Adult Changes in Thought (ACT) U19 RESEARCH PROGRAM DATA SHARING PLAN
VERSION 3.0 12/01/2023

Purpose

The ACT U19 is a complex, multifaceted research program, and the ACT Data Repository, built over 25 years, is an important national data resource. ACT investigators are developing standardized procedures to ensure that the ACT Data Repository data are thoughtfully stewarded to maximize scientific productivity while minimizing risk to study participants. While the U19 provides substantial resources to facilitate wide data sharing with qualified investigators, those resources are still finite, and it is important to outline policies and procedures to marshal those resources.

This document describes the ACT Data Repository and outlines the **Data Sharing Plan** and the **Data Request and Review Process.** These processes are designed to accomplish the following objectives related to scientific merit, programmatic fit, and resource availability:

Objectives:

1. Ensure that the scientific work outlined in the U19 proposal is able to proceed. In particular, ACT investigators are located at Kaiser Permanente Washington Health Research Institute (KPWHRI) but also at many other institutions. It will be essential for these personnel to be able to share ACT data with each other safely and linked to a coded identification number that is consistent across the various aspects of the ACT study.
2. Ensure that new requests for data (i.e., for research proposals and publications) are congruent with ACT's scientific aims and mission.
3. Track internal and external requests for data to ensure that new requests do not duplicate or overlap with existing work. When overlap is found to exist, we encourage collaboration and identification of mutually beneficial relationships to maximize the scientific reach of the ACT study.
4. Monitor development and maturation of ACT as an international resource and document its growing reach and productivity, including for new collaborations and training purposes.
5. Review the overall scientific rigor and feasibility of submitted data requests, applying standard and consistent processes for how requests are reviewed, approved, and addressed.
6. Protect the confidentiality and integrity of the ACT data.
7. Facilitate the allocation and availability of ACT resources and personnel.
8. Assure business continuity and sustainability of the ACT Program by using structures that are efficient and repeatable.

Data and resource sharing are an integral part of the Adult Changes in Thought (ACT) U19 Research Program. This document describes the following: 1) the ACT data resources currently available and those planned for collection and curation during the initial U19 funding period, 2) the U19 Research Program's current and planned approaches to data sharing, and 3) the specific processes by which ACT data resources may be used and shared between the ACT U19 Research Program's collaborating institutions and by external researchers and entities.

1. ACT Data Repository

The ACT Data Repository is broadly defined as all data related to ACT research participants. At a high level, data sources that make up the ACT Data Repository include **data collected directly by the ACT study**, such as self-reported risk factor data, cognitive testing data, and research diagnoses produced by the ACT study team in the course of work directly with participants.

Beyond these data, the ACT Data Repository further includes:

Data derived from samples. The ACT study collects blood samples from participants; data derived from these samples, including genetic data from DNA from those blood samples, are all incorporated in the ACT Data Repository. ACT investigators seek consent for brain and tissue donation from ACT participants and over the years about one-third of participants consent. Data derived from brain tissues from ACT participants are all incorporated in the ACT Data Repository. These data include routine neuropathology data used in evaluation of Alzheimer's disease and related conditions, but also other data derived from the brain tissues, including such data as gene expression data and DNA methylation data. Raw neuropathology data and some key variables essential to perform and interpret the neuropathology evaluations are housed securely at UW with the neuropathology core, as well as raw imaging and other data produced from neuropathology samples.

Data from ancillary studies and data derived from samples or investigations from ancillary studies. ACT has had the good fortune to attract several ancillary studies that have collected and will collect additional data from ACT participants. All of these data are also incorporated in the ACT Data Repository. If these ancillary studies collect samples from ACT participants, all data derived from those samples are also incorporated in the ACT Data Repository. Examples of these data include research MRI scans on ACT participants from a variety of funding sources, and fundus photographs and optical coherence tomography (OCT) data collected by the Eye ACT study. Additionally, the ACT Air Pollution project collected air pollution data from the residences of ACT participants. All of those data are incorporated in the ACT Data Repository, though may require additional review and approval by ancillary grant PIs triggered by submission of a standard ACT Proposal Form requesting these data.

The ACT Data Repository also includes **data from clinical care**, including linked **Kaiser Permanente Washington (KPWA) clinical delivery system data** such as paper-based and electronic medical records. The ACT Data Repository includes all such records housed at KPWA, but also includes **records and data housed at other institutions**. Several ACT-affiliated studies have made use of these records, including, for example, the ACT Imaging Records project led by Dr. Mac Donald which is identifying, procuring, and processing clinical MRI data generated from clinical care. All medical record data for ACT participants are conceptually within the ACT Data Repository, regardless of the location of the care (within KPWA or anywhere else); however, previously unlinked data or medical record sources may require additional funding, staffing resources, release of information for non-KPWA records (if not already obtained) and IRB or other approvals to obtain for a new study. For the purposes of the ACT Data Repository, the location of the care (within KPWA or anywhere else) has no impact on whether the data are conceptually within the Repository; all medical record data for ACT participants are incorporated in the ACT Data Repository, though previously unlinked data or medical record sources would require additional funding, staffing resources, and IRB approvals to obtain for a new study.

Data that can be linked to ACT participants. In many cases, there are exciting opportunities to link data to other data in the ACT Data Repository. For example, addresses of ACT participants can be used with recent geographical information system (GIS) approaches and data to characterize exposures for the ACT cohort. The address data themselves are incorporated in the ACT Data Repository, as are other data linked to those addresses. Similarly, outside of GIS efforts, we plan to use publicly available data such as US Census data to further characterize ACT study participants. All of these data will also be incorporated in the ACT Data Repository.

Over the course of the U19 funding period, collection and linkage of these data elements will continue, and the collection of several new data elements will be added to the ACT Data Repository. Below is a list detailing these domains:

Domains of ACT Data Elements		
Data Element	***Historical Data Description*** ***(prior to May 2021)***	***Collection Plans for U19*** ***(May 2021 and beyond)***
Data collected at ACT study visits	Data elements such as demographic and health characteristics, cognitive and physical function assessment tests, etc., collected via	Collection will continue as before. Some forms were revised to streamline elements collected. We

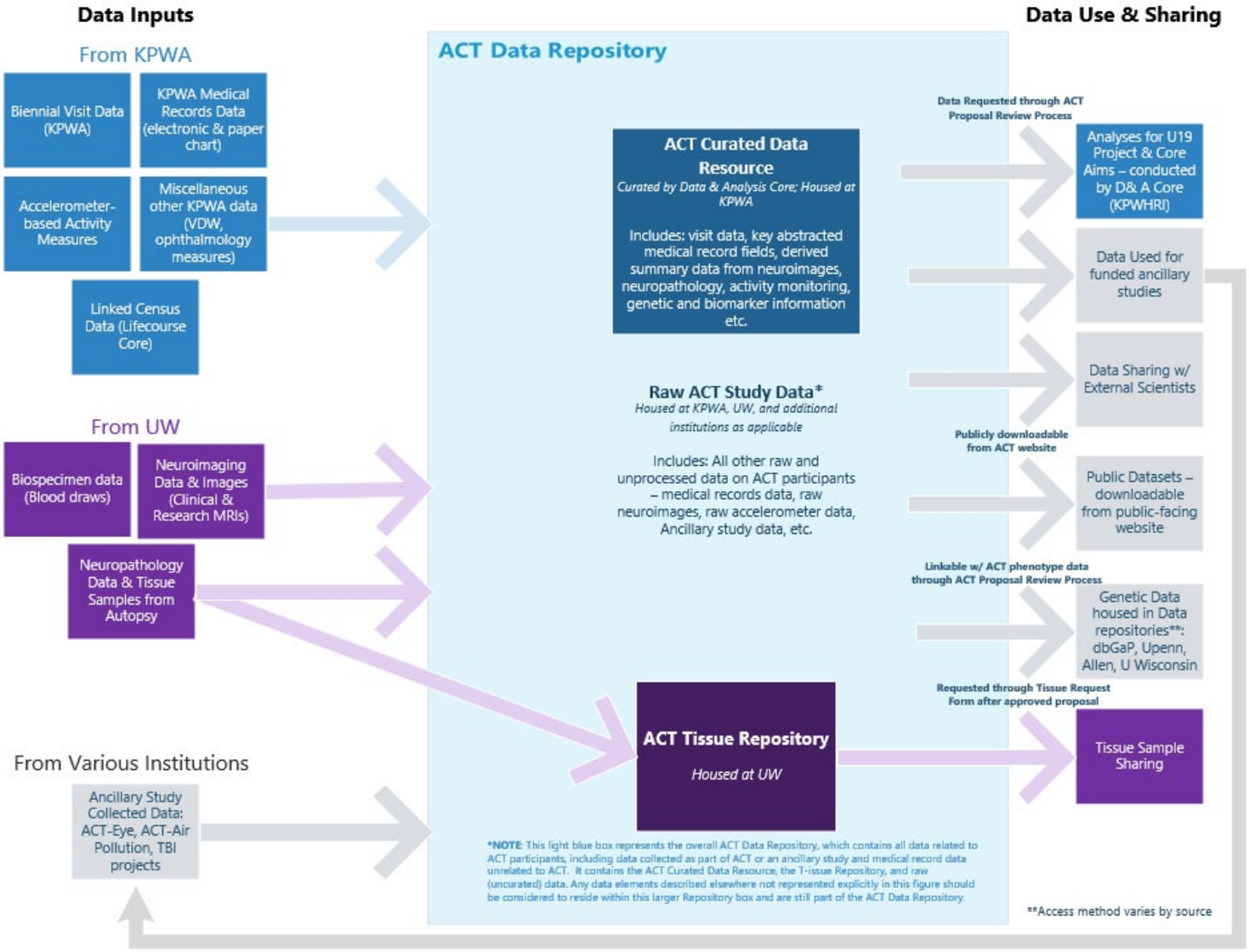
	forms and self-report surveys at study visits on all participants	envision tablet-based data collection beginning in this initial U19 funding period.
Activity Measurement device data	Data collected using activPAL and ActiGraph from a subset of consenting participants (typically in the week after a biennial visit), along with accompanying self-reported sleep log data for their device wear period and data from a survey of self-report activity and built environment variables.	ActivPAL data collection will continue (along with sleep log and self-report survey data). New Sleep watch data will be collected, and the device sub-cohort will be expanded.
Data from the KPWA medical record	Data from ACT participants' KPWA medical record: • Data from the KPWA virtual data warehouse (VDW) (e.g., KPWA enrollment, pharmacy, diagnosis/procedure codes, clinical encounters, etc.) • Additional data (beyond what is in the VDW) that could be pulled/derived from clinical sources and the electronic health record • Data obtained from manual review of EPIC and/or abstraction from paper charts	Data linkage and collection will continue. Additional data elements may be abstracted to meet U19 aims. By definition this category of data involves data generated from clinical care of ACT participants. As clinical care evolves, so too do these forms of data.
Neuropathology data	Data elements derived from neuropathological evaluation of ACT subject brain and other tissues conducted at UW. These raw and derived data, including whole slide imaging, quantitative neuropathology data, 3D scanning data and brain images, are housed securely at UW. Derived data such as ADRD scores from structured neuropathology exam and other quantitative data are also returned to KPWA and incorporated into the ACT Data Repository, making them available for sharing. Neuropathology specimens and tissue samples from which these data are derived are housed securely at UW and managed by the neuropathology core. Requests to share these tissue samples are managed separately, unless linkage to data from the ACT Data Repository is required, in which case the standard ACT data request process outlined below applies.	Data collection will continue. Many enhancements to routine procedures are outlined in the Neuropathology Core proposal.
Genetic, biomarker, or other specimen data	DNA samples were and are collected from all ACT participants. *APOE* genotype is routinely obtained from these samples and used in most ACT analyses. Additional data gleaned from ACT DNA samples include genome-wide SNP data ("GWAS data") and more recently whole exome and whole genome sequence data.	Genetic data will be housed at the University of Wisconsin during the U19. There may be interest in (and funding for) obtaining more / different genetic data during the U19. We also plan to obtain new blood samples from participants at study visits. Data generated from these blood samples – including plasma

		biomarkers – will be part of the ACT Data Repository and used for future biomarker studies.
Neuroimaging data from clinical scans	Data elements derived from clinical scans of ACT participants, whether those scans are housed at KPWA or elsewhere (e.g., Swedish, Virginia Mason, etc.).	There are new initiatives in the U19 to use artificial intelligence with clinical scans with UW's eScience Institute. Currently these are being identified, obtained, and processed under the auspices of the ACT Imaging Records R01. The scan data and data derived from the scan data are part of the ACT Data Repository. The raw data are housed securely under Dr. Mac Donald's control at UW. Scans and the derived data such as the Common Data Elements (CDE) from structured neuroradiologist reads of the scans are also returned to KPWHRI and will be incorporated in the ACT Data Repository and made available for sharing in the future.
Neuroimaging data from research scans	Data elements derived from research scans of ACT participants. These are obtained and processed as part of the ACT Imaging Records R01. The raw data are housed securely at UW. Research scans include MRI sequences not used in clinical practice such as diffusion tensor imaging (DTI), functional connectivity MRI (fcMRI), and arterial spin labeling (ASL). Scans and the derived data such as the Common Data Elements (CDE) from structured neuroradiologist reads of the scans are also returned to KPWHRI to be incorporated into the ACT Repository.	The ACT U19 includes specific funding to obtain research MRI scans on a subset of the ACT cohort.
Neuroimaging data at the time of autopsy	Current protocols spearheaded by the Neuropathology Core include scans of fixed brains or hemibrains.	Arrangements have been made for a portable MRI scanner to be available in the autopsy suite to facilitate in situ MRI scans of whole brains for every ACT autopsy case.
Historical life course and social determinants of health data	The ACT study collected these sorts of data and has linked other sources of data in the past such as birth certificates. The Life Course Core will be adding to these resources under the U19.	Planned activities include a survey administered to participants, as well as enhanced use of geocoded and economic data by U19 investigators. This includes data elements derived from Census linkages for ACT participants, new surveys, etc. generated by the Life Course Core. Economic data are also envisioned by the Life Course Core.

Data generated on ACT subjects from other ACT-affiliated studies	This includes a variety of data types not collected as part of any of the data streams above, added for the explicit purpose of answering a research question funded by an ancillary grant working with the ACT cohort. Examples include the ACT Air Pollution study, various TBI projects, ACT-eye, etc.	Data collection will continue according to the timelines of each ancillary study.

Within each type of data domain outlined above, numerous data elements exist (e.g., raw data fields and variables, calculated or derived analytic constructs, metadata, etc.). While all these data elements are part of the ACT Data Repository, only a subset of those data constitute the "ACT Curated Data Resource." The ACT Curated Data Resource contains primarily data from the ACT study visits and derived variables from autopsy and from the KPWA medical record that are used most routinely for ACT analyses, are most readily shared externally (with necessary approvals; see the "Data Request and Sharing Processes and Procedures" section below) and are under full purview of the Data & Analysis Core for data curation. Other elements from the Data Repository may be made available to external requestors, pending the necessary approvals and resources, but those elements have not been curated to the same level as the elements in the ACT Curated Data Resource.

The majority of ACT data are collected and stored at the Kaiser Permanente Washington Health Research Institute (KPWHRI) within Kaiser Permanente Washington (KPWA). However, certain data elements are collected and housed at the University of Washington or other institutions. The figure below depicts the data elements described above, outlining where each is collected and stored in the ACT Data Repository as well as the avenues through which data from the ACT Data Repository are requested and used. Processes for accessing data from the ACT Data Repository represented in the figure are detailed in the "Data Request and Sharing Processes and Procedures" section below.



2. Current and Future State of ACT Data Sharing

The U19 Research Program's data and resource sharing plan is multi-faceted and emphasizes the scaling up of data sharing resources from current state to include a public facing website, carefully vetted downloadable de-identified datasets with extensive documentation, an improved Data Query Tool, depositing carefully vetted data in large multi-site repositories, and holding public seminars and interactive webinars to highlight ACT data.

Current ACT Data Sharing Activities	Future Planned Data Sharing Activities
ACT Data Query Tool. https://act.kpwashingtonresearch.org/dqt/ A custom-built online system that allows users to obtain preliminary, aggregate counts of ACT data to	The Data and Analysis Core will work to enhance the Data Query Tool and update it regularly, including adding data in new fields collected under the U19 mechanism. All available data elements through the

explore study feasibility. It includes demographic characteristics, risk factors, comorbid conditions, dementia outcomes, and neuropathology results. It tracks the number of autopsy consents, genetic data availability, medical record reviews, and KPWA administrative data so users can generate counts of potentially eligible subjects for new proposals or grant applications.	Data Query Tool will be derived from the ACT Curated Data Resource in order to facilitate data sharing of those data elements with which the Data & Analysis Core have extensive expertise.
Custom datasets for external investigators. Following the data-sharing policies, procedures, and forms described below, the Administrative Core will work with the data requestor and their institution to obtain IRB approval, a Data Use Agreement, and/or a Material Transfer Agreement before any data or specimens are shared. The Administrative Core will oversee the progress of each request and track all manuscripts, presentations, and related grants through regular progress reports.	The creation of custom datasets will continue and expand throughout the U19 period, supported by the establishment of a more robust process for intake, tracking, and review of new requests as described below in the **Data Request and Sharing Processes and Procedures** section.
N/A – new to U19	ACT public website (https://actagingresearch.org/. Developed in the early phase of the U19 period, a public-facing website allows easy sharing of clear and detailed information on ACT study protocols, clinical research forms, and existing data resources, the process for data requests, and, once developed, freely downloadable public use datasets (described below).
N/A – new to U19	Deidentified public datasets. These datasets will be curated and will be freely available for download from our website. These will be based on prior published ACT papers and be *limited in scope* (to ensure maintenance of confidentiality) and approved by the ACT Proposals & Publications Committee prior to posting. They will not require prior approval to use and will not require human subjects approval or data use agreements, though downloads of the data will be tracked by the ACT team. They will also not be linkable with each other as each dataset will have a unique ID numbering system.

3. Data Request and Sharing Processes and Procedures

All requests to use data from the ACT Data Repository, both those that directly support an aim of the ACT U19 and those by the broader research community, are governed by the ACT Proposals & Publications Committee. The P&P Committee is comprised of 5-6 standing nominated representatives from each U19 project (3 individuals), the Data & Analysis Core (1 individual), the Admin Core (1 individual) and one of the remaining cores on an annual rotation (1 individual). The Committee is arbitrated and managed by a Chair nominated from the membership of the P&P committee. Any matters for which the Proposals & Publications Committee is unable to make a final determination will be escalated to the ACT Steering Committee, which includes all Core and Project Leaders and the ACT U19 Multiple PIs.

Data Request and Manuscript Proposals

When an investigator (defined here as any researcher or student, regardless of whether they are a subcontracted ACT U19 collaborator or external to the ACT U19) wishes to use data from the ACT Data

Repository for a paper, presentation and/or grant proposal, they must complete a standardized ACT Data Request and Manuscript Proposal Form or ancillary study proposal form and submit the completed proposal for review by the ACT Proposals & Publications Committee prior to grant approval, provision of data, or new analysis initiation of data from a prior request. External investigators will be expected to collaborate with an ACT investigator in preparing a proposal. Information on how external investigators connect with an appropriate ACT collaborator is outlined and available on the ACT external website (https://actagingresearch.org/collaboration). The purpose of proposal review is to ensure feasibility of the project, avoid duplication with previously approved projects and planned U19 aims, and provide scientific input and review, especially focused on ensuring that ACT's design and methods are represented correctly and compatible with the planned proposal, and that analysis plans meet current best practices for scientific rigor.

With minor exceptions, all submitted proposals to use ACT Data Repository data will be reviewed by assigned members of the Proposals & Publications Committee via email review and/or discussed on Proposals & Publications Committee calls as needed. Investigators can request the necessary form from kpwa.actproposals@kp.org, or download the current form from the ACT website (https://actagingresearch.org/). Manuscript proposals should specify planned collaborators and should follow standard ACT manuscript writing guidelines. The lead investigator for any approved proposal will be required to sign and comply with the ACT Collaborative Research Agreement upon proposal approval and prior to the release of any ACT data or initiation of analyses. (*Note, for all key documents referenced here—ACT Data Request and Manuscript Proposal Form, Ancillary Proposal Form, ACT Writing Guidelines, and the ACT Collaborative Research Agreement—the format and the specific requirements and stipulations therein may be refined and modified over the course of the U19. All changes will be reviewed and approved by the ACT Steering Committee prior to use.*

In the case that an ACT investigator and Subrecipient under the U19 award require a Limited Data Set (LDS) as defined by HIPAA, this disclosure shall be governed by the terms set forth in the ACT Collaborative Research Agreement and tracked via the ACT Data Request Process. However, in the case that an ACT U19 subrecipient requests PHI beyond the definition of a LDS for release from the ACT Data Repository to an institution outside KPWA, an additional Data Use Agreement will be required beyond the standard ACT Collaborative Research Agreement. For all external requestors of a LDS or PHI beyond the definition of a LDS, an additional Data Use Agreement will be required in addition to the ACT Collaborative Research Agreement. Sharing data from the ACT Data Repository with collaborators that are not Subrecipients under the U19 award is considered an external secondary disclosure that must be approved via the ACT Data Request process noted above prior to redisclosure of the data. Subrecipients shall refrain from external data disclosures until they have received approval and appropriate data use agreements with the Administrative Core or Subrecipient have been executed. Each data set may include unique identifiers for each participant's data. Crosswalks relating these ID numbers to ACT ID or other identifying information are carefully protected at KPWA. In general, those crosswalks are not distributed. It may on occasion be useful for a crosswalking dataset to be released to an investigator to link disparate sources of data. If a crosswalk is needed and such sharing meets the definition of a LDS or PHI, a separate Data Use Agreement may be required before the crosswalk is provided, in accordance with the data sharing guidelines above. All data will be shared via secure file transfer or another designated secure method.

Access to ACT data at the Alzheimer's Disease Genetics Consortium (ADGC) is only granted after review and approval by both the ADGC Steering Committee and a designee of the ACT Proposals and Publications Committee. ADGC members can submit special analysis group (SAG) proposals to perform specific analyses. This requires a written proposal which is reviewed by the ADGC Steering Committee. The terms include that the data are kept confidential, used only for the analysis proposed, and accessed only by ADGC members who are involved in the analysis. Due to the collaboration between eMERGE/ADPR/ACT and the ADGC, Paul Crane, ACT MPI, is an active member of the ADGC Steering Committee. If an ADGC affiliated investigator needs ACT data stored at ADGC to answer a research question, they must obtain approval first. They must submit an ACT Proposal form following the ACT Data Request process detailed above. The ACT Proposals and Publications Committee designee approves any release of data related to ACT subjects. Full ACT Proposals and Publications Committee approval is not required unless additional ACT variables not stored at ADGC are required.

Requests for tissue samples that require linkage to data in the ACT Data Repository will utilize the ACT Data Request process detailed above. Once a proposal including request for tissue is approved by the Proposals and Publications Committee, a separate Tissue Request form will be completed by the requestor and coordinated directly with UW Neuropathology. UW Neuropathology has supported the ACT study nearly since its inception. ACT participant tissue samples provide a critical foundation for the robust tissue sharing and national impact of the ACT study. As before, the scientific integrity, quality, and biospecimen availability for ACT tissue research is sustained by thorough review of every request by a panel of neuropathologists and data and research coordinators on the Neuropathology Core tissue committee. When a tissue request for ACT participant biospecimen(s) collected under ACT does not require linkage to data in the ACT Data Repository and the tissue, cells, or biofluid itself will not be fully expended as a result of the proposed external research, UW Neuropathology review, moderation, and fulfillment of the request will proceed according to standard workflow through the Neuropathology Core tissue committee. Generally, human brain tissue is robust and tissue sharing does not result in depletion of the tissue resource. Indeed, most tissue requests are for unstained sections of formalin-fixed paraffin-embedded tissues, of which hundreds are available from each tissue block, and many more tissue blocks can be made from banked fixed tissues. UW Neuropathology Tissue Committee, as part of its standard review of tissue requests, has as a requirement to consider whether a resource will be exhausted. This can occasionally happen for small brain regions, such as hippocampus, in which case the request is denied and the tissue resource reserved for ACT-specific research, such as ACT U19 projects or linked projects such as ACT-Eye. In the rare case that a biospecimen collected under ACT will be fully expended and unavailable for future analyses as a result of an external request, UW Neuropathology will consult with the ACT Proposals & Publications Committee for guidance and prioritization of the use of that biospecimen. As in the past, the Neuropathology Core will report back to the ACT Steering Committee annually on tissue samples obtained and details of requests filled to facilitate sample tracking, collaboration, and reporting. Continued coordination and data communication between ACT and UW Neuropathology are essential to sustaining and promoting the ACT study's prominent contribution to brain aging and neurodegeneration science. Researchers shall acknowledge the ACT U19 grant in any publications or other presentations. Investigators will be referred to ACT for any requests that require data from the ACT Data Repository (more than the standard ACT participant neuropathology core-associated data). Data from ACT brain donors are protected through robust deidentification, encryption, and access control.

Requests for biospecimens such as blood, plasma, or DNA will utilize the ACT Data Request process detailed above. Once a request has been approved, a Material Transfer Agreement (MTA) will need to be signed, along with the Collaborative Agreement and potentially a Data Use Agreement as described above. ACT Data Repository staff will coordinate with the appropriate labs, sending lists of required IDs via secure file transfer. Staff at the designated lab will aliquot the requested volume of blood or DNA for requested specimens and will label tubes with the designated IDs. Specimens will then be shipped according to specifications outlined in the MTA to the designated recipient. ACT Data Repository staff will retain any linking files between the lab and designated IDs for the recipient.

Final Manuscript Review

Prior to journal submission, final manuscripts or presentations based on previously approved proposals must also be reviewed and approved by the Proposals & Publications Committee. The purpose of manuscript review is to ensure adherence to publication policies designed to protect the identity of ACT participants; to acknowledge participants and funding sources; to appropriately reflect the ACT study design and data; to ensure the analysis follows what was outlined in the approved proposal, and to allow for thorough tracking of research products resulting from ACT data and resources. Information on the manuscript review process can be found on the ACT study website (actagingresearch.org).

Restrictions to Data Sharing

A primary goal of the U19 Research Program is to encourage and facilitate meaningful data and resource sharing by offering programmatic, analytic, and scientific expertise to help collaborators understand ACT data. The ACT U19 leadership is committed to ensuring that ACT resources are stewarded and shared thoughtfully. The principles described below are in place to ensure that data sharing is truly meaningful and maximizes use of limited programming and analytic resources:

- Requests must be scientifically sound, and an appropriate use of ACT data as determined by the ACT Proposals & Publications Committee. This is an iterative process, in which ACT scientists and staff work with the data requestor to ensure they are interpreting ACT data appropriately and have the resources to conduct analyses, rather than simply share data without any follow-up. Upon approval of a proposal, the requestor must sign a Collaborative Research Agreement indicating willingness to follow ACT study and KPWA research policies in conducting analyses and publishing results. This process does not apply to downloadable datasets, which will be made freely available to anyone with internet access later in the U19 period.
- The ACT Program does not share data in any manner that would identify individuals without proper participant consent, Institutional Review Board (IRB) approvals, or Health Insurance Portability and Accountability Act (HIPAA) requirements.
- The ACT Program does not share data in any manner that may be deemed commercial or seen as selling data.

Data Deidentification Procedures

It is critically important to respect privacy and minimize risk of identifiable information disclosure of participants. The ACT Program has well-developed internal policies and procedures in place to make sure that confidentiality is maintained and will build on ACT's existing secure data architecture and management systems to accommodate new U19 Program data. When data are transferred across participating institutions, the Data and Analysis Core will work closely with the Administrative Core to ensure data are protected in compliance with HIPAA and IRB requirements, and, when applicable, appropriate Data Use Agreements. Only authorized project staff can access identifiable data. Data handling procedures will be clearly documented and comply with KPWA guidelines for data storage, transfer, and destruction.