In June 2014, the H3Africa Working Group on Ethics convened a consultative meeting with members of research ethics committees from across Africa to discuss ethical challenges in H3Africa research, with particular focus on issues relating to broad consent, sample and data sharing and the proposed policy framework developed by H3Africa. For this meeting, the Working Group aimed to invite a member of each ethics committee reviewing H3Africa research, including members of institutional and national ethics committees. In total, the Working Group invited members of 66 committees in 21 countries. The meeting was attended by approximately 80 people including about 60 members of about 40 ethics committees from 18 African countries. Also in attendance were a number of H3Africa PIs, members of the H3Africa Working Group on Ethics, and representatives of the two funding agencies that are supporting H3Africa research, namely the Wellcome Trust and NIH.

The meeting started with a welcome address by Dr. Fred Nakwagala, who is a member of the H3Africa Independent Expert Committee and Chair of the Mulago Hospital Research and Ethics Committee. Dr. Nakwagala emphasized the potential for H3Africa research to redefine the way scientific research is conducted in Africa, ensuring that African scientists become true partners in the global scientific enterprise. He was followed by Professor Himla Soodyall, member of the H3Africa Working Group on Ethics, who stressed the centrality of consultation and engagement with a broad range of stakeholders for the success of scientific projects. They were followed by two presentations by Professor Charles Rotimi of the NIH Centre for Research on Genomics and Global Health and Dr. Julius Ecuru of the Uganda Council for Science and Technology. Charles Rotimi gave an introduction to H3Africa research and explained the basic features of genomic research. To date, H3A research is involving researchers from over 25 countries in Africa. He identified two main bottlenecks for genomic research in Africa: first, the difficulty of getting access to high-quality samples, and second, the challenges around the capacity of African scientists to analyse genomic data. As Charles poignantly said, in his view, the main ethical challenge for H3Africa research does not lie in questions about the ownership of samples, but rather in the ownership of the intellectual capability to understand the information contained in samples. Julius Ecuru stressed that genomics research is
introducing a new way of thinking in Africa, including new ways of thinking about the ethical issues in research. Informed consent is certainly part of the challenge, but equal attention needs to be paid to issues such as respect for communities, ownership and the responsible use of samples and data, and risks and benefits of research including thinking about social value of the research. With regard to broad consent, Julius reported that Uganda is already using broad consent and this has not raised any significant ethical concerns, as long as it is embedded in a transparent and robust governance framework. Uganda operates as trusteeship model, where the sample donors retain ‘ownership’ over samples, but organisations hold samples in trust on their behalf. Also essential for broad consent to work is that it is embedded in community engagement activities.

A general questions and answers session was followed by small group discussions during which meeting participants a) raised any additional ethical challenges not identified or considered by the Working Group, and b) discussed more in-depth their views on issues relating to broad consent, sample and data sharing. Lunch was then followed with a presentation by Professor Ames Dhai of the University of Witwatersrand. Ames Dhai shared with us her experiences of developing and chairing a Biobanks Ethics Committee that only reviews applications for biobanks. Particular challenges arise from the absence of good ethical and regulatory guidance relating to biobanking research internationally as well as nationally; the open and evolving nature of biobanks, and clashes in national positions relating to biobanking research which is inevitably international in character. Instability in the political context in Africa, as well as a strong belief in traditional medicine (and therefore public unawareness or scepticism of modern medicine) create particular challenges in the African context. The presence of a good governance framework, which addresses essential questions about control, ownership, and prevention of risks, should build trust and address some of the concerns relating to biobanking. Ames Dhai’s talk was followed by a talk by Professor Akin Abayomi of the University of Stellenbosch, who introduced the H3Africa policy framework around sample and data sharing (see below).

During the question and answer sessions, the small group discussions and the talks a range of ethical concerns were raised. The main issues are discussed below, but throughout these discussions, the issue of trust was highlighted as key in addressing the ethical concerns arising at each step of the process. It features in sample collection and consent, in relations between the ethics committees and researchers, but also between ethics committees and the H3Africa biobanks and the policy framework that governs research. Importantly, participants, communities and ethics committees need to trust researchers to use samples and data properly, and researchers and ethics committees need to trust data and sample repositories to look after resources responsibly. Some participants suggested that trust may be achieved through a robust governance structure which has been informed by appropriate community engagement. The ethics consultation meeting – as a process of engagement in its own right – was also seen as an important first step in the process of building trust between ethics committees and H3Africa researchers.

(Broad) Consent

Much of the days’ discussion focussed on consent, including some discussion about how best to get consent for genomic studies. Meeting participants referred to traditional knowledge about inheritance – for instance, that particular disease traits are more common in some families – as a way to explain genomic research. The most pertinent topic of discussion, however, related to consent for sample sharing and biobanking principles. The Briefing Document that was circulated
prior to this meeting referred to a need for ‘broad consent’ – also mentioned by Charles Rotimi and Akin Abayomi in their presentations – without offering a definition of the concept. This created considerable discussion about what ‘broad’ consent means, and how it relates to open, substitute, restricted, targeted and blanket consent – other terms used by meeting participants. Open and blanket consent were taken to mean consent without any restrictions on sample use and period of storage, whereas broad consent indicates that there are some restrictions to sample use and storage timeline. Restrictions on sample use could be that samples could only be used for research on a particular (set of) condition(s), for instance research on cardiovascular disease. Meeting participants questioned whether ‘broad’ consent was still informed consent, and there was some discussion about this. Some participants argued that providing participants with adequate information about future use of samples would be considered ‘informed’. Another condition for broad consent could be that the future research use of stored samples is reviewed by a relevant ethics committee.

A concern in relation to broad consent for biobanking research is that participants must be given the option to refuse broad consent, but to agree to participate in the primary research project. If participants do not have an option to refuse sample sharing and future re-use then some of the participants felt that this could compromise the validity of consent, particularly because people often give consent on the basis of trust, not knowledge. In Uganda when broad consent is used, then people normally record consent for sample sharing and future use in a separate sheet, or in a different box on the main form. Such concerns were not articulated for data sharing, which seemed to be less controversial for meeting participants.

There was also some concern about how projects would manage changing relationships over time – for instance, consent given by children who reach the age of maturity or people who pass away – and whether there would be possibilities for those samples to be withdrawn from the biobanks. There was considerable variation in the acceptability of broad consent for research for the different meeting participants and committees or countries that they represent. Some participants indicated that their committees do not support the use of broad consent, and that their countries had developed regulations that exclude broad consent as a valid option. In addition, it was noted that clear and practical processes for withdrawal of samples from storage also take some of the heat off challenges relating to broad consent. Many of the other RECs did not have experience of broad consent and could not recall having ever reviewed studies that proposed to use broad consent.

It was highlighted that many countries have placed restrictions on the number of years that samples can be stored, either in legislation or through regulations or national and institutional guidelines. Where such restrictions exist, researchers will have to follow these and samples will need to be destroyed when the timeline expires. It was noted, however, that in the presence of a robust and transparent governance framework, destruction of samples may not always be ethically desirable. Overall, it was clear from the discussions on consent for biobanking research that there is an urgent need for further empirical work in this field. Such work should explore the views of a variety of stakeholders including research participants, ethics committee members and policy makers, investigate what they understand broad consent to be, and outline the criteria under which broad consent can (not) be used in medical research in Africa.

Community Engagement

Community engagement was identified by multiple meeting participants as being of key importance in ensuring ethical conduct in health research in Africa. Community engagement was considered as an integral component of building trust in the researchers and project. It was considered particularly
important in the case of biobanking research where broad consent for secondary sample use is used. In those cases, community engagement could be one way of understanding what future types of sample use are appropriate, and to keep the link with original sample donors alive (through the communities they belong to). It was considered important to understand past and present experiences with community engagement for genomics research in Africa – a project currently undertaken by the H3Africa Working Group on Ethics – and to foster empirical research to understand the role it could play in biobanking research.

**Stigma and discrimination**
The potential for genomic research to stigmatise communities and patient groups was raised as a concern by several participants as a risk. It was emphasized that this needs to be better understood as a concern. Suggested solutions were a) encouraging of ‘responsible reporting’, possibly with development of a responsible dissemination plan, and b) careful discussion with either the communities or populations involved in the research to understand the most appropriate ways to refer to/name them.

**Governance framework for biobanking research**
What became exceedingly clear during the meeting is that in order for deposition of samples in biobanks to be acceptable for ethics committees, research needs to be accompanied by thorough community engagement and embedded in a robust and transparent governance framework. Such a governance framework would inspire trust, optimise beneficial use of samples and prevent harm. Meeting participants identified particular essential elements of the governance framework that they would like to see in place. These were:

- Clear mechanism for withdrawal of samples from the biorepository;
- (Annual) monitoring mechanism for RECs to know the status of the samples;
- Compliance with local and national guidelines and regulations;
- Plans for sustainability of the biobanks;
- Transparency over IP arrangements, commercialisation of samples and data and ownership over samples.

**Policy Framework for H3Africa**
Akin Abayomi in the afternoon gave a presentation about the current proposed policy framework for H3Africa research, which includes policies for data and sample sharing. The current proposal is that H3A genomic data will be submitted to a central data repository within a year after it is generated. It will be under embargo for a further twelve months, so that African researchers will have two years in total to publish their analyses of data. Samples will be made available through the H3Africa biorepositories two years after they were submitted. After that, for three years they will be made available either to researchers based in Africa, or to those outside of Africa who collaborate with researchers in Africa and who articulate a clear plan for capacity development. The proposal is that there will be one committee – the Data and Biospecimen Access Committee (DBAC) – to grant data and sample access for all (3 or 4) H3Africa biorepositories. The DBAC will be composed of members who are (preferentially) based in Africa, or with experience of conducting research in Africa. Sample access will be aligned with informed consent and conditions stipulated by the ethics committees ‘on record’ (i.e. the committees that originally approved sample collection). Access will only be granted to researchers with ethics approval that they obtained from their ethics committee of choice (e.g.
the committee at their institution). For practical reasons, it has been proposed that the ethics committees on record will not be contacted to approve secondary sample access, unless this is a specified condition of the ethics committee that originally approved sample collection.

Overall, the policy framework developed for H3Africa sample and data sharing seemed acceptable to the meeting participants, with expressed recognition of the work that has gone into developing it. There was some discussion about the proposed timeline for granting exclusive access to African researchers. It was suggested that African researchers should be collaborators on all future studies, including ones that are approved after the three year period expires. Overall the policy framework seemed to offer a good starting point. It was recognised throughout the meeting that a robust and transparent governance framework is of key importance in establishing trust between researchers, ethics committees, policy makers and communities that participated in research.

Considerable discussion arose about whether it is appropriate that the original ethics committees that approved sample collection, are not to be involved in subsequent sample access decisions by the biobanks. Many participants felt that this is not an appropriate model. On the one hand, there was recognition that an overly restrictive system would prevent effective sharing of the samples, thus slowing down African-led research that could benefit patients in Africa. On the other hand, there was a recognition of the importance of involving local ethics committees in secondary sample access decisions. Several suggestions were made to resolve this, for instance by ensuring annual feedback to the ethics committees about the sample sets that they originally approved, by establishing a pan-African ethics committee that could consider issues at a continental level or by identifying which ethics committees would specifically want to be consulted about access decisions for samples the collection of which they initially approved. There was also a question about who appoints the DBAC members and whether the composition will be representative enough to protect the interest of research participants across the continent. Currently, the H3Africa Consortium is considering these discussions and is amending the policy framework to reflect these discussions. Further consultation with ethics committees will be required to ensure the final mechanism is broadly supported by all ethics committees. The sharing of data seemed less controversial.

**Training Ethics Committees**

Throughout the day, the need to train ethics committees in the review of genomic and biobanking research was emphasized repeatedly. Training would need to focus on:

- Explaining what biorepositories/biobanks are, and what ethical challenges they raise. These include:
  - Broad consent
  - Community engagement to support the biobank
  - Ownership of samples;
  - Regulation of sample access, including relations with the ‘IRB on Record’;
  - Governance framework.
- How those challenges need to be considered;
- The documentation to be reviewed by a REC;
- Ongoing monitoring of biobank operations.

Training would need to be extended to both Francophone and Anglophone countries. It is not exactly clear what the best model for this would be: in person or online training, at regional or
national workshops, targeting entire committees or individual members. It is also not clear whether and how the H3Africa Working Group on Ethics can facilitate the development and delivering of such training.

In addition to building capacity in ethics review, there was also some discussion about the need to build the ‘ethical reflection’ capacity of researchers and their moral integrity – so that ethics becomes integral to doing good science.

**Building ongoing links with and between ethics committees**

It became clear during the day that there is real value in bringing together ethics committees from across different countries and regions, particularly in enabling exchange of experience and guidelines. It was considered really important that the Working Group collects documents, guidelines and experiences for and with biobanking and genomics research from the various meeting participants, and distribute these to the group.

**Main meeting outcomes**

1. Overall, there was widespread support for the ethos and aspirations of H3A, and the meeting managed to build a greater understanding of the goals, ambitions and policy framework of H3Africa;
2. Many of the more ‘traditional’ ethical issues – for instance relating to inducement and voluntariness in informed consent – are also pertinent for H3Africa research. They are not new issues in research, but affect the way in which H3A research happens on the ground and need to be taken into consideration;
3. H3Africa has the ability to make African researchers true partners in global health research and to be world leading in the way in which ethics and science can work together. It also gives African people an opportunity to contribute to the global good, by contributing knowledge beneficial to all of humankind. The banking and sharing of good quality research samples is central to this aim;
4. The lack of regulatory infrastructure in this area gives a wonderful opportunity for science and ethics (and law) to co-evolve. Ongoing discussion and consultation with and between stakeholders is essential for this to happen effectively. It will also be important for H3Africa researchers to engage with the African Union to develop a sample regulatory or legislative framework for adoption by its members;
5. African researchers can become global leaders in relation to questions around community engagement and how it can support genomics and biobanking research;
6. Broad consent for biobanking research may be acceptable for use in Africa, provided that it is embedded in thorough mechanisms of community engagement and a robust and transparent governance structure that prevents harm to and protects the interests of participants and their communities, and ensure appropriate benefit sharing. Also important is a feasible mechanism for withdrawal of samples from the biobanks;
7. There is a need to consider how ethics committees ‘of record’ can be involved in secondary sample access decisions, for instance through annual reporting, the identification of particular areas of research or committees that require consultation or through other means. This will require a revision of the Terms of Reference of the Data and Biospecimens Access Committee.
**Action Items**

1. Continue the process of engagement between H3Africa researchers and ethics committees that was started in this meeting through regular communication, sharing of materials and further consultation on topical areas of debate in H3Africa;

2. Update the H3Africa Guidelines for Informed Consent and provide clear definitions of the spectrum of informed consent, including of broad consent;

3. Review H3Africa policies on Sample and Data Sharing in light of the discussions at the meeting, and specifically reconsider the relations between the DBAC and ethics committees on record. This includes developing a clear plan of reporting back to ethics committees about sample access decisions and identifying which ethics committees specifically want to be consulted about secondary access requests;

4. Develop a clear and practicable plan for withdrawing of samples from the H3Africa biorepositories;

5. Collect and catalogue experiences and documents pertaining to genomics and biobanking research from across Africa, and share these with the meeting participants;

6. Explore funding opportunities and feasibility of developing and delivering training opportunities in the review of genomics and biobanking research for research ethics committees in Africa;

7. Foster, in as far as possible, academic dialogue and research on ethical issues raised by H3Africa. Topics of research should include broad consent, biobanking research, and the role of community engagement in supporting genomics and biobanking research in Africa.

The Human Heredity and Health in Africa (H3Africa) Consortium and its meetings are funded by the National Institutes of Health and the Wellcome Trust.