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 (https://h3africa.org/wp-content/uploads/2018/05/Final-Framework-for-African-genomics-and-biobanking_SC-.pdf) 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 to determine the underlying genetic predisposition to diseases in diverse African populations while building capacity. It is envisioned that all sharing of biospecimens will be aligned with 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;
- Enriching the existing H3Africa data repository with additional data including genomic, epigenetic and DNA methylation derived from H3Africa biospecimens

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 a Data and Biospecimen Access Request Form submitted to the H3Africa DBAC (Appendix D).

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. Details about the DNA

sample processing and QC are available on the H3Africa Biorepository website at https://www.biorepository.africa.

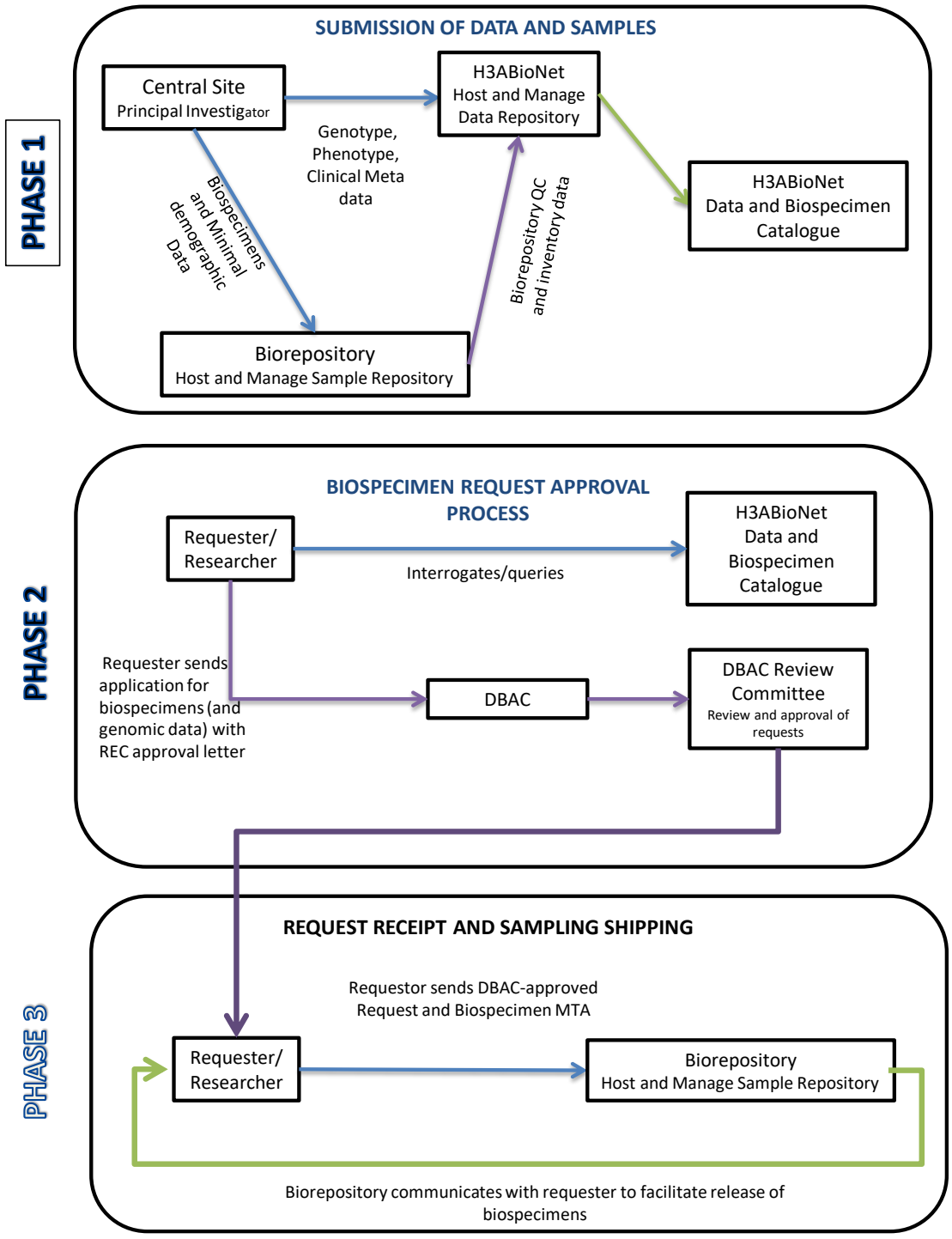
During the first three years of availability, beginning with the date a biospecimen is listed in the H3Africa Data and Biospecimen Catalogue, the DBAC will prioritise release of biospecimens to applicants who seek to use the biospecimen in collaboration with African researchers and who aim to build African research capacity. After this restricted period, the biospecimens will be released to the international scientific research community regardless of their involvement of African collaborators or their potential to build African research capacity.

In compliance with current international standards to protect participant confidentiality, data generated from H3Africa biospecimens are expected to be shared only 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 those cases, all phenotype data associated with participants should also remain exclusively available through 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 Data and Biospecimen Access Request Form in Appendix D) and, in the first three years of biospecimen availability, a statement of collaboration from an African scientist based at an African institution as well as a statement of how the proposed research would lead to the development of research capacity in Africa. The review of requests will include ensuring that proposed use complies with both the consent that was obtained when samples were collected and any research priorities that accompanied the collection of materials. Additional information about policies regarding biospecimen deposition in the H3Africa Biorepositories can be found in Appendices A and B.

Biospecimen access decisions will be based on the description of the research presented in the Data and Biospecimen Access Request Form and, in the first three years after samples become available, its potential value to African health and/or research capacity building in Africa. Evidence of rigorous scientific peer review (for example, an approval letter from funding source) must accompany the **Data and Biospecimen Access Request Form**. It is also 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, a biospecimen request proposing to generate equivalent data without strong justification, will not be approved. Justification could for instance include the development of new and improved methodology. The H3Africa DBAC will also check for overlap of the requestor's research with future work by the primary H3A principle investigator that has been previously approved by the H3Africa Steering Committee. Complete information (for example, applicant(s) names and institution(s) and the research proposal summary) on projects for which biospecimen access has been granted will be made available on the H3Africa or another appropriate website.

Once the Data and Biospecimen Access Request has been approved by the DBAC, the requestor 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 and the primary researchers and governs the terms and conditions under which access will be granted. The MTA will require users to agree to:

a) Include documentation that the proposed research has been approved by the requestor's Research Ethics Committee;
b) Use the biospecimen only for the approved research;
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 the biospecimens obtained from the H3Africa biorepository or data derived thereof with individuals other than those listed in the request;

h) Submit genomic and related (e.g. epigenomic) data generated from the biospecimens to EGA under the H3Africa project via H3ABioNet;
i) 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;
j) Report, in a timely manner, any violations of the H3Africa Biospecimen Sharing, Access and Release policy to the DBAC Secretariat as identified in the H3ABioNet Data and Biospecimen Catalog;
k) Adhere to the H3Africa policy with regard to publication and intellectual property;
l) Acknowledge the H3Africa Consortium in any publications arising from the acquired biospecimens;
m) Provide annual progress reports and publications on research using the biospecimens.

The MTA must be signed by the responsible institutional official (e.g. a representative of legal, intellectual property, scientific ethics or similar offices) and the requesting PI who attests that they have read and understood the MTA.

A list of projects for which access has been approved (principal 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 the original Data and Biospecimen Access Requests. These "pre-approval" requests will not be made public but will be available to the H3Africa Steering Committee for oversight purposes.

Data and Biospecimen Access Committee

Requests for Data and Biospecimens will be managed through the Data and Biospecimen Access Committee (DBAC) (Appendix C). Investigators and institutions seeking biospecimens from the H3Africa biorepositories will be required to submit an electronic Data and Biospecimen Access Request Form, 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 is novel and will be made available to the general research community through EGA.
- Any residual material from a biospecimen will be rendered unusable for scientific research and will be disposed of according to local safety practice and regulation.
- Only one (1) vial of a biospecimen per research participant for a given research project has been requested. Future requests for additional vials will require submission of a separate Data and Biospecimen Access Request for novel research.

The DBAC will also review requests for biospecimen access to ensure the proposed use of the biospecimens does not conflict with the constraints or informed consent limitations identified by the H3Africa Investigators that submitted the biospecimens to the Biorepository. In the event that biospecimens 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.

Release of Participant Identifying Data:

In order to minimize risks to study participants and their communities, biospecimens will be identified by a code generated by the original researcher according to the Deposit Guidelines (Appendix A,). This code, which contains the unique specimen number, a de-identified participant ID, the Study Name, and other prescribed information will be mapped across all processing, storage and distribution of the biospecimen and also across all accompanying and derived data. The H3ABioNet Data and Biospecimen Catalog will assign a "catalogue number" to the biospecimen and associated data (phenotypic, genomic, demographic, etc.) at the time it is listed in the H3Africa Catalogue for distribution. When the data is sent to the European Genotype Archive (EGA), an EGA accession number will also be generated. Thus, there are several discontinuities in the identity chain to ensure patient confidentiality. Additional details are provided in the EGA Submission Guidelines (Appendix F). Data which might be used to identify a participant would not be readily available to a secondary researcher.

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. Upon request, these reports will be available to the H3Africa Steering Committee, the H3Africa Coordinating Centre, individual H3Aftrica principal investigators, and ethics committees that approved access and release of the samples.

Researchers receiving H3A biospecimens and/or genomic and metadata should undertake to inform the DBAC Secretariat immediately if any provisions of the H3Africa Biospecimen Sharing, Access and Release policy are inadvertently breached.

A breach of any of the conditions of the Material Transfer Agreement (MTA) brought to the attention of the H3Africa Secretariat will result in termination the MTA and recipients will be required to return or destroy the biospecimens immediately and to send documentation of the action. Future access may also be denied to individuals found responsible for a breach of the conditions of the MTA.

Ensuring Benefits to African Research Participants and Communities

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 biospecimen access requests should be aligned to these principal aims. One key way of doing so is by articulating how the proposed use of the biospecimens would benefit African people and communities. For example:

- Innovations which directly impact diagnosis or treatment of disorders in African populations in particular.
- 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.
- Publications in which African scientists have provided meaningful intellectual leadership at all stages of the research process, including data analysis and writing. African contributors should be included as co-authors or otherwise acknowledged in alignment with the publication ethics guidelines of the NIH and Welcome Trust.
- 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 how the proposed research will benefit African people and communities will be given priority. 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 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 the biospecimens are intended to 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