Preparation/Transfer of NIA-Funded Biospecimen Collection(s) to the AgingResearchBiobank

Overview

This document discusses the transfer of custodianship of an NIA-funded biospecimen collection to the NIA, including relocating biospecimens and the clinical study data to the AgingResearchBiobank. In this role, the NIA becomes the caretaker and assumes responsibility for maintaining the collection. In addition, custodianship also includes the rights to determine conditions under which the biospecimens are accessed, used, and retained. Key benefits of transferring custodianship to the NIA include 1) Long term storage in an established facility, at no cost to the study; 2) Biospecimens are inventoried and tracked in a secure centralized database and made available online through the AgingResearchBiobank website; 3) All requests undergo a scientific and technical review; and, 4) The original Study is acknowledged in publications.

- Only quality biospecimen collections from NIA-funded clinical studies with potential scientific utility and that can meet the requirements below will be considered for transfer to the AgingResearchBiobank:

- An Institutional Review Board (IRB) has reviewed and verified that submission of the collection to the AgingResearchBiobank for subsequent sharing with non-study investigators for research purposes is consistent with the informed consent of study participants.

- A data file in SAS or Excel/CSV format can be provided electronically of the current biospecimen inventory. This file should include the variables described in the Incoming Biospecimen Collection Questionnaire available at http://AgingResearchBiobank.nia.nih.gov/static/docs/AgingResearchBiobank_Incoming_Biospecimen_Collection_Questionnaire.pdf and should be included in the initial collection application.

- The Parent Study PI(s) will sign an Incoming Human Materials Transfer Agreement (IHMTA) prior to shipment of vials/samples to the AgingResearchBiobank.

- The Parent Study acknowledges that biospecimen collections in the AgingResearchBiobank are subject to periodic utilization assessments and possible reduction.

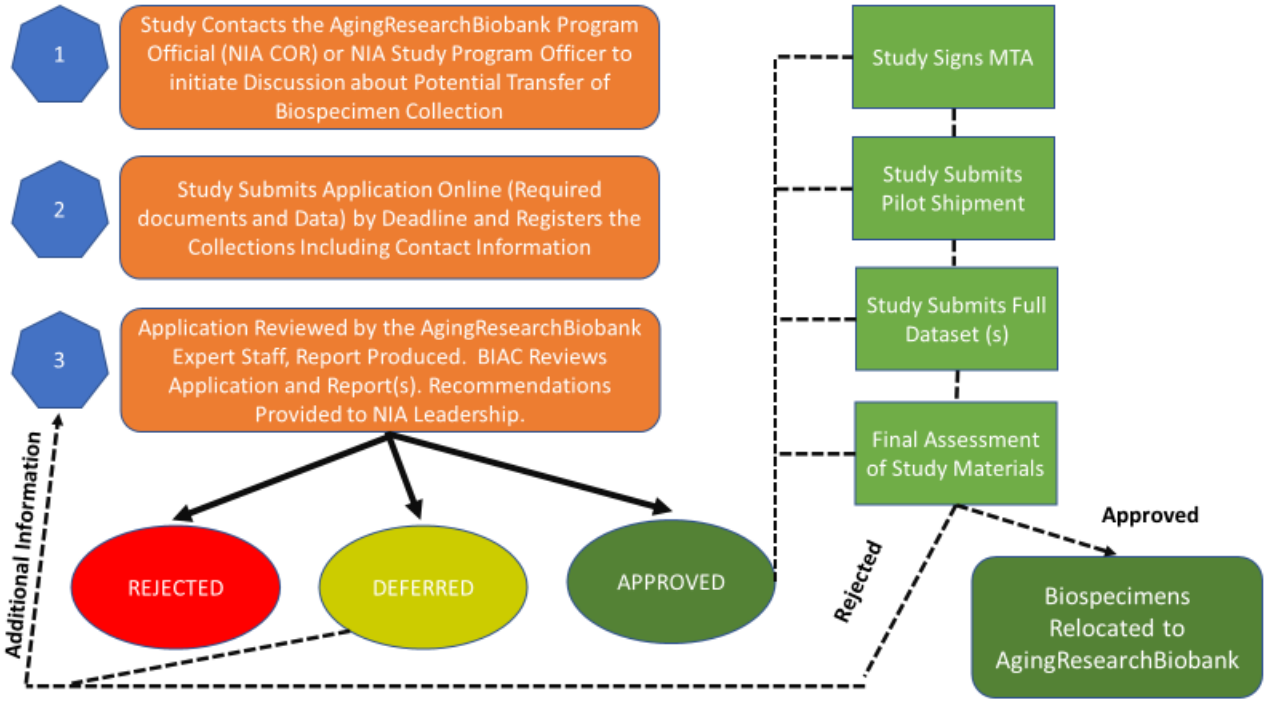
All biospecimen and data collections undergo an assessment for potential scientific utility and quality prior to acceptance into the AgingResearchBiobank. The quality of a study collection is based on the completeness of the collection and on procedures used by the study to ensure the quality of the biospecimens and data. Building a quality biospecimen collection suitable for study and/or future use by the broader research community requires careful planning and deliberated practices, as well as adequate resources to build, store and sustain such collection when the study's primary funding ends.

The assessment for scientific utility is performed by the Biobank Internal Advisory Committee (BIAC). The BIAC membership includes a Chair and one or two representatives from each NIA extramural research division. The BIAC meets two times each year to review applications to transfer biospecimens to the Biorepository to serve as "open" scientific resources through the AgingResearchBiobank website. The review is based on information provided by the study in the questionnaire referred to above as well as in

reports prepared by the AgingResearchBiobank staff with expertise in data management, statistical programming, biorepository management and biospecimen collection, processing, labelling and analysis. These staff members provide assessments throughout the transfer process regarding the quality and completeness of the biospecimens and data. BIAC recommendations regarding the suitability of the collection as an "open" scientific resource through the AgingResearchBiobank website are sent to the NIA Leadership for acceptance and implementation. Not all requests to maintain a collection in the AgingResearchBiobank are approved. Studies should always have an alternate plan(s) in place for providing sustainability for their study resources.

OF NOTE: A Study should contact the NIA COR at least 18 months before the proposed transfer date to discuss the process and a transfer timeline. The biospecimen collection cannot be transferred until the data have been received and reviewed by AgingResearchBiobank expert staff. Studies must take this into account when developing their timeline. Missing and/or incomplete data/information will result in delays and potential rejection of the transfer.

Figure 1 Summarizes the steps and key components of the biospecimens and data transfer process.



Requesting to Transfer Biospecimens to the AgingResearchBiobank

Preparing to transition a collection from Study use to an "open" scientific resource requires considerable planning to curate the Study documents and data, assess the scientific utility of the collection and complete all the activities necessary to transfer the biospecimens. Experience from NIH biorepository programs demonstrates that it takes a minimum of 18 months to successfully accomplish this goal. Therefore, study Principal Investigators (PIs) or the NIA Program Officials (POs) responsible for study oversight should initiate discussions with the AgingResearchBiobank Program Official (NIA COR) regarding the transfer of the custodianship of the collection and the relocation of the biospecimens and data to the AgingResearchBiobank at least 18 months prior to the anticipated transfer date.

Transfers that are supported are reviewed by the AgingResearchBiobank Program Official (NIA COR) to ensure all steps in the process are followed, a transfer timeline is set, and the resources needed to acquire the biospecimens and data are available. The NIA COR will present the proposal to the BIAC for final approval including a budget decision.

To be eligible for inclusion in the AgingResearchBiobank, the study must demonstrate that the collection is of interest to the scientific community, has been collected in a rigorous and well documented manner, that biospecimens can be shared with non-study investigators, that the study data can be linked to the appropriate vials in the collection, that an electronic inventory with the location of each vial is available, and that the study will sign an Incoming Human Materials Transfer Agreement (IHMTA). Requestors should be aware that biospecimens cannot be transferred until the study data have been submitted to, and accepted by the AgingResearchBiobank. In addition, the collection will be "open" immediately to investigators in the broader community following a quality control of the biospecimen inventory. Storage of collections for study investigator use only is not provided.

Submitting an Application to Transfer Biospecimens to the AgingResearchBiobank

All applications to transfer a collection to the AgingResearchBiobank undergo a rigorous assessment for potential scientific utility and biospecimen quality. The reviews assess the completeness and quality of the study data and documentation, the ability to link each sample to its study data, the integrity of the biospecimens based on the study procedures, and the collection's potential scientific future use. Applications are reviewed by the AgingResearchBiobank BIAC two times a year at scheduled meetings. The application submission dates are available at https://AgingResearchBiobank.nia.nih.gov/submit-biospecimens-and-datasets/. Given that unanticipated delays may occur, applications should be submitted at least 18 months before the proposed transfer date. The time to complete the assessment depends on the ability of the study to submit the required documents and to respond promptly to review questions.

Registering the Study to Initiate he Application

The assessment is initiated by registering the study on the AgingResearchBiobank website following approval by the NIA (see above). Registration information includes basic identifiers such as the study name and acronym, and contact information for the study PI(s) and NIA PO(s). A list of study contacts who are

key to the transfer of the data and biospecimens must be provided. The NIA PO(s), the Study PI(s) listed on the registration form and the additional contacts **MUST** be registered as AgingResearchBiobank website users to ensure receipt of correspondence regarding the application. AgingResearchBiobank website user accounts are free and may be obtained at https://agingresearchbiobank.nia.nih.gov/wayf . Upon request, AgingResearchBiobank staff can schedule a call to review the registration and application process.

Submitting Application Documents

Following registration, the required information must be uploaded to the registration page. These materials are essential to completing the initial scientific and technical review of the biospecimens and data. Incomplete submissions will not be sent to the BIAC for review. Studies will be informed of the status of their submission through their AgingResearchBiobank website account. Required application documents and files include:

a) The NIA Biospecimen Collection Questionnaire: http://AgingResearchBiobank.nia.nih.gov/static/docs/AgingResearchBiobank_Incoming_Biospecimen_Collection_Questionnaire.pdf. This document includes detailed information regarding the scientific value and technical quality of the collection.
b) A SAS or Excel/CVS data file and data dictionary that includes the variables listed in the Questionnaire which details the biospecimens. The data file should be structured to list one observation for each individual biospecimen sample in the inventory and include all the samples that the Study proposes to transfer. The data dictionary should include a description of the variables and their formats. For variables that are not captured electronically, the data dictionary should indicate if this information is captured non-electronically and, if it is, where and what data are captured.
c) Study protocol (most current version).
d) Study informed consent template.
e) A summary of the informed consent documents used at the collection sites to collect the biospecimens with information on:
    a. restrictions on biospecimen use by non-Study investigators
    b. restrictions on biospecimen use by research topic (e.g., disease or organ- specific), genetic use restrictions, use by commercial entities, etc., if applicable
    c. changes to the restrictions for biospecimen use over time, including the effective date (s)
    d. site specific changes to the Study informed consent related to biospecimens and data use
f) The Study document(s) with the procedures used to:
    a. collect, process, label, aliquot, track, store, and ship each biospecimen type
    b. validate and monitor the biospecimen collection throughout the Study
    c. perform the laboratory assays performed on fresh and frozen biospecimens
g) The names and contact information for Study staff (data coordinating center and laboratory) essential to the maintenance of the collection.

Reviewing Applications to assess the Scientific Utility and Technical Quality of the Biospecimen Collection

Prior to the review, reports are prepared by the AgingResearchBiobank as described previously and below. Questions related to incomplete submission of required study application documents and files, difficulties encountered when trying to find required information, concerns about the utility of the collection for future sharing, and other potential problems will be shared with the study applicant(s)through their AgingResearchBiobank website account. The NIA COR will be included in all correspondence. Delays in responding to questions or incomplete submissions may affect the BIAC review schedule. Using the information submitted through the AgingResearchBiobank website, the AgingResearchBiobank expert staff prepare a report describing the technical quality and possible limitations of the collection. The report includes information on:

- The potential utility and limitations of the biospecimens based on the procedures used by the Study to collect, process, label, store, and document the collection.
- The types of research that may or may not be possible, based upon specimen processing and storage methods, such as additives, preservatives, and pre-draw patient preparation and other considerations.
- An estimate of funds needed to transfer, consolidate and/or re-label samples.
- The potential overlap with stored Biorepository collections.

A separate report is provided by the AgingResearchBiobank subject matter experts on the submitted data files. This report includes information on:

- The ability to associate vials in the specimen inventory with subject and visit data.
- Descriptive tabulations of the number of subjects with biospecimens available at all visits, and the number of vials at each time point.
- Tabulations of the numbers of vials, by material types and visit, within the proposed transfer.
- Descriptive tabulations of biospecimen availability by consent restrictions.
- Tabulations of the number of sample boxes and number of vials within the boxes to assess freezer requirements and the potential need to consolidate the collection.

The PO(s) sponsoring the Study request may attend the BIAC meeting to discuss the request and address questions related to the utility and size of the collection. Based on the information provided and the meeting discussion, the BIAC makes its recommendations to the NIA Leadership. The overall recommendation may be to 1) Approve the application to transfer the biospecimens, or 2) Ask the Study to provide additional information to address questions in the next BIAC meeting, or

3) Reject the application to transfer the biospecimens. Additional recommendations from the BIAC may include suggestions regarding size of the inventory transfer (i.e., the entire collection vs. a subset). The overall BIAC recommendation and specific suggestions are compiled for review by NIA Leadership to make decisions on whether to proceed with the application process, defer it pending additional information or reject the application. Final decisions are communicated to the Study PI(s) and additional contacts through their AgingResearchBiobank account.

Transferring a Collection to the AgingResearchBiobank

Studies with applications that underwent the scientific assessment by the BIAC and are accepted for transfer to the AgingResearchBiobank will work with the Biorepository Program Official (NIA COR) and both components of the AgingResearchBiobank to establish a timeline to complete the transfer process. The process includes signing an Incoming Human Materials Transfer Agreement (IHMTA), submitting a pilot shipment of biospecimens to assess the physical condition of the vials and labels, and submitting the full study data and documentation. Questions that arise during the transfer process that impact the scientific utility of the collection are sent to the study through their AgingResearchBiobank account and these must be addressed by the study prior to relocating biospecimens to the AgingResearchBiobank. Incomplete responses to these questions may result in a re-review of the application by the BIAC. The types of questions include questions related to the quality and/or completeness of the biospecimens, data or documentation.

Initiating the Transfer

The AgingResearchBiobank will schedule a call using the contact list provided at registration to review the process and establish a timeline with milestones. Study participants on the call must include the Biorepository Program Official (NIA COR) and other expert staff, the study PI(s), and the study members responsible for preparing the datasets and the pilot shipment of biospecimens. The AgingResearchBiobank will prepare action items which include the timeline and milestones agreed to on the call. Based on the milestones established, the AgingResearchBiobank will send automatic reminders for upcoming milestones through the study's AgingResearchBiobank website account. It is the responsibility of the study to inform the AgingResearchBiobank of any changes to the milestones in a timely manner. Missed milestones typically result in delays and may lead to the termination of transfers.

Signing the Material Transfer Agreement Prior to Pilot Shipment

All transfers require the submission of a pilot shipment of biospecimens to assess the physical condition of the biospecimen vials and labels and the accuracy of the inventory file. Prior to arranging a pilot shipment, the Study must complete the Incoming Human Materials Transfer Agreement (IHMTA). The IHMTA is generated by the AgingResearchBiobank using information already provided through the AgingResearchBiobank account. The study will be instructed to download the IHMTA, obtain the appropriate signatures and upload the signed IHMTA to their

AgingResearchBiobank account. Materials cannot be transferred to the AgingResearchBiobank until the IHMTA has been signed by the appropriate study signatories and the AgingResearchBiobank Program Official (NIA COR), and posted in the study application.

Pilot Shipment

Following completion of the IHMTA, the study will be informed through their AgingResearchBiobank website account of the steps to arrange a pilot shipment of biospecimens. Shipping expenses will generally be paid for by the study. The AgingResearchBiobank, can, however, provide shipping materials. Prior to scheduling the pilot shipment, the study will be asked to send a current electronic file of the biospecimen inventory to enable the AgingResearchBiobank to select a representative sample of biospecimens. The pilot shipment will typically consist of between 300 and 800 specimens and include all material types and storage conditions, time points, and collection sites. A listing of the biospecimens to include in the pilot shipment will be provided through the Study's AgingResearchBiobank website account and the study will arrange the transfer of the listed vials with the AgingResearchBiobank expert staff. Shipments will be scheduled to occur on Mondays, Tuesdays or Wednesdays and on a date convenient for both the study and the AgingResearchBiobank biospecimens storage/management component.

OF NOTE: A manifest of the vials must be included with the shipment and an electronic copy of this manifest must be sent to the Biorepository at the time of shipment. The AgingResearchBiobank can provide shippers and shipping protocols, if requested.

The AgingResearchBiobank expert staff will assess the shipment by comparing the data elements listed on the shipping manifest to the information on the vial labels and characteristics that can be observed (i.e., material type, hemolysis, volume). A report will be provided to the NIA and the study that includes discrepancies and recommended corrective actions. The AgingResearchBiobank will schedule a call with the NIA COR, the study PI(s) and the key study members to discuss the pilot shipment report. During this call the timeline and milestones will be reviewed and adjusted if needed. Discrepancies found during the pilot shipment will require correction prior to transfer of the full collection. Discrepancies that cannot be resolved with the study may result in delays or the withdrawal of the approval to transfer the collection.

Data Submission

Prior to the transfer of the collection, clinical data must be submitted to AgingResearchBiobank (see sections above). In addition to the required documentation, the study protocol included in the data submission should be the final version and should be accompanied by a summary of changes from previous protocol versions. A road map document that would serve to guide a researcher unfamiliar with the data must be included in the submission and should include such information as a listing of the submitted materials; the names of datasets, their function, and their source(s); guidance/code for importing and using the data; and a list of any changes made to redact/modify variables from their original state. A linking file that allows the specimens to be associated with the data must be provided.

For studies that have published, the data submitted to the AgingResearchBiobank will need to be reflective of the data reported in the primary manuscript. This can be accomplished by including a frozen set of data used at the time of the primary manuscript, in addition to final adjudicated data. Alternatively, variables can be included in the data that indicate the study population(s) used in the primary manuscript. The AgingResearchBiobank will review the submission for completeness of the documentation and clarity of the data and will verify that all specimens in the proposed collection transfer can be linked to the submitted data and that these specimens are properly consented for future use by researchers who would be requesting them through the AgingResearchBiobank website. The AgingResearchBiobank will also assess the replicability of the tables in the primary manuscript using the submitted data.

Relocation of the Biospecimens to the AgingResearchBiobank

Approval to transfer the collection will be made following the successful completion of the pilot shipment and the receipt and review of the full study data and documentation. Biospecimens will not be transferred to the AgingResearchBiobank until the study data have been accepted for inclusion. The facility storing the study collection will receive a request via the Study's AgingResearchBiobank website account to initiate discussions to finalize the arrangements to transfer the collection. Typically, a conference call with study staff to discuss the details will be arranged. The AgingResearchBiobank expert staff will provide guidance on packing, shipping and logistics. Transfer expenses will generally be paid for by the study or by NIA pending approval by NIA Leadership and availability of funds. Upon receipt, a subset of the collection will undergo the same inspection and reporting process as described for the pilot shipment. The study site and data management center must be able to provide corrective actions for any discrepancies found during the inspection process.