H3AFRICA CONSORTIUM BIOSPECIMEN SHARING, ACCESS AND RELEASE POLICY

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Background

The goal of the Human Heredity and Health in Africa (H3Africa) Initiative (http://h3africa.org/) is to enhance the capacity of African researchers to conduct state of the art genomics research, to advance understanding of the genetic and environmental determinants of common diseases in Africa and to use this knowledge to improve the health of African populations. The H3Africa biospecimen sharing, access and release policy is built upon H3Africa principles of ethics, governance and resource sharing that have been established by the NIH and Wellcome Trust (http://h3africa.org/ethics_governance_resourcesharing.cfm) and the H3Africa consortium members. These principles aim to strike an appropriate balance in ensuring that adequate safeguards are in place to protect participants, while maximizing the ability of investigators to advance research.

The H3Africa project was initiated by the Wellcome Trust and National Institutes of Health to determine the underlying genetic predisposition to diseases in diverse African populations while building capacity. It is envisioned that all sharing of biospecimens should take place within the context of these aims. The principles for sharing both data and biospecimens, therefore include:

- Maximizing the availability of research materials, in a timely and responsible manner.
- Protecting the rights and privacy of human participants who took part in research studies.
- Recognizing the scientific contribution of H3Africa researchers who developed cohorts and collected biospecimens.
- Considering the nature and ethical aspects of proposed research whilst ensuring the timely sharing of resources
- Ensuring the deposition of genomic and related data (for example, epigenetic and DNA methylation) derived from H3Africa biospecimens in existing public, managed access data repositories whenever possible.

General Guidelines

The H3Africa Initiative is committed to providing DNA biospecimens generated by the H3Africa research projects to the research community. The H3Africa funders require that data and biospecimens generated by the H3Africa consortium projects are publicly accessible, with access controlled by the H3Africa Data and Biospecimen Access Committee (Appendix C). H3ABioNet, together with members of the H3Africa Biorepositories and research projects have developed the H3Africa Data and Biospecimen Catalogue -for searching H3Africa metadata and samples. The aim of the catalogue is to allow users to identify datasets, along with their EGA accession numbers and matching biospecimens. The sets of interest (data or biospecimens or both) can then be requested via an Access Request Form submitted to the DBAC (Appendix D). Since considerable attention has been paid to the accompanying genomic and metadata as this annotation adds considerably to the value of the biospecimen, it is thought that the biospecimen and data will be sought simultaneously.

Presently, only DNA biospecimens are available from H3Africa Biorepositories. Most DNA biospecimens contain high molecular weight human DNA in aliquots of at least 50 µl of 100 ng/µl DNA. In some cases, volumes and concentrations are lower than this and will be noted in the H3ABioNet Data and Biospecimen Catalogue description.

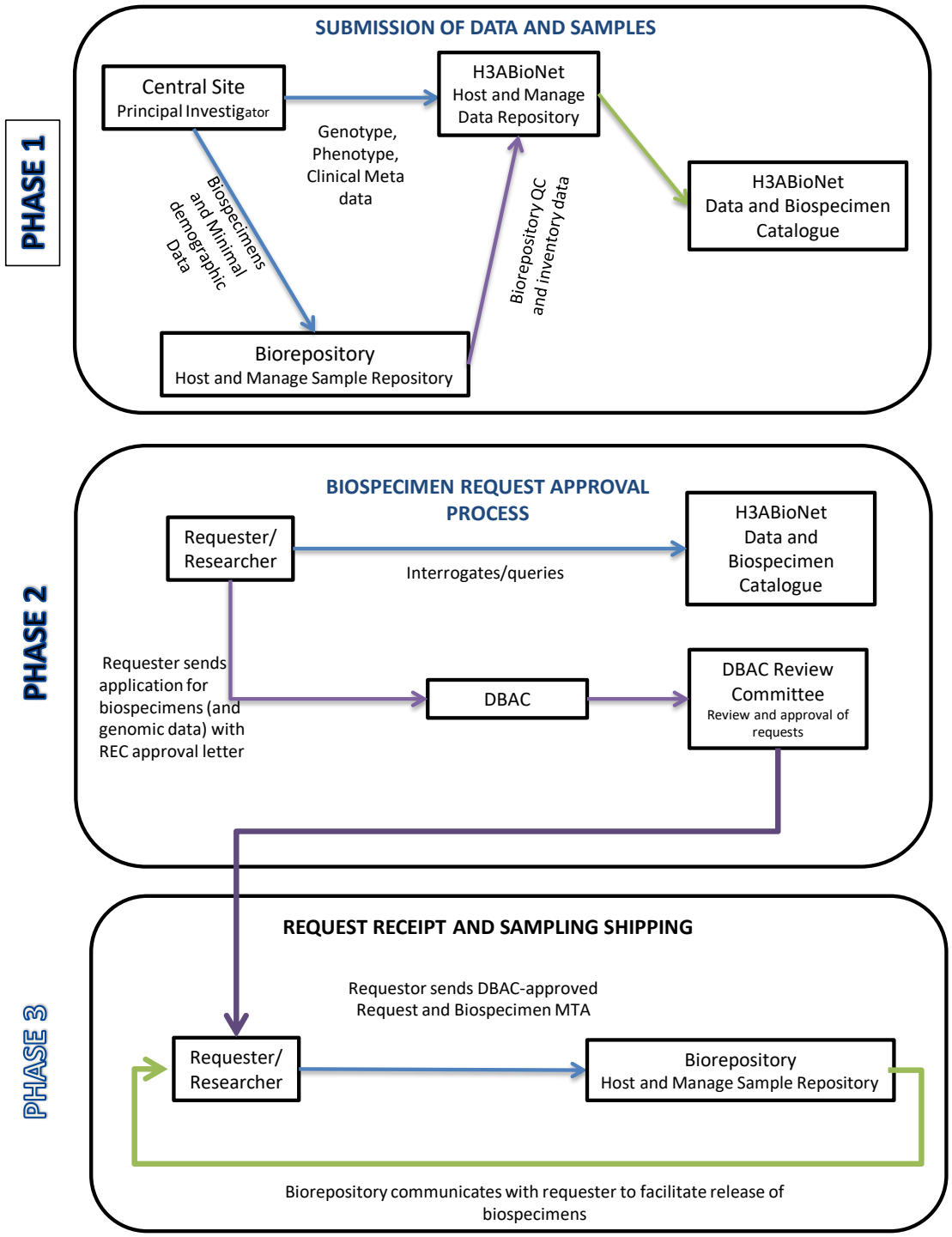
During the first three years of a biospecimen's availability, the DBAC will prioritise release of biospecimens to applicants who seek to use the biospecimen in collaboration with African researchers and who aim to build African research capacity and capabilities. After this restricted period, the biospecimens will be released to the international scientific research community according to the DBAC guidelines.

In compliance with current international standards to protect participant confidentiality, data generated from H3Africa biospecimens are expected to be shared with qualified researchers via established controlled access processes at the European Genome-phenome Archive (EGA). Please consult appendices F and G for additional information regarding data protection policies and procedures.

Note, investigators generating microbiome/metagenomics data from the H3A biospecimens can choose to deposit these data in open access databases; but if they do so, it is important that any human sequence contamination is removed prior to submission. In addition, all phenotype data associated with participants remains in the EGA.

The process and lifecycle of an H3Africa Biospecimen is shown in Figure 1.

LIFE-CYCLE OF A BIOSPECIMEN



Biospecimen Access

Potential biospecimen users will be required to provide a summary of their proposed research (see Biospecimen Access Request Form in Appendix E) and, in the first three years of biospecimen availability, a statement of collaboration from an African scientist at an African institution as well as a statement of the benefit of this research for the African continent. The review of requests will include screening for appropriate use and ensuring that proposed use complies with the ethical consent associated with the biospecimens. Access decisions will be based on the description of the research presented in the Biospecimen Access request and its potential value to African health and/or research capacity building in Africa. While there will not be a rigorous scientific/peer review of the research proposal, it is expected that use of the biospecimen not be duplicative; i.e., if certain data from that biospecimen, such as whole genome sequence, are already publicly available, the biospecimen will not be approved for use to generate equivalent data without strong justification, such as new and improved methodology. DBAC will also check for overlap of the requestor's research with pre-approved future work by the primary H3A principle investigator. Complete information (for example, applicant(s) names and institution(s) and the research proposal) on projects for which biospecimen access has been granted will be made available on the H3Africa or another appropriate website.

Approved biospecimen users will be required to agree to the Terms and Conditions of a Material Transfer Agreement (MTA), which aims to protect the privacy and interests of the research participants as it governs the terms and conditions under which access will be granted. The MTA will require users to agree to:

a) Use the biospecimen only for the approved research;
b) Inclusion of a Research Ethics Committee-approved protocol
c) Protect participant confidentiality and not attempt to identify individual participants from whom biospecimens were obtained;
d) Follow appropriate security protections;
e) Follow all applicable laws, regulations and local institutional policies and procedures for handling human biospecimens;
f) Not sell any of the H3Africa biospecimen; including any material incorporated in progeny or modified/unmodified derivatives (for example, fractions or aliquots, products of whole genome amplification or PCR)
g) Not share with individuals other than those listed in the request any of the biospecimens obtained from the H3Africa biorepository;
h) Allow the listing of a summary of approved research uses on the H3Africa or another appropriate website along with his or her name and organizational affiliation;
i) Report, in real time, any violations of the H3Africa Biospecimen Sharing, Access and Release policy to the DBAC Secretariat as identified in the H3ABioNet Data and Biospecimen Catalog;
j) Adhere to the H3Africa policy with regard to publication and intellectual property;
k) Acknowledge the H3Africa Consortium in any publications arising from the acquired biospecimens;

l) Provide annual progress reports and publications on research using the biospecimens. This information may be shared to third parties or on a public facing website at the discretion of the H3Africa DBAC Secretariat.
m) Submit genomic and related (e.g., epigenomic) data generated from the biospecimens to EGA under the H3Africa project via H3ABioNet.

The MTA must be signed by a responsible institution official (e.g. a representative of legal, intellectual property, scientific ethics or similar offices) must sign a Material Transfer Agreement (MTA) on behalf of the recipient institution. In addition, the applicant must provide a signed statement assuring that they have read and understood the MTA.

A list of projects for which access has been approved (principle investigator names and institution, date of request, and title of the research) may be made publicly available on the H3Africa or another appropriate website. The DBAC Secretariat will also keep detailed records of any researchers who requested access to biospecimens. These "pre-approval" requests will not be made public but will be available to the H3Africa Steering Committee for oversight purposes.

This policy may be subject to review in light of novel technological applications and/or data analytical tools.

Data and Biospecimen Access Committee

Biospecimen access requests will be managed through the Data and Biospecimen Access Committee (DBAC) (Appendix D). Investigators and institutions seeking biospecimens from the H3Africa biorepositories will be asked to submit an electronic biospecimen access request, including a brief description of the proposed research use of the requested biospecimens (see Appendix D). The DBAC Secretariat will be responsible for receiving and managing the review of applications for access to H3Africa biospecimens and determining whether:

- The principal investigator is a *bona fide* researcher.
- The research use is consistent with signed informed consent and the broad aims of H3Africa.
- Within the first three years of biospecimen availability: the research will be done in collaboration with African scientists and will benefit African communities.
- The data to be generated from these biospecimens are novel and will be made available to the general research community through EGA.
- Any request for biospecimen must include a description of the plans for disposition of any residual material. Ordinarily, this will be disposal according to local safety practice and regulation.
- Researchers will be able to request only one (1) vial of a biospecimen for a given research projects. Requests for additional vials require submission of a separate Data and Biospecimen Request for novel research. Once access is granted, an MTA (Appendix E) must be completed, including all required signatures and documented ethical approval by the recipient's institution for the proposed research. The MTA must be signed by the designated Institutional Official(s) and co-signed by the investigator

The DBAC will review requests for access to determine whether the proposed use of the biospecimens is ethically appropriate and does not conflict with constraints or informed consent limitations identified by the H3Africa Investigators that submitted the biospecimens to the Biorepository. In the event that requests raise concerns related to privacy and confidentiality, risks to populations or groups, or other concerns, the DBAC may consult with other experts at their discretion as necessary to resolve conflicts.

***Release of participant identifying data**:*

In order to minimize risks to study participants and their communities, data submitted to the EGA will be de-identified and coded using a random, unique code to ensure the identities of data participants cannot be readily ascertained or otherwise associated with the data. Further details are provided in the EGA Submission Guidelines (Appendix F) and Data Access Agreement (Appendix G).

Ethical Use of H3Africa Biospecimens in Compliance with MTA

Biospecimen users will be expected to submit annual reports to the DBAC Secretariat describing the use of the biospecimens to ensure that use continues to comply with the terms of the MTA and the provisions laid out in the associated informed consent. This information may be shared with the H3Africa Steering Committee, the H3Africa Coordinating Centre, individual principal investigators, or primary ethics committees at the discretion of the DBAC Secretariat.

Researchers receiving H3A biospecimens and/or genomic and metadata should undertake to inform the DBAC Secretariat immediately if conditions of privacy are inadvertently breached.

A breach of any of the conditions of the Material Transfer Agreement (MTA), will terminate the MTA and recipients will be asked to return or destroy the biospecimens immediately. Future access may also be denied to individuals found responsible for a previous breach of the conditions of the MTA. In addition, when a breach of the MTA is suspected or takes place, the H3Africa Steering Committee and/or the DBAC Secretariat will contact the relevant authorities with evidence that biospecimen use conditions have been breached and to request that appropriate action be taken.

Benefit Sharing

The broad aims of H3Africa are encapsulated in the following statement:

> "H3Africa empowers African researchers to be competitive in genomic sciences, establishes and nurtures effective collaborations among African researchers on the African continent [and other researchers globally] and generates unique data that could be used to improve African and indeed global health."

All access requests should be aligned to these principal aims and indicate how they would promote benefit sharing.

Benefit sharing is understood broadly within this policy and may include:

1. Innovations which directly impact diagnosis or treatment of disorders in African populations
2. Training of African scientists particularly (but not exclusively) those based in African institutions. This may include technical training in genetic analyses, training in other techniques and training in grant writing and scientific writing
3. Publications on which African authors are acknowledged or included as co-authors in alignment with the publication ethics guidelines of the NIH and Welcome Trust.
4. Formal collaborations with African scientists particularly (but not exclusively) those based in African institutions

Although it is not within the mandate of the DBAC to ensure that all of these outcomes arise from secondary use of stored biospecimens, applications with an explicit statement on benefit sharing which will arise from the proposed research will be given priority. Please note that this requirement for benefit sharing in no way removes the MTA provision that biospecimens cannot be used for purely commercial reasons. While H3Africa biospecimens or biological products derived from them may not themselves be used in the manufacture of commercial products, there is no restriction on development of commercial products resulting from the knowledge gained from studies using the H3Africa biospecimens. In addition, the embargo periods and the necessity that an African scientist is involved within the first 3 years (under the Biospecimen Access Policy) cannot be subordinated to any other stipulation as detailed in this policy.

Open-Access, Patents, and Intellectual Property

It is the aim of H3Africa that data derived from H3Africa biospecimens be made available through the EGA and that this data which is derived directly from them will remain freely available, without any licensing requirements, for uses such as, but not necessarily limited to, markers for developing research innovations and guides for identifying new potential targets for drugs, therapeutics, and diagnostics. H3Africa discourages any premature claims on pre-competitive information (such as the naturally occurring DNA sequence of the H3Africa biospecimens) that may impede research, though it encourages patenting of technology suitable for subsequent private investment that may lead to the development of products that address healthcare needs. The filing of patent applications and/or the enforcement of resultant patents in a manner that might restrict use of H3Africa biospecimens and data could diminish the potential public benefit they could provide. Approved users and their institutions, through the execution of a MTA, will acknowledge the goal of ensuring the greatest possible public benefit from H3Africa biospecimens and the derived data.

NIH Genomic Data Sharing Policy:
https://osp.od.nih.gov/wp-content/uploads/NIH_GDS_Policy.pdf

The Wellcome Trust Intellectual Property policy:
https://wellcome.ac.uk/funding/guidance/policy-intellectual-property