become known to people who should not have this information. There is a small risk that someone who should not have your information could learn something about you.”

J. Risks to groups and other unknown risks (e.g., group discrimination, stigmatization)

There may be unknown risks to participation that an investigator might want to share with participants. For instance, research results could have the potential under certain circumstances to be misconstrued and used to discriminate and/or stigmatize a population. Whether this is a risk may depend on the disease you are investigating and the population groups you are including in

the study. You may need to take this challenge more seriously if either the population group or the diseases under investigation are already stigmatized.

Some ethics committees may insist that such unknown risks are mentioned in the consent form, and so we have included it here for completeness. However, considering a) that most participants will already find it challenging to understand genomic research and the consent documents and b) that the nature of these risks remains elusive and the risk small, we suggest one considers leaving this section out of the consent documents. Researchers should of course remain aware of the possibility of unknown risks arising for the community or population group. Where an ethics committee insists that these unknown risks are included, the following can be used as sample language.

Sample Language:

“It is possible that when we report our study results, they will change the way others see your community. We will do our best not to let this happen, but cannot always prevent it.”

“Since your sample will be stored in an H3Africa Biobank, in the future, your blood could be used to do research that we are not able to predict with our current knowledge. If this happens there is a chance that something could go wrong and we can’t be sure how it might affect your privacy or affect your community.”

K. How participants' privacy will be protected

As is standard practice for clinical research, 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 or in password protected databases. However, before making promises that cannot be kept, it is important to think about the practicalities of ensuring confidentiality in your own laboratory. Expectations regarding confidentiality should be clearly stated. Also, investigators should think through the practicalities of assigning code numbers to samples as they are collected/ arrive in the laboratory. It also important to recognize that genomic data is unique and that it is therefore always theoretically possible that participants will be identified.

Sample Language:

“Your blood samples will be stored in a locked freezer in our laboratory and your personal information on a secure computer. Also, after they are sent to the biobank they will be stored under lock and key. But your genomic information is unique to you, and also tells us something about your family. It is always possible that someone may find out that you participated in this project. However, it is very unlikely that this will happen. and we will do our very best to ensure that it will not.”

L. Potential benefits associated with the research

With regard to benefits resulting from the research, it is important not to exaggerate. The most important outcome of H3Africa studies will be ‘knowledge’ and capacity building. Even though a cure for a disease might in 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 an H3Africa study. If you offer something in return for participation, such as nutritional supplements or food, then be brief about this (and possibly mention them under ‘compensation’ rather than benefits). Focusing too much on such benefits might lead to false inducement. The points you may want to mention in the informed consent are:

- Benefits to society;
- Likely lack of immediate benefit to participants (that the study involves research, not medical care).

Sample language:

“This study will not help you [or your children] to get better but we hope it will benefit others in the future. What we are trying to do is very difficult and could take a long time. Whether you decide to join this study or not will not affect your treatment in our clinic. Your decision to join is of your own free will.”

M. Participant compensation

This information should be optional and will depend on the budget of the grant and on national (legal or ethical) regulations about compensation. Compensation should be limited to legitimate out of pocket expenses and should not be so large as to be an inducement for participation.

Sample language:

“We would like to pay you back for the time and money spent to participate in the study. We will cover the costs of your time away from work and travel to get here today.”

N. Return of results

It is generally considered good practice for investigators to feed back general study results, but there is no consensus about whether individual genomic study results should also be fed back. The decision on what individual results to feed back, if any, is very challenging and the specific context is important to make an appropriate determination. There are a number of considerations such as whether the test done is reliable, that is has it been done to accredited diagnostic standards, as well as whether the finding is clearly linked to a disease. There are also those that argue that investigators or biobanks should only consider feeding back results indicating serious conditions that are medically actionable – but exactly what qualifies as ‘medically actionable’ in the African context may not always be clear. It will be important for the wider H3Africa Consortium to explore

what kinds of results could meaningfully be returned to participants. Our recommendations here reflect this and are deliberately generic to allow for a tailored approach to be developed.

At the least, investigators should provide participants with information about whether or not individual research results will be returned in the consent documents. If investigators plan to return any individual results to participants, is planned, it is important to describe when and through what mechanisms this will happen. The investigator may wish to consider the potential for disclosed information to confuse the participant or to cause distress. If individual research results are returned to participants then investigators need to ensure that there are clear pathways to ensure participants are referred to properly qualified and resourced professionals including genetic counselors. Careful consideration of the likely resources needed to do this effectively must be made before embarking on any projects and be presented to ethics committees for review where appropriate.

Sample language:

“When the study is finished we will share the study’s general research findings with you and with your community. We think this will take about (x time in months /years). (Investigator will need to add some language as to how this will happen, e.g., text message, in the course of care at the time they return to the clinic, etc.)”

“In general, individual results from this research project will not be given back to you or put into your medical records. “

If choosing to return results to participants, you can add:

“In some situations, the results might be important to your health or medical care. If this occurs, we will contact you to see if you want to learn more”.

Or

“If we find anything that is important for your health, we will contact you and put you in touch with doctors who can help you.”

O. Assent from children

In some studies, samples and clinical data from children may also be collected. In that case, parents or guardians will be asked for consent but children will be asked for their assent. Whether or not you need to obtain consent or assent depends on the age and maturity of the child, and is often articulated in national laws or national ethical guidelines. If children are old enough to understand the study but have not yet reached legal maturity, then you may need to obtain consent from both the child and the parent or guardian. If you are unsure about the age of assent or how to proceed, then your ethics committee will be able to provide guidance.

Sample language:

"I am X, working for the Y Research Institute. We are doing research on [Disease ABC]. We would like to know what causes this disease. Hopefully this will help us make people with this disease better in the future. We would like to ask you if you will help us with this study. If you agree, we will need to collect some blood from your arm. The prick of the needle causes some pain, in the same way as an injection. You are allowed to say that you don't want to be in the study. Nobody will be angry with you if you say no. Before you decide, you can ask us questions, or you can talk to your mother and your father about this."

6. Recording consent

Standard practice is now to document consent with a signature on a separate sheet. In some cases in the African context, this may be challenging, for instance because participants cannot write or because signatures on documents carry negative associations (of the policy, for instance). In that case, you should consider asking someone to witness the consent process and sign the consent document to confirm that the information provided was accurately explained to and apparently understood by the participant and that consent was freely given. If the participant is unable to sign the consent document, an alternative is to ask people to thumbprint the signature sheet. Sometimes, participants may not like to sign or give a thumbprint or other mark. In that case also, it may help to ask a witness (for instance, a nurse who is not involved in the study or a family member) to affirm that the participant gave consent voluntarily.

7. Beyond individual informed consent: considering the appropriateness of community engagement

Genetics and genomic research may have implications for the research participants, and may affect the broader communities and populations of which they are a part. This is because the research involves the potential for comparing allele frequencies among groups whose ancestors come from different geographic regions, sometimes in a context where societal, racial, or ethnic discrimination exists.

Thus, in some situations, in addition to obtaining informed consent from individual participants, it may be appropriate to conduct a process of community engagement or community consultation. This is increasingly coming to be seen as an important part of ethical research practice. Community engagement should take place before, during and after the study takes place. The goal of community engagement or consultation is to give an appropriate, usually broad range of members of the communities in which the research will be conducted an opportunity to:

- Obtain information about the study so that individuals will be better informed when deciding whether or not to participate in the study;
- Share their views about the ethical, social, and cultural issues the study raises for them, their immediate communities, and the broader communities and populations of which they are a part;
- Provide input into such matters as to how the samples from their locality will be collected and described;
- Remain informed about how the samples and the data are being used and about findings from future studies that use the samples or the data from individuals in their community.

In some cases, if this is not already in place, it may be appropriate to establish a Community Advisory Group or similar body to facilitate the providing of ongoing feedback about the study and about how the samples and data are being used.

8. References

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9. Recommended further reading

Books

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Articles

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Guidelines

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4. South Africa Good Clinical Practice Guidelines. Second Edition. 2006. Department of Health, South Africa. Available at: <http://www.nhrec.org.za/wp-content/uploads/2008/09/gcp.pdf>

Websites

1. National Human Genome Research Institute website on 'Ethical Issues': <http://www.genome.gov/10000006>
2. Stanford Medical School's Centre for Integration of Research on Genetics and Ethics (CIRGE): <http://cirge.stanford.edu/>

Online courses

GlobalHealthTrials have got an online course entitled '**Introduction to Reviewing Genomic Research**'. The course is free but requires registration. Those completing the course will receive a personalized certificate. The course is available here: <http://globalhealthtrials.tghn.org/elearning/other-resources/> (number 10 in the list).