



ADNI RARC & Biosample Policies

BACKGROUND

ADNI has always collected biosamples (CSF, blood, and in ADNI 1, urine) to measure and track biologically informative analytes. The initial focus was on β -amyloid, tau, and hyperphosphorylated tau, and the Biomarker Core measures these peptides in CSF as part of the ADNI database. NIA and the ADNI investigators realized that biosamples - collected longitudinally from carefully phenotyped subjects - would be a valuable resource for replicating important new findings, and validating novel biomarkers developed in the future. However, unlike the neuroimaging and clinical data shared by ADNI, the biosamples collected in ADNI can only be used once: each aliquot of CSF or sample of genomic DNA is a precious, non-renewable resource.

As a condition of funding, NIA required the ADNI investigators to curate and store biosamples collected in ADNI, and to share them with non-ADNI scientists. NIA was to be the gatekeeper for these biosamples, and the ADNI Executive Committee created a Resource Allocation Review Committee (RARC), made up of non-ADNI investigators, to review requests for biosamples and advise NIA. Biofluid (CSF, plasma and serum) samples collected in ADNI are stored at the Biomarker Core, at the University of Pennsylvania. The RARC review process, and instructions for investigators wanting access to ADNI biofluids are explained in the document titled Applying for ADNI Biofluids.

After ADNI began in 2005, it soon became clear that genetic materials would be important in the future. ADNI 1 included ApoE genotyping and GWAS on subjects, and collected and immortalized lymphocytes to provide a renewable source of DNA. A limited amount of genomic DNA - remaining from the GWAS - was kept, but the quantities are such that access to ADNI 1 genomic DNA is possible only under extraordinary circumstances. ADNI 2 collected genomic DNA and RNA, along with blood cells (e.g., PBMCs) on a longitudinal basis. ADNI 3 has continued these collections and is considering creating iPSC cell lines. ADNI genetic materials are stored at the National Cell Repository for Alzheimer's Disease (NCRAD) at Indiana University. The RARC review process, and instructions for investigators wanting access to ADNI genetics materials are explained in the document titled Applying for ADNI Biofluids.

It has always been clear that postmortem neuropathologic evaluation of ADNI subjects would be essential. A Neuropathology Core was added to ADNI 1, and over time, as ADNI subjects passed away, having consented to brain donation, brains were collected, evaluated, and stored by the Neuropathology Core at Washington University. Neuropathology reports are available here ([LINK NEEDED](#)). While still quite limited, there are now enough subjects to allow qualified investigators to apply for access to ADNI postmortem brain tissue. The RARC review process and instructions for investigators wanting access to ADNI postmortem tissue are explained in the document titled Applying for ADNI Biofluids.

ADNI BIOSAMPLE POLICIES

All data from studies using ADNI biosamples must be shared and included in the ADNI database. A list of previously completed, and currently active RARC studies can be found here (LINK NEEDED). Data from completed studies can be downloaded from the ADNI database

There are 3 RARCs advising NIA on applications for biofluids (CSF and plasma), genetics material, and postmortem tissue. 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) that co-funds ADNI.

NIA and the ADNI Executive Committee have formulated certain 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. Since ADNI works in a non-commercial, pre-competitive space, development of commercial products cannot be a priority. 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).

FUNDING & GRANT APPLICATIONS: Neither ADNI nor the RARC provide 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: Biomarkers, Drs John Trojanowski, trojanow@upenn.edu and Leslie Shaw, Leslie.Shaw2@uphs.upenn.edu; Genetics, Dr. Andrew Saykin, asaykin@iupui.edu; or Neuropathology, Dr. John Morris, jcmorris@wustl.edu. A letter of support does not substitute for RARC review, and should explain that access to ADNI biosamples is controlled by NIA, advised by an RARC.

BLINDING & INTELLECTUAL PROPERTY: All analyses on ADNI biosamples should 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 upload their results and associated data dictionary and method files to the ADNI database. The database will merge the correct subject ID codes needed by investigator to analyze and correlate results with the rest of ADNI data. ADNI does not allow an embargo period, and as with all ADNI data, all users will have access to results as soon as data are uploaded.

NIA and the 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.