H3Africa Data and Biospecimen Access Committee Guidelines

1. Preamble

The Human Heredity and Health in Africa (H3Africa) Data and Biospecimen Access Committee (DBAC) will review and approve or reject all requests from the research community for access to biospecimens collected and data generated by the H3Africa Consortium. Data includes candidate gene association studies, genome-wide association studies (GWAS), sequencing studies and other genotype-phenotype studies (including sequencing and molecular diagnostic assays). The H3Africa Consortium will generate a range of biospecimen sample types. However due to funding priorities, most biospecimen collections in H3Africa Biorepositories currently are limited to DNA. A minimum set of essential data is associated with each sample in these collections.

The Committee will evaluate whether the request conforms to H3Africa policies and procedures including consistency of the proposed research use with data or biospecimen use limitations stipulated by the submitting H3Africa Investigators for each study.

The H3Africa DBAC will maintain records of all researchers who have been given access to those controlled biospecimen and datasets for programmatic oversight and research purposes.

2. Composition of the Committee

H3Africa's DBAC will be composed of 8 core members with appropriate scientific, bioethics, data and human subjects' research expertise. Since some requests to the committee will be for data or biospecimens only, while others will be for both data and biospecimens, a range of expertise will be included on the committee and some or all may be required, depending on the request. The committee members should include senior representatives that represent the following fields: (i) scientists involved in research relevant to H3Africa, (ii) scientists with specialist expertise in biobanking, (iii) a data expert, (iv) individuals qualified/well versed in ethical aspects of research into human health in an African setting, (v) the legal fraternity and (vi) a lay member (e.g. a community representative, advocacy group or nurse). They should not be members of the H3Africa Consortium and should have no conflict of interest with regard to the sharing of data and biospecimens in terms of any of the H3Africa projects. The Steering Committee will consult broadly to identify appropriate members of the DBAC. Selection of members will be done by the H3Africa Steering Committee together with Funders. The aim is that the majority of DBAC members are people residing in Africa.

An ex-officio PI or Independent Expert Committee member may be included on the Committee to provide insight as a non-voting member. If necessary, the DBAC can call on external expertise for advice, and although H3Africa PIs cannot be involved in any decisions of the DBAC, they will be consulted as appropriate.

a) Terms of Appointment

The Chair shall be appointed by a majority vote of the Steering Committee of the H3Africa Consortium. The Chair may be appointed for a maximum of two three-year terms.

Members will be appointed for a term of up to 3 years, with the possibility of serving a further three-year term if agreed. Rotation of members will be staggered to allow for continuity of membership; at least three committee members should remain on the committee while others are replaced.

In considering the re-appointment of the Chair and the members, the H3A Steering Committee shall take advice from the Secretariat.

b) The Secretariat

Support of the DBAC will be provided by the Wellcome Trust, NIH and the H3Africa Coordinating Centre.

c) Accountability

The Committee is accountable to the H3Africa Steering Committee for acting within its remit and carrying out its functions.

3. Scope of Work

What the H3Africa DBAC will do:

The H3Africa DBAC will review and approve (possibly subject to minor revision) or reject all requests from the research community (the "Research community" also includes members of commercial enterprises) for access to datasets and/or biospecimens assigned to them, as long as the request conforms to H3Africa policies and procedures including compliance of the proposed research use with data or biospecimen use limitations stipulated by the submitting institution/investigators for each study. Researchers who qualify to submit a request are defined as scientists or medical professionals employed at, or legitimately affiliated with academic, non-profit or government institutions, or commercial companies. If necessary, the DBAC will delay a decision pending a request for additional information from the submitter.

The H3Africa DBAC will only consider requests for access to data and/or biospecimens submitted through the Data and Biospecimen Access Request Form.

Data

Prior to DBAC review of an incoming access request, DBAC staff will review the relevant websites for any current ban on research with human subjects involving the Requesting Investigator or his/her institution. Submission of a DAR indicates that the Requesting Investigator (Requester) and his/her institution have agreed to the terms and conditions for data use specified in the Data Access Agreement (DAA) for each

dataset requested. For example, the H3Africa Data Access Policy (detailed in the DAA agreement) requires that Requesters, at a minimum, agree to:

- Abide by the agreed upon research uses of the requested dataset,
- Not seek to identify individuals within the dataset,
- Not distribute the data in any form to any entity or individual other than his/her research staff or trainees or independent collaborating investigators listed in the DAR under "Research & Related Senior/Key Person Profile,"
- Keep the data secure, and
- Acknowledge H3Africa as appropriate in publications and presentations.

Biospecimens

The DBAC will review new Biospecimen Access Applications from qualified researchers and notify applicants of results within 30-60 days of receipt. During the first three years of a biospecimen collection's availability, the DBAC will only grant access to applicants outside the H3Africa Consortium who seek to use the samples in collaboration with African researchers and who aim to build African research capacity and capabilities.

The DBAC will approve the specific terms of release in the Material Transfer Agreement (MTA) that was drafted by the Biorepositories based on the donor and recipient's study terms and the application details. The DBAC will use information from participating Biorepositories, such as inventories of limited and depletable collections, when considering new applications as well as requests to extend use periods. The DBAC will also review information on the optional PI Input form submitted by donor PIs to the Biorepository, including comments or caveats for future use and preferences for direct contact with the DBAC about access requests. The Biorepository will send this information to the DBAC within 30 days of receipt of the first Shipment Manifest form. Donor PI information may be particularly helpful when considering requests to access sensitive collections involving vulnerable populations, limited quantities of material, and/or local ethics or legal restrictions. However, the DBAC will consider this information in light of the need to identify potential conflicts of interest and take steps to prevent any identified conflict from influencing access decisions. If the PI changes institution or otherwise relinquishes responsibility of the biospecimen collection, the DBAC must be notified with 30 days of transfer of responsibility. Also, if the DBAC contacts the PI about a request, the PI has 2 weeks to respond. No response within this time frame will be considered a consent.

All reports need to include a plan for the disposal or transfer of unused biospecimens, which can be revisited by the DBAC at completion of the project. The DBAC will mediate any disputes between biospecimen recipients, donating researchers, and participating Biorepositories, in matters related to quality control, access, appropriate use or other issues specified in this policy.

Recipients must also agree to specific conditions, of which at a minimum include:

- The disclosure of information regarding researcher background, intended use, timeline for completion of research, and ethics, technical, and publication aspects

- Adherence to the regulations as per the MTA, unless a modification thereof is required, which would be evaluated on its own merit
- Any remaining biospecimens cannot be used for other research unless a new request has been submitted to the DBAC
- Complying with the set rules that guide procedures for disposal of biospecimens following said research, where applicable
- Acknowledgement of the H3Africa consortium in publications arising from the acquired biospecimens

Given that samples are a finite resource, all research projects seeking to use H3Africa biospecimens will need to undergo scientific review and have a letter demonstrating institutional support. The DBAC will evaluate whether the scientific review was adequate or additional review is necessary. Prior to submission of a funding application, applicants may contact the H3Africa Biorepository Program to obtain a letter about biospecimen availability and access procedures to include in their research proposals. The DBAC will only grant final approval for biospecimen release to appropriately reviewed funded applications. Applications will be judged in competition against existing and potential future applications and evaluated for the appropriateness of sample quantity versus research proposed, in light of sample availability.

The H3Africa Secretariat will develop and circulate an annual report to the ethics committees involved in the original approval of H3A research projects on applications made for sample access. This will include both approved and rejected applications.

4. Conflicts of Interest

Conflict of interest for DBAC members includes, but is not limited to: scientific publication with a Requester or a Co-Investigator listed on a data or biospecimen access request within three years of the submission date of the Request (excluding consortium publications with large numbers of authors, e.g., publications by case-control consortia or cohort consortia); supervisory relationship with a Requestor or a Co-Investigator listed on a data or biospecimen access request or listed as a Requester or a Co-Investigator on a data or biospecimen access request.

DBAC members are expected to review data and biospecimen access requests in advance to identify conflicts and communicate them to H3Africa Secretariat staff. DBAC members will recuse themselves from, and will not be present for, discussion and voting for requests for which they are in conflict. Any conflicts of interest will be recorded in the minutes.

5. Operations

Review schedule

Using a standardized request review checklist (Appendix A), the H3Africa Secretariat staff will review requests to determine whether applications are complete prior to sending the request for a full H3Africa DBAC review. Prior to a full H3Africa DBAC review, H3Africa Coordinating Centre staff may ask for more information from the Requester and/or her/his institution if necessary. Following this preliminary review, H3Africa Coordinating Centre staff will post the request and completed checklist in a place accessible to the DBAC only. DBAC members will then have the opportunity to review each request prior to voting. From an initial request, the H3Africa DBAC will aim to reach and communicate a decision in 30-60 days depending on whether it is data, biospecimens or both.

Quorum

A quorum is defined as 5 out of 8 of the H3Africa DBAC members.

If it is anticipated that a quorum will not be present for making decisions about requests at a DBAC meeting, the meeting will be moved to a date such that a quorum is reached. At least one H3Africa DBAC member or alternate with experience in bioethics or human research participant issues, and at least one H3Africa DBAC member or alternate with experience or expertise in genetics or genomics research will be present for making decisions about requests at H3Africa DBAC meetings. In addition, a DBAC member who is a biobanking expert must be present for decisions involving biospecimen requests. Applications that have specific issues not covered by expertise on the Committee can be deferred for further consultation.

Decisions about Data and Biospecimen Access Requests

Evaluation criteria

Applications from qualified researchers that maximize use of biospecimens for biomedical research in accordance with participant consent, and without identification of individuals, will be further evaluated to assess:

- Scientific merit of the request, including originality and innovative use of materials, valid design and methodology capable of answering proposed research question, consideration of alternative resources;
- Institutional and researcher capacity, including researcher qualifications, adequate funding, ability to complete study within a defined time period;
- Potential for research to be published, lead to patents or aid in discovery and development of new therapies.

Requests will be reviewed by H3Africa DBAC members who will vote via e-mail to approve, reject, or discuss the request. Voting responses will be tracked by the Secretariat. If a quorum of H3Africa DBAC members vote by the stated deadline and the vote to approve or reject a request is unanimous, the request can be approved/rejected without discussion at a DBAC meeting. The decision will be reported at the next H3Africa DBAC meeting. If the vote is not unanimous, the Chair will have the final decision-

making vote. The DBAC will aim to hold regular meetings in person, or via telephone or video conferencing software. If there is a disagreement that relates to an ethical matter, this should be referred to external ethics experts, and if agreement is still not reached it can be deferred the original ethics committee(s) for the project. Other disagreements maybe addressed by the project PI or the funder.

If an H3Africa DBAC member is not able to attend a meeting at which a request will be discussed, the member can raise issues and vote via e-mail. If the H3Africa DBAC member votes by e-mail prior to the meeting and important issues are raised at the meeting that may affect the member's vote, as judged by the members attending the meeting, the member who voted by e-mail will be informed of the discussion and given the opportunity to reconsider her/his vote.

The decision-making process will be reviewed by the H3Africa DBAC members at least once a year to determine whether changes need to be made.

Procedures for Checking Elements for Research Use

Authentication and Terms of Access

Applicants and their institutions are checked by the Coordinating Centre staff who do the first check of all requests. To successfully submit a request, Requesters and their institutions must agree to the terms of access specified in the DAA. Thus, authenticating Requesters and confirming agreement to the DAA require no further steps by the H3Africa DBAC.

Ethics approvals

Ethics approval or a letter of exemption will be required for access to data and/or biospecimens, depending on the scope of the research. For example, ethics approval is expected for requests of data sets with detailed phenotypic information linked to biospecimens, whereas data alone, or biospecimen derivatives and products such as anonymized cell lines, may be exempt from approval according to local policies. By agreeing to the terms of access in the DBAC, Requesters and their institutions are certifying that any applicable Federal, State, and Local laws are being followed and that, if applicable, a Requester is in compliance with local human subjects' protections. While the H3Africa DBAC is not responsible for reviewing the ethics approval letter, it must be provided if required (https://mail.nih.gov/owa/#_msocom_1). If required, the DBAC can seek the opinion of the original ethics committee that approved sample collection.

Single institution application

The Principal Investigator (applicant) must be a faculty member or government/private sector equivalent employed by the requesting institution.

The Principal Investigator of the request and all collaborators listed as part of the request must be from the same institution. If they are not, then all participating institutions must be listed on the request form and H3Africa DBAC staff will contact the Requester to explain to her/him that collaborators from different institutions will have to submit separate access agreements if access is granted.

Compliance with any data use limitations identified by the institutions that submitted the dataset(s):

The DBAC members will review the research use statement provided by the Requester and information provided by the submitting institution, to determine whether the proposed research use is consistent with any data or biospecimen use limitations identified by the institutions that submitted the dataset(s).

Decision feedback

Decisions on requests for access to datasets registered with the European Genome-phenome Archive (EGA) and the European Nucleotide Archive (ENA) are relayed in an automated fashion through the EGA mechanism. Any decision by the H3Africa DBAC not to grant access will be conveyed to the Requester with feedback on the reasoning behind the determination, for instance, a brief summary of the points considered about the proposed use and how these were not consistent with the data use parameters for the dataset in question. All approved requests will be listed on the H3Africa website.

Reconsideration of DBAC decisions

If a Requester contests the H3Africa DBAC's decision regarding the appropriateness of his or her access to data and/or biospecimens, the Requester may contact the H3Africa DBAC Chair to discuss the issues or resubmit her/his request. The H3Africa DBAC Chair can approach the H3Africa Steering Committee for their advice in problematic cases, if appropriate.

DBAC Annual Reports

Annual Reports summarizing DBAC activities will be generated by the H3Africa DBAC Chair and will be due to the Steering Committee annually.

Appendix A: Request Review Checklist

The H3Africa Coordinating Centre will review requests for data and biospecimens prior to submission to the DBAC to ensure that all documents are present and in order. They will check the following:

- Is the H3Africa Data and Biospecimen Access request form complete, correctly filled in and signed?
- Review the relevant websites for any current ban on research with human subjects involving the Requesting Investigator or his/her institution.

Specifically for Biospecimen requests:

- For the first three years of a biospecimen collection's availability, check that requester has a collaboration with African researchers.
- Check inventories of limited and depletable collections, to ensure the sample requested is available.
- Check evidence of scientific review and letter demonstrating institutional support

The H3Africa Secretariat will:

- Gather information on projects and their aims for the H3Africa website
- Maintain a list of granted access requests on the H3Africa website
- Check publications from requesters to ensure acknowledgement is provided and relevant H3Africa publications are cited.
- Develop and circulate an annual report to the ethics committees involved in the original approval of H3A research projects on applications made for sample access. This will include both approved and rejected applications.