ADNI BIOSAMPLE POLICIES AND PROCEDURES

Alzheimer's Disease Neuroimaging Initiative (ADNI) Biosample Policy and Procedures Statement (August 2024). The Biosample Policies and Procedures are subject to change as ADNI progresses and further experience is gained.

One of the goals of ADNI is the collection of biospecimens, including blood, CSF, genetics (DNA, RNA, etc.), and postmortem brain tissue from participants. An accounting of ADNI biospecimens available and biomarker data can be found in the database.

Biomarker data and several analyses of general interest in the ADNI database comes from:

- ADNI Core labs including:
    - Biomarker Core (Drs. Leslie Shaw and Edward Lee, University of Pennsylvania)
    - Genetics Core (Drs. Andrew Saykin and Kwangsik Nho, Indiana University)
    - Neuropathology Core (Dr. Richard Perrin, Washington University in St. Louis)
- Outside labs which run analyses and provide them to LONI

Interested investigators are encouraged to apply for use of these limited resources but should be aware of ADNI biosample and RARC policies. NIA and the ADNI Executive Committee have formulated policies governing access to ADNI biosamples:

PURPOSE: ADNI biosamples are not usually provided for exploratory studies or methods development. Preliminary data, establishing the validity and reliability of all proposed methods, must be provided in RARC reviewed applications. The overall goal of ADNI is to provide scientific information to the community. Most critically, all applications should be justified by their scientific value. We recognize and appreciate that development/improvement of commercial products may be facilitated by this process and may be an aim of RARC applications. NIA will request input from the PPSB, as well as the RARCs, in those (rare) instances when NIH policy or public health impact support using ADNI biosamples in development of commercial products (for instance, an FDA or CLIA approved diagnostic).

APPROVAL FOR BIOSAMPLE REQUESTS: Interested parties must follow instructions outlined here: Apply for Access to Samples. RARC review is required for all access to ADNI biosamples, except for studies that are part of the ADNI cooperative agreement, itself. Any qualified scientist – whether domestic or foreign, in government, academia, or industry - may apply for biosamples collected by ADNI. No special preference is given to applications by ADNI investigators, or from sponsors of the Public Private Scientific Board (PPSB).

DISTRIBUTABLE ALIQUOT SIZES:

Sample Type	Distributable Quantity
Genomic DNA	5ug
Cell Line DNA	5ug
Lymphoblastoid Cell Lines	1 vial
PBMC	1 vial
RNA	2ug
RBC	1000 µl
Plasma	0.5 mL
Serum	0.5 mL
CSF	0.5 mL
Urine	0.5 mL
Brain tissue	Formalin-fixed paraffin-embedded (FFPE) tissue sections (4-8 um in thickness)
	Fresh-frozen brain tissue (stored at -80°C)
	Formalin-fixed wet tissue (limited availability)

APPROPRIATE USES FOR SAMPLES:

The ADNI Cores have performed several analyses of general interest (CSF and plasma, multiple species of tau and Aβ, APOE genotyping, GWAS, whole genome sequencing, glial fibrillary acidic protein, neurofilament light, and more). Non-ADNI investigators may apply for use of the samples and have contributed additional results to the ADNI data available via LONI-IDA. Use of ADNI samples for technology development or comparisons among different technologies is not recommended for well-established analytes unless there is preliminary data showing clearly superior performance.

Impact on sample inventory will be considered in all requests. Access to ADNI1 genomic DNA and baseline CSF is limited to high priority research. PBMCs are a highly limited resource banked for iPSC development. iPSCs will be available and are a renewable resource. Brain tissue samples from brain areas that are relatively small and/or commonly requested (e.g., hippocampus, dorsolateral prefrontal cortex) are limited and require a strong justification for why those areas are requested. Blood plasma samples are increasingly of interest and biobank supply of this resource is closely monitored, especially requests for participant baseline samples.

Each restriction imposed by sample inclusion/exclusion criteria (e.g., postmortem interval, age at death, APOE genotype, co- existing neuropathologies) may negatively affect sample availability.

- Previous ADNI studies can be found in the ADNI dataset: https://adni.loni.usc.edu/data-samples/adni-data/
- Previous add-on studies (RARC-approved studies) can be found here: https://adni.loni.usc.edu/data-samples/adni-samples/previously-approved-rarc-studies/
- See RARC policies for criteria under which sample requests are evaluated: https://adni.loni.usc.edu/wp-content/themes/adni_2023/documents/rarc/ADNI_RARC_Policies.pdf

SPECIFIC ADVICE ON APPLICATIONS FOR SAMPLES: Provide a very strong scientific justification for the request, along with as much supporting data as possible. It will be very helpful to your application if you download the ADNI database and choose those samples from specific individual subjects at specific timepoints and provide a table or list of these very specific samples in your application. Requesting samples from "Cognitively normal or MCI participant with amyloid PET scans" is too vague. Be highly specific, and base your power analyses on the data available.

FUNDING & GRANT APPLICATIONS: Neither the ADNI study, nor the RARC provides funding to applicants. Investigators should have funding and all necessary resources in hand before applying. Investigators needing proof of access to ADNI biosamples to prepare grant applications, should contact and ask for a letter of support from either ADNI's Principal Investigator (Dr. Michael Weiner, michael.weiner@ucsf.edu), or the Project Leader(s) of the relevant ADNI Core:

- Biofluid Biomarkers, Dr. Leslie Shaw, leslie.shaw2@uphs.upenn.edu and Dr. Edward Lee, edward.lee@pennmedicine.upenn.edu
- Genetics, Dr. Andrew Saykin, asaykin@iupui.edu and Dr. Kwangsik Nho, knho@iupui.edu
- Neuropathology, Dr. Richard Perrin, rperrin@wustl.edu

In your request, please provide the grant title and submission date. A letter of support does not substitute for RARC review, and should explain that access to ADNI biosamples is controlled by NIA, advised by a RARC.

DATA SHARING: All data resulting from studies using ADNI biosamples must be shared and included in the ADNI Database on LONI. Instructions for accessing the ADNI database can be found here (https://adni.loni.usc.edu/data-samples/adni-data/). A list of previously completed, and currently active RARC-approved studies can be found here (https://adni.loni.usc.edu/data-samples/adni-samples/previously-approved-rarc-studies/). Data from completed studies can be downloaded from the ADNI database.

QUARTERLY UPDATES ON STUDY PROGRESS: Each quarter that passes after an investigator has received samples and not yet uploaded data, the requesting investigator must send a quarterly update on their study's progress to catherine.conti@ucsf.edu.

In their Full Application, the investigator provides a timeline for expected results to come back to ADNI. If the originally proposed timeline is expected to be delayed more than a few weeks**, the investigator must notify ADNI immediately**. However, we strongly recommend that all investigators keep within their proposed timeline.

If an investigator's ability to provide the data is substantially delayed, **ADNI reserves the right to request that the samples be returned ASAP**.

RESIDUAL SAMPLES AND ADDITIONAL STUDIES: Investigators should not dispose of unused ADNI biofluid/tissue samples and are required to notify ADNI if there are residual samples left after completion of the RARC-approved study. Investigators may return residual biofluid samples to the Biomarker Core, where they will be pooled and used for assay standardization. Residual brain tissue is not to be used for additional unapproved studies. Investigators are required to receive NIA approval (and RARC concurrence) before using any ADNI residual samples in a new study (any analyses outside of what was proposed in original RARC-approved study application).

BLINDING & INTELLECTUAL PROPERTY: All analyses on ADNI biosamples must be carried out blind to

clinical data. Samples sent to investigators will be identified by code numbers not linked to ADNI clinical data. The relevant ADNI Core will work with investigators to ensure methodological reliability and rigor (e.g., technical replicates, sample assay sequence, plating, etc.). Once analyses and QC are completed, investigators will send their completed data submission form, methods, results (.csv data file), and data dictionary to be unblinded. ADNI will then add associated subject ID codes to the data file which will permit correlation of results to ADNI clinical data. The NIA is now allowing investigators with RARC approved ADNI biosample research applications to request a data embargo period of up to 2 months. This will give the investigator a 2-month period of access to the unblinded data before it is released to all ADNI users via LONI. After the blind is broken, investigators must notify ADNI if they perform any additional analyses. They must promptly report the results of any subsequent analyses to ADNI for posting. Investigators are not allowed to share the individual participant data with anyone else. All ADNI data must be shared through the LONI website. Investigators may not submit any data for publication unless that data is posted on the LONI website.

NIA and the RARC/BRC/NP RARCs will not disseminate or release investigator applications for access to ADNI biosamples, but non-disclosure and confidentiality agreements cannot be honored by ADNI, the RARCs, or NIA.

MTA FOR SENDING SAMPLES:

- **Biofluids** - No Material Transfer Agreement (MTA) is required.
- **Genetics** - Subject to additional policies including signing of a Master Agreement for Transfer of Materials to NCRAD. See https://ncrad.org/access-samples/request-samples/mta-out
- **Brain Tissue** - A signed Master Agreement for Transfer of Materials will be required.

COST OF SAMPLE DISTRIBUTION:

- **Biofluids** - There is no charge to the investigator for review or sample preparation, processing, and transfer.
- **Genetics** - See NCRAD Pricing Schedule for costs of genetic sample distribution. While we do not charge for samples, there are associated costs for aliquoting, shipping, etc. which the investigator must cover.
- **Brain tissue** - Due to the variety of brain tissue sample types available, please inquire for costs of sample acquisition. Inquiries can be sent to ADNI-NPC@email.wustl.edu.

PROPER CITATION OF ADNI IN PUBLICATIONS: Requesting investigators must review and follow instructions for appropriate citation of ADNI in any publications resulting from ADNI sample and data use. https://adni.loni.usc.edu/wp-content/uploads/how_to_apply/ADNI_Manuscript_Citations.pdf

CONFLICT OF INTEREST POLICY: The RARCs will follow the COI policy as described by the NIH (review here: https://ethics.od.nih.gov/coi). Reviewers must declare any COI with any application and recuse themselves from any review, discussion, or decision about that application.