Ethics and Governance Framework for Best Practice in Genomic Research and Biobanking in Africa

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Preamble

The number of genomics research and biobanking projects taking place on the African content is growing steadily. A critical feature of such research is the broad sharing of data and samples for secondary use by investigators who were not originally involved in their collection. Such 'open science' holds considerable potential for facilitating scientific discovery but it also evokes important ethical challenges that need to be addressed for its successful implementation, not least where research takes place in the African research context, which evokes questions about equity and fairness. Whilst the ethical and regulatory constructs to allow sharing and re-use of scientific resources are being developed, it is not surprising that the ethical review and regulatory infrastructure in Africa does not yet accommodate sharing and secondary use. Yet African people's broad genetic diversity could be a key to addressing the high burden of disease in the continent and Africa offers many unique opportunities to advance an ethic of sharing. This Framework aims to set out the principles and actions that should be considered as pertinent ethical concerns for genomic research and biobanking in Africa.

The Framework takes account of pertinent concerns raised regarding scientific and medical research in Africa. One such concern is the perception that research collaborations have been largely unfair for African researchers and participants. This Framework seeks to foster a progressive regulatory ethos that will empower African research participants, communities and researchers to engage with, and benefit from, genomic research and biobanking in a fair and mutually beneficial manner.

This Framework is inspired by communal or solidarity-based worldviews that are important in many African countries. Such worldviews recognize that individuals are shaped by their relations to people around them, and emphasize respectful and harmonious relationships between individuals. It places central importance on reciprocity, consultation and accountability as key ethical values. This worldview would suggest that sharing to contribute to the ultimate wellbeing and humanness of others would be broadly supported in Africa. But such sharing must always be matched with reciprocity – i.e. as much as the individual contributes to the community, the community also contributes to the individual's sustainable wellbeing. Similarly, sharing should happen responsibly, with input from all those affected and with mechanisms by which to hold research teams accountable. By supporting genomics research in this way, African populations could contribute to cutting edge research, which, though expensive at the moment, has strong potential for better returns in reduced health care costs from diseases amenable to improved control as a result of a better understanding of their genomic determinants.

Purpose

The purpose of this Framework is to provide a principled and practical approach to promote best practice for genomic research and biobanking in Africa. In recognising that the standards and principles outlined here may not be currently achievable in all countries and may need to be adapted to the local context, its primary goals are to:

- Promote responsible conduct of genomic research and biobanking in Africa that fosters shared decision making, accountability, transparency and fairness;

- Guide development of national regulation for genomic research and biobanking in African countries that will promote social value and maximize benefits to African scientists and nationals who engage in biobanking and genomics research;
- Provide a framework for evaluating the ethical soundness of genomic research and biobanking by ethics review committees across the African continent.

Intended Audience

This Framework is intended to support all stakeholders involved in the design, conduct, participation, regulation and ethical review of genomic research and biobanking across the African continent. This includes research conducted in Africa by African and non-African researchers as well as research on African samples and data conducted outside of the continent to the extent that this is feasible. More specifically, the Framework is intended to inform the development of national (African) regulation of biobanking and genomic research, for instance through its endorsement by stakeholders at national levels or by incorporation into national ethics guidelines and contract templates. Furthermore, it is envisaged that the Framework would be considered by scientific organisations and research programmes involved in conducting African genomic research and biobanking, as well as sponsors and funding organisations.

Whilst the Framework offers generalized guidance on what should constitute ethical best practice for genomic research and biobanking in Africa, we recognise the importance of ensuring that what happens on the ground in genomic research and biobanking is appropriately adapted to local cultures, languages, practices and national legal frameworks. We therefore strongly encourage stakeholders to consider how the principles and elements set forth in this Framework can be adapted to best suit particular local research contexts.

Core Principles

- Research should be sensitive to and respectful of African values and cultures;
- Research should be for the benefit of African people recognizing that it likely also yields benefits to the global population;
- Research and the dissemination of data in publications should take place with genuine and active intellectual participation of African investigators and other African stakeholders;
- Research should promote ways of relating typified by respect for individuals and communities, fairness, equity and reciprocity.

Elements

African intellectual leadership

Considering that the primary objective of African biobanking and genomic research should be to benefit African people, the contribution of scientists based at African institutions should be meaningful and substantive, and include effective intellectual leadership or co-leadership.

Note: We recognise that achieving this requires support from political and traditional leaders. Political and traditional leadership in Africa needs to be made aware of biobanking and genomics research and help to ensure sustainability and strengthen capacity. African organizations such as the African Academy of Sciences (AAS), the African Union (AU) and the New Partnership for Africa's Development (NEPAD) should play a key role in mobilising funding and resources and creating awareness.

Consent

One of the important advantages of genomic research and biobanking lies in the ability for samples and data to be re-used by investigators not involved in the original collection of these resources. In order for this 'secondary use' to be effective, the samples and data need to have been collected with consent that allows for such sharing and re-use. Broad consent can be defined as consent for the use of samples and/or data for unspecified future studies, but with conditions. These conditions can involve for instance a restriction on the types of studies or diseases that samples/data can be used for; a specified oversight and approval process for future use; ongoing consultation with sample donors about future use, if possible; and a process allowing participants to withdraw samples or data from the storage facility that holds them. Broad consent is acceptable in most African countries, at least in the sense of ethics guidelines and legal infrastructure and can be an ethically appropriate consent model if used responsibly. Most importantly, care should be taken to explain genomic research and biobanking, and their implications, to research participants in the consent process.

- Broad consent should be the consent model of choice to be used in genomic research and biobanking. This can include tiered consent where participants select different options for use of data and samples using tick boxes;
- Broad consent needs to be accompanied by thorough information and communication processes to ensure participant comprehension and voluntariness, and should be supported by community engagement activities;
- Broad consent should only be used in conjunction with appropriate safeguards outlined in a governance framework (see Section on Good Governance below), which provides an additional layer of protection for participants;
- Ethics review in Africa is a condition for re-use of samples and is essential in ensuring the responsible use of samples in future research;
- Broad consent is not the same as unrestricted (open/blanket) consent, and there may be legitimate reasons for restricting secondary use of samples and data to for instance certain disease categories or user groups. Such conditions on sample and data use should be outlined early in the research process and incorporated into the consent documentation. Potential restrictions on sample re-use should be ethically justifiable to an ethics committee;
- Researchers should consider whether and to which extent it will be possible for participants to withdraw from study participation, and details on whether and how this can be done should be provided to the participants during the consent process.

Community Engagement

Genomic research and biobanking have implications not just for individuals but also for their families and communities. Community engagement is a process of informing, consulting and actively involving relevant communities that have a legitimate interest in the research process. In many African contexts, individuals often take decisions in consultation with family, friends and community members. Frequently, there are also clear authority structures that must be respected in the engagement process such as permission from village chiefs and elders. In genomic research and biobanking, community engagement offers an important opportunity to:

- Build respect and trust between research teams and the respective communities;
- Demonstrate respect for the ways that people may have chosen to commune with one another;

- Identify and incorporate the collective legitimate interests of the community, community values and concerns in the research process;
- Seek community support for research processes, particularly on issues relating to the storage and re-use of samples;
- Strengthen or facilitate the consent process by providing information over time and support the use of broad consent in genomic research and biobanking;
- Discuss and address community concerns and misconceptions about research and be available for further enquiry by community leaders over time;
- Disseminate information on genomic research and provide feedback of research results.

In this respect, community engagement must be an integral part of all genomic research and biobanking in Africa. In order to be done well, researchers should take time to become acquainted with the community, its culture and other relevant dynamics that need to be taken into consideration in the design of context-specific research processes. Research institutions, and not just individual researchers or research teams, also play an important role in this regard. The institutions need to build trust with the community and should be seen to be serving the interest of all stakeholders, including communities involved in research. In conducting community engagement for genomics and biobanking, the following key points should be taken into consideration:

- Goals and process of community engagement should be clearly defined;
- Target group/community should be clearly defined with sensitivity towards the possibility of some groups within a community being unrepresented;
- Community engagement strategies should be appropriately planned and designed in a collaborative process at the start of the research project;
- The impact of community engagement efforts should be appropriately evaluated;
- When researchers are not originally from the communities where research takes place, then translators should be available as necessary.

Ethics review

Ethics review of proposed studies is one of the cornerstones of human research protection; promotes ethical conduct of research while providing assurances to the public that their welfare is being well taken care of as they contribute to knowledge and development. The role of ethics committees is particularly important when research involves vulnerable people and communities. Many people in Africa continue to live in areas that are characterized by a high burden of disease, poor access to basic necessities and healthcare, low average income and literacy levels compounded by unfamiliarity with biomedical research generally and genomic research specifically. In these cases, ethics committees play an important role in safeguarding their interests.

- All new genomic research and biobanking studies must be reviewed by a competent ethics review committee based in the country where samples are collected or stored;
- Ethics review in Africa is a condition for re-use of samples and is essential in ensure the responsible use of samples in future studies. Research studies proposing to use samples derived from primary genomics studies also need to be reviewed by an ethics review committee(s). Depending on country regulations, this could be the primary approving ethics

committee or by another ethics review committee. An example of the latter could be a committee linked to a biobank, or the institutional committee where secondary use will take place. Where an ethics committee other than the primary review committee approves secondary sample use, then there should ideally be a mechanism for feedback to the primary approving ethics committee about secondary sample use;

- In addition to ethics review, sample users also require approval by a sample access committee or a relevant authority designated to undertake similar functions;
- Research studies that only involve the use of data from genomics studies should be timeously reviewed by data access committees with periodic feedback provided to the primary approving ethics committee(s);
- Mechanisms that support joint review or reliance on the review of one REC in a collaborative study should be promoted.

Avoiding group harm or stigma

Africa is home to a vast number of population groups characterised by unique languages, cultures and belief systems, some of which may be marginalised or discriminated against. Similarly, research may involve groups of people suffering from stigmatised conditions or outlawed and stigmatised behaviours, phenotypes or lifestyles. The reporting of genomic research results involving such groups has the potential to aggravate existing stigma or marginalization, or even punishment, for individuals belonging to these groups.

- Investigators should relay to potential donors and ethics committees any likely risk that re-use of samples or data could aggravate group harm or stigma before research is conducted;
- Where concerns about stigma are linked to the sharing of genomic materials and samples, for instance because important contextual information about existing stigma may not be shared with secondary users, or because the interpretation of results requires researchers to be knowledgeable of group dynamics, researchers should liaise with relevant stakeholders (including ethics review committees, funders, and community representatives) to discuss the appropriateness of sharing data and samples, and to identify any limitations to secondary use;
- Where there are concerns about stigma and to the extent possible, individuals from the countries and/or institutions where samples were collected should be involved in secondary research projects to ensure appropriate interpretation of research results, capacity building, and potential translation of pertinent research findings into health policy and clinical practice;
- Researchers should always be mindful of how communities and population groups are described and identified in research publications, and be aware that some descriptions could be perceived to be prejudiced or stigmatising. Where possible, and where there is an identified risk that research could increase stigma, the researchers should consider possibilities to obscure the group identity, for instance by only referring to the broader population that the community is part of, or by not naming particular locations for sample collection;
- Researchers should consider the role that community engagement could play in managing some of the stigma-related risks that may arise.

Benefit Sharing

The main benefits of genomic research and biobanking in Africa should be health and welfare benefits to African populations, as they are shouldering the research burdens and risks. Benefit sharing regulates that benefits and burdens are distributed fairly and it is therefore key to ensuring that research collaboration is fair. The benefits of genomic research and biobanking can be thought of as those arising from the use, whether commercial or not, of genetic resources or biological samples, and may include both monetary and non-monetary returns. What constitutes benefits for different stakeholders is influenced by their particular needs, values and cultural expectations and could therefore take varying forms, for example sharing information on results arising from the use of resources in the biobank with study communities, research capacity building, or the sharing of profits in cases where genetic research leads to commercial products or where samples are sold at a profit.

- Feedback of general study results to research participants is a benefit, which can be expected in all types of research;
- In cases where there are realistic expectations of tangible benefits that will accrue to an identifiable group (e.g. a biobank), a benefit sharing arrangement should be discussed and agreed with relevant stakeholders, which normally should also include those individuals that participated in the research project. Representatives of local communities should be involved in those discussions;
- Where there are no expectations of tangible benefits arising as a result of research, researchers should explore other ways in which genomic research and biobanking may confer benefits on research participants and their communities. These could take the form of social recognition, support for local infrastructure, feasible ancillary care for diseases discovered in the course of a study and capacity building (see below);
- In all cases and to the extent possible, researchers should clearly articulate expected benefits associated with research, and consider how research participants and their communities are likely to partake in such benefits. This involves ensuring that no unrealistic expectations are raised, especially about monetary benefits.

Capacity building

It is of key importance that genomic research and biobanking conducted in Africa lead to substantive building of research capacity, including both human resources and research infrastructure. The building of a critical mass of scholars in genomics and biobanking is an essential component in ensuring the sustainability of these research approaches in Africa. Similarly, such a critical mass is needed to ensure that this research can be conducted by African teams and under African intellectual leadership in the future. The expectation is that this would ensure that research is responsive to the health needs of Africans, is sensitive to African ethical, legal and social issues, and that there is a stronger avenue for implementation of relevant research findings into clinical practice.

- Projects should have a clear plan for capacity building in all aspects of genomic research and biobanking, not just through training of junior staff members but also by supporting (the development of) more senior academic staff and through development of infrastructure. Such plans should arrange for project members based in Africa to be involved in all aspects of genomic research and biobanking, including in sample processing, data generation and

analysis, and preparation of manuscripts for publication, in which they should be granted co-authorship;

- Where absent, studies should build leadership capacity for senior project members, empowering them to actively participate in all aspect of genomic research and biobanking;
- Similarly, projects should build capacity in financial grant administration, ensuring that institutions will in future be able to hold and manage their own grants;
- Capacity building should also focus on career development in science, bioinformatics, and entrepreneurship in the public and private sector. The latter is particularly important in countries with high unemployment rates, where graduates struggle to find employment;
- Capacity building of ethics committees will ensure thorough and appropriate review of genomics and biobanking studies;
- Capacity building plans should also be a part of proposals involving secondary access to research samples collected in the African research context.

International Collaboration and Export of samples

Genomic research and biobanking is collaborative in nature and often involves the collection and analysis of huge amounts of human biological samples and associated data across different research sites and countries. In some cases, projects require the analysis of these samples outside the countries where they were collected. In other cases, data or samples donated by African research participants may be kept and distributed by entities outside of the continent. International sample export can happen both within Africa and outside the continent. These research practices can sometimes raise concerns and tensions between collaborating researchers and/or institutions.

- International collaboration and export of samples should promote the goals of reducing global health inequality and exploitation and strengthening the research system in the country where the samples were collected;
- The rationale for sample export should be clearly justified in the research protocol and be reviewed by the relevant research ethics committee. This would include how many samples will be exported, the recipients of the samples, the purpose of export and how the status of exported samples would be monitored as well as plans for archiving and/or destroying samples;
- International collaboration and sample export should provide opportunities to strengthen the capacity of local African researchers through their meaningful involvement in all aspects of research collaboration. For instance, this could include the training of a student or staff member in procedures occurring overseas, involvement of investigators in data analysis and in manuscript preparation. This involvement should not be tokenistic but substantive, preferably with African researchers in (joint) intellectual leadership roles;
- The rationale for sample export should be clearly described in informed consent documents;
- Template consent documents need to be included when samples are exported to ensure that the interests of sample donors are taken into account in the analysis process and in potential secondary use of samples;
- There should be clearly defined and agreed upon material transfer agreements (MTAs) between the collaborating institutions. African researchers should not take the content of the MTA for granted; they should be aware how to negotiate the terms of the MTAs so as to safeguard their interests;

- Pertinent African stakeholders (including relevant ministries or biobanking organisations) should develop procedures that allow for regular updates on the status of exported samples to research ethics committees based in the countries where the samples were collected.

Feedback of individual genetic research results

The feedback of individual genetic research results is a topic of considerable debate in the international research context. As this debate has scarcely been extended to the African research context, efforts must be made to initiate such a discussion on the continent. The African research context generates strong ancillary care obligations, which also extend to decisions about whether individual genetic research results should be fed back to research participants. Challenges relating to the feedback of findings in the African research context relate to difficulties of validating research findings in a diagnostic facility, the absence of healthcare workers trained in genetics that could provide feedback, and limited validation of genomic research findings in African populations. Whilst the detection of actionable variants is expected to be rare, it is important that the African research community considers what is to constitute best practice for feeding back individual genetic findings.

- Pertinent African stakeholders, including medical genetics healthcare professionals, medical genetics researchers, ethicists and other relevant actors, should come together to develop a context-informed approach to whether and under what conditions individual genomic research findings ought to be fed back. The considerations that should feed into such an approach relate to, for instance:
    - what findings are to be considered 'actionable' in the various healthcare contexts;
    - which findings have been sufficiently validated for the various populations;
    - how feedback should be done and by whom, particularly in the absence of genetic counsellors;
    - what researchers would reasonably be expected to do w.r.t. feedback of findings;
    - how obligations for the feedback of genetic research results should be considered in the context of biobanking and genomics research;
    - whether it is ever advisable to return individual genetic research results without diagnostic validation, considering that there are scarce opportunities for diagnostic validation across the continent.
- Until national policies are developed about the feedback of individual genomic research findings, researchers should develop a plan for how to manage genetic variants with strong scientific evidence that are associated with disease causation. This plan should be included in the research protocol and consent documentation and should be specifically reviewed by the ethics committee;
- Where possible, researchers should work with international collaborators to develop modalities and language for feeding back results. This could include, for instance, the use of internet-based communication methods to feedback results as has been successfully done in some cases. Similarly, researchers should also explore possibilities of using diagnostic facilities outside of Africa to validate research results, particularly if projects involve international collaborations;
- Every effort should be made to ensure that pertinent findings are translated into population-specific diagnostic assays/tests in cases where current and often Euro-centric assays/tests are inadequate in the African settings.

Good Governance

Good governance is a precondition for working with integrity. It helps to build and maintain public trust by making provision for issues of accountability of researchers, confidentiality of participants and transparency of the system from sample collection through to storage, future use of data and samples and feedback of findings. Involving the community in the development and evolution of the governance framework can promote trust and a trustworthy research culture. There are important ethical concerns around sample and data sharing and their appropriate use following broad consent. Good governance ensures the application of ethical principles and responsible use of stored samples and data in line with the consent permissions from study populations and other relevant authorities, while maintaining and upholding public trust.

- The governance framework supporting African genomic research and biobanking should be responsive to the core principles set out in this Framework. The governance framework should promote fairness, reciprocity and accountability, foster trust and integrity, and promote African intellectual leadership and capacity building;
- The governance framework needs to articulate a mechanism for review by an oversight committee to provide permission for the re-use of samples and data;
- Researchers, biobanks and institutions at which samples and/or data are stored should comply with national and international guidelines and/or regulations that govern data and sample access that lead to wide-spread data sharing without disadvantaging researchers;
- For international biobanks, entities charged with controlling access to samples and data derived from African countries, such as Sample Access Committees and Data Access Committees should be primarily constituted by members residing on the African continent, international researchers with expertise in sample sharing and data access as well as researchers working in Africa or on African samples;
- Sample and Data Access decisions should be sensitive to the need to promote genomics scholarship from African scientists and make provisions that allow for preferential use of data and access to samples for such scientists for a reasonable period of time. Provisions should however be balanced with the risk of over-protection which may hinder good science and any potential benefit to humanity derivable from it;
- Sample Access Committees and Data Access Committees should communicate regularly with the ethics review committees with primary ethical oversight of the samples and data being overseen by the SAC and DAC, thus enabling the ethics committees to know what is happening with the samples;
- Unnecessary bureaucracy surrounding research governance and oversight should be reduced to the barest minimum. We recommend centralisation of access review requests and promoting ethics review equivalency (particular as pertains to secondary access requests);
- MTAs/DTAs/research contracts should outline directions for handling commercialisable outputs including benefit sharing arrangements.

Implementation mechanisms and amendments

This Framework should be considered as the basis for locality-specific guidelines by organisations and bodies involved in African genomic research and biobanking, either those based in Africa or elsewhere. Particularly, the Framework is relevant to researchers, ethics committees, communities,

governments and funders involved in the ethics review or regulation of genomic research and biobanking in Africa. Ideally, the framework should be the basis for further discussions and engagement with regulators, researchers and bioethicists across Africa. The Framework is recommended to scientific entities including for instance the African Academy of Sciences, H3Africa, B3Africa and other similar organisations, collaborations or projects. The H3Africa Working Group on Ethics can facilitate the further development of country-specific guidelines and can be contacted through the H3Africa Coordinating Centre. It will track the development of country-specific guidelines for genomics research and biobanking; where available, identify cases studies on the use of the Framework in the development or review of national guidelines and make these available online for possible use by other countries, while respecting any restrictions to sharing.

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