DOMINANTLY INHERITED ALZHEIMER NETWORK (DIAN)

Data and Tissue Sharing, Notifications, Publications, and Authorship Policies

These policies are intended to promote collaborative, high quality dissemination of DIAN study findings in a timely, accurate, and just manner. They address: access to data; notification of presentations and publications; internal manuscript review; and writing group membership and authorship. We adopt a broad definition of 'investigator'; in general the term applies to any faculty person at a DIAN site (or who is on the DIAN Steering Committee) who is directly involved in the DIAN study. An investigator may nominate someone at their site who is not usually involved with DIAN to work on a specific study.

ACCESS TO DIAN DATA/TISSUE

We follow the principles of Productivity (with Recognition of the investigator who develops a research idea and does the work to publish it), Transparency, Fairness, and Inclusiveness. The following policies regarding access to DIAN data are intended to provide structure to the request process, respect for intellectual contributions, and standards regarding security/confidentiality. For specific policies on the sharing of tissue and biospecimens, please see the section below on DIAN Biospecimen Sharing for biospecimen restrictions and review procedures.

Priority of Access and Review/Approval Process: To respect intellectual contributions of DIAN investigators and collaborators, the following system has been adopted.

DIAN-affiliated requests: Data analyses to support manuscripts can be developed and proposed by anyone in DIAN: Core Leaders, Site Leaders, other Steering Committee members, or any student, fellow, or investigator designated by a DIAN Site Leader. All data requests will be reviewed by the relevant Core Leaders and the Principle Investigator of DIAN. Upon approval, these requests will receive the most recent data freeze modules.

External requests: For requests from those not affiliated with the DIAN study, upon approval, access to the previous data freeze will be granted. Such projects/manuscripts will follow the "DIAN-affiliated request" review and approval process (see next section). Publications by investigators outside DIAN would list the DIAN Study Group in the acknowledgments with the required paragraph at the end of this document.

Review and Approval Process for Data-Only Access

All DIAN Data Requests/Proposals should be submitted to DIAN's Administration Core through the online resource request system on the DIAN Website: http://www.dian-info.org/resourcedb/default.htm. The Deputy Director of DIAN (ie., Administrative Core) will review the request and determine the relevant Cores that are required for review the proposal. Then the application will be sent to those Core Leaders and the Principle Investigator to review and approve or deny the request. When Core Leaders do not reach consensus about the request or agree not to approve, further review by the Steering Committee may be necessary. To avoid overlapping effort, investigators are be encouraged to use the search option on the DIAN request website to see what other requests might be similar to theirs.

Summary of Data Access Procedures				
	Who	**What**	**Data Access**	**Review process**
DIAN-Affiliated Requests	Any DIAN Core or Site Leader and/or their designated DIAN investigator from a DIAN site	DIAN data request nominated by an investigator affiliated with DIAN	Most recent data freeze	Approval of PI and relevant Core Leaders
External Requests	Non-designated investigators within or external to DIAN sites.	DIAN data request nominated by investigators not affiliated with DIAN	Access to previous data freeze (ie., 1 year prior)	Approval of PI and relevant Core Leaders
• Declaring an intention to pursue a topic does not guarantee approval of the project. A formal request must be submitted to the DIAN Administration Core for review (Resource Request website: http://www.dian-info.org/resourcedb/default2.htm).				

Requesting Data

De-identified DIAN data will be made available to investigators to conduct analyses after approval by the PI and the relevant DIAN Core Leader

All requests for data must be submitted in writing via the electronic data request form available at the resource sharing website (http://www.dian-info.org/resourcedb/default.htm). The request form will include investigator affiliation, contact information, funding support, institutional review board (IRB) approval (if applicable), an NIH-style biosketch, and a brief description of the project, including specific aims, study design, characteristics of the data requested and analysis plans. Investigators requesting data also will be required to sign a data user agreement and an acknowledgement agreement, as specified below. Applications for data use will be reviewed by the Principle Investigator and relevant DIAN Core Leaders. The number, type and disposition of the requests will be tracked by the DIAN Administration Core and a data sharing report will be generated for progress and final reports to the National Institute on Aging (NIA). Each data request will specify the data elements required for the planned analyses. The Biostatistics Core personnel will prepare a file containing only these data elements, together with a participant identification number (not the DIAN ID# but identifier recoded to protect confidentiality) so that questions about particular individuals can be resolved without the investigator's knowledge of the participant's identity. Image data will be available to approved investigators in raw and post-processed formats via the DIAN Central Neuroimaging Data Archive (CNDA) after a formal Data Use Agreement (DUA) has been signed by both institutions.

Data Documentation: The research community at large will be informed of the procedures to utilize data from the study through a project website. The website will provide information about the data that are available, a detailed description of the cohort, and an overview of the methods by which data have been collected and stored. The website will also provide an electronic data request form.

Criteria for Review: Data requests will be reviewed based on the following criteria:

- Scientific merit and feasibility (e.g. availability of DIAN resources to fulfill the request)
- Appropriateness of the investigator's qualifications and resources to protect the data.
- Appropriateness to DIAN goals/themes

Preparation of data: There will be one data freeze of the DIAN data each year that includes all data that have passed relevant quality control processes at the time of the 'freeze.' Biostatistics Core personnel will prepare modules (ie., clinical, fluid biomarker, imaging, etc.) of the frozen dataset and provide statistical consultation if appropriate.

All precautions to ensure confidentiality must be taken by recipients of DIAN data. The final dataset will be stripped of DIAN identifiers and re-coded with dummy IDs prior to release and be transferred only with encryption and password protection by the Biostatistics Core. The code linking a subject's identity to data will be maintained only at the DIAN site where the participant is enrolled. This link will only be accessible to research staff on a need to know basis. All United States sites are required to have a Certificate of Confidentiality before they are approved to enroll subjects. The exact mutation will not be recorded in the National Institutes on Aging (NIA), National Cell Repository for Alzheimer's Disease (NCRAD), Central Neuroimaging Data Archive (CNDA) databases nor will it be entered into DIAN on-line electronic data capture system. Separation of this sensitive data is to prevent accidental disclosure of participant mutation status to a member of the research team. Any research data that goes outside of the study group will be coded with a second unique identifier (which is different from the study ID, another unique identifier) to limit the risk of loss of confidentiality. However, there is always the possibility of deductive disclosure of participant identity because participants are associated with specific institutions, and the dataset contains detailed demographic information, as well as detailed prospective information about their disease and mutation status, living situation, etc. Thus, we will make the data and associated documentation available to users only under the following prerequisites:

1. Recipient of data will:
    a. Provide documentation of IRB approval valid for the analysis of DIAN data (or acknowledgment from their IRB that receiving coded data without access to other identifiers is not considered "research" requiring review).
    b. Provide assurance of ability to secure dataset in accordance with the most stringent protections possible compliant with local IRB and Health Insurance Portability and Accountability Act (HIPAA for US sites) standards for such sensitive data.
    c. Provide a signed Code Access Agreement (CAA) or Data Use Agreement (DUA) for data usage
        i. CAA: a simple statement that the recipient of the data signs, verifying they will use the data only for research purposes and will not attempt to identify any individual participant.
        ii. DUA: a contractual document used for the transfer of non-public data that is subject to some restriction on its use. This contract outlines the terms and conditions of the transfer.
    d. Guarantee that individual mutation status data will be destroyed when analyses are complete.
2. If a DIAN dataset is to be shared with a DIAN Site, the site leader must identify a third party at the site who will conduct the analyses. This individual must not have contact with participants nor play any role in data processing that involves interpretation or judgment to avoid un-blinding of study personnel or biasing of the data.

Genetic data sharing: Participants also will be asked to participate in the NIA/NIH genetic data sharing program. The genetic data sharing program is a national resource supported by the NIA that prepares and stores cell lines and DNA samples and makes them available to scientists who would otherwise have no access to this information. Transformed cell lines from all DIAN participants are created and stored at the National Cell Repository for Alzheimer's Disease (NCRAD) where the DNA is extracted, stored, and provided to investigators after review and approval by the DIAN Steering Committee. Relevant clinical and biomarker data would be obtained from the DIAN Biostatistics Core.

DIAN Informed Consent: The DIAN consent forms include a statement informing participants that de-identified data may be shared with authorized investigators, following guidelines for preserving confidentiality through coded identities and consistent with HIPAA requirements. DIAN participants and/or their relative/guardians have the right to have the material and/or data destroyed or made anonymous at any time. If consent to participate in the study is withdrawn, and the participant and/or his/her relative/guardian no longer wish their DNA to be used, NCRAD will destroy any unused samples. However it may not be possible to retrieve or destroy samples that have already been distributed to other investigators.

Samples and data may be shared with commercial entities with the possibility that the research done may be used to develop new products. The participant will receive no financial compensation for the development of new products that result from the use of his/her biological sample (blood, cell line), clinical and demographic data, biomarker data, and/or genetic data.

BIOSPECIMEN SHARING

Scope: A major goal of the DIAN project is the creation of a participant registry, database and biospecimen repository to support research toward discovering antecedent biomarkers and therapeutic targets for Alzheimer disease (AD). DIAN reviews and processes requests from qualified investigators seeking access to biospecimens collected from DIAN research participants and banked for this purpose in the DIAN Biomarker, Genetics (including at the National Cell Repository for Alzheimer Disease [NCRAD]), and Neuropathology Cores. These biospecimens include cerebrospinal fluid, plasma, serum, cell lines, DNA, fibroblasts and brain tissue; please see “Data and Biospecimens Available for Sharing” on the DIAN website. Please see the Biomarker and Neuropathology Core procedures manuals for details of biospecimen collection.

Restrictions on Access to DIAN Tissue: Tissue from DIAN participants cannot be used for exploratory research. Investigators seeking access to this resource must first demonstrate the hypothesized effect in tissue from sporadic AD compared to cognitively normal controls, unless a mutation specific effect is hypothesized. Demonstration of the effect in animal or cell models is good, supporting evidence but does not replace the need to demonstrate the effect in sporadic AD tissue.

Authority: Whether banked in a DIAN Core or NCRAD, or transferred to another laboratory, these biospecimens remain under the authority of the DIAN Steering Committee. Investigators receiving DIAN biospecimens acknowledge this authority and will only use the materials in accordance with the ways approved by the DIAN Steering Committee. Third party sharing is not permitted without DIAN approval.

Unless approved for a longer period of time, all requests are "active" for a maximum of 18 months or until the number of approved samples has been provided, whichever comes first.

Disclaimer: Screening for infectious agents is **NOT** performed on samples provided by the DIAN Cores at Washington University School of Medicine. The investigator must take appropriate precautions.

Requesting Biospecimens: Investigators seeking access to DIAN biospecimens are strongly encouraged to contact and discuss their request with the relevant DIAN Core Leader in advance of submitting a request. Such questions should address biospecimen collection protocols, types of tissue available, etc. Please avoid questions that would require database inquiries (ie., how many samples have XX?) Specific questions regarding DIAN biospecimens should be directed to the relevant Core Leader according to the biospecimen type:

- Plasma, serum, or cerebrospinal fluid (CSF)-Biomarker Core Leader, Dr. Anne Fagan, email: fagana@wustl.edu
- Autopsied brain material-Neuropathology Core Leader, Dr. Nigel Cairns, e-mail: cairns@wustl.edu
- DNA-Genetics Core Leader, Dr. Alison Goate, alison.goate@mssm.edu

- Cell lines and Fibroblasts – Dr. Celeste Karch, karchc@wustl.edu

Investigators should complete the tissue request webform on the DIAN Website (http://www.dian-info.org/resourcedb/default.htm) and forward the required documents to the Administrative Core for review (Katrina Paumier, Deputy Director: kpaumier@wustl.edu).

Review Process: The review process for DIAN Biospecimens is different than for data-only requests. Requests for DIAN biospecimens should detail the associated data elements to accompany the samples. After initial review, the request is assigned to two to three reviewers selected in consultation with the DIAN PI, at least one of whom must be a DIAN Steering Committee member. Biospecimen requests are disseminated to the DIAN Steering Committee for voting. A simple majority is required for approval. Upon final approval from the Steering Committee, the request will be forwarded to the relevant Core to prepare and ship the samples, in consultation with the DIAN Biostatistics Core. A Material Transfer Agreement also is needed and will be sent to the investigator following approval of the request. The criteria for review are:

- scientific merit and feasibility
- demonstration of preliminary data from sporadic AD
- appropriateness of the investigator's qualifications for proposed methods
- relevance to DIAN goals/themes
- burden on DIAN biospecimen resources
- burden on DIAN staff

Obligations incurred when accepting DIAN data or biospecimens:

- Acceptance of DIAN data obligates the recipient to cite/reference the NIA grant (Dominantly Inherited Alzheimer Network, U19AG032438) in any presentation or publication that may result from this research. Publications should also acknowledge the funding agencies from the DIAN self-funded sites including the following: the German Center for Neurodegenerative Diseases (DZNE), Raul Carrea Institute for Neurological Research (FLENI), Partial support by the Research and Development Grants for Dementia from Japan Agency for Medical Research and Development, AMED, and the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI).
- Specific language should be included in each DIAN publication detailing DIAN as an author (Please see paragraph at end of this document). If fibroblasts (or iPSCs) are shared, the DIAN Pharma Consortium should to be acknowledged for support. The full list of Pharma Consortium members can be found at: http://www.dian-tu.org/Pharma/Consortium.htm.
- Should publications result from the use of DIAN data now or in the future, the recipient agrees to notify the DIAN Deputy Director with details (reference or PubMedCentral ID#) and provide a copy of the publication to the DIAN Administration Core so that DIAN may report productivity derived from our resources to the funding agency, the NIA. Such publications require compliance with National Institutes for Health (NIH) public access policies.
- Should funding result from this research now or in the future, please notify the DIAN Executive Director (contact information below) with details (grant title, sponsor, number, dollar total, and dates) so that DIAN may report productivity derived from our resources to NIA.
- No sharing of data or biospecimens with a third party is allowed without permission of the DIAN Steering Committee.

- Any costs generated in sharing data or biospecimens will be paid by the recipient investigator.
- Recipient of data/biospecimens will provide documentation of IRB approval valid for the analysis of DIAN data/biospecimens (or acknowledgment from your IRB that receiving coded data/biospecimens without access to identifiers is not considered "research" requiring review).
- Data generated by recipients of DIAN biospecimens "belong" to the recipient investigators, but the principle of data sharing is endorsed.

Suggested timeline for resource requests:

1. Allow 30-60 days for the review process
2. Allow 30 days for interaction with the Biostatistics Core to provide dataset.

NOTIFICATIONS, MANUSCRIPT REVIEW AND AUTHORSHIP

The DIAN publication policy applies to all public and scientific communication of unpublished data that result from any DIAN-related activity. All investigators must abide by established DIAN policies and procedures. The Principal Investigator of DIAN adjudicates all disputes over leadership of analyses, authorship, etc. and decisions will be final.

Notifications:

Communications from the DIAN Study may be classified as press releases, interviews, public web site postings, presentations (includes poster and accompanying abstract) or publications that contain unpublished DIAN data. The DIAN Administration Core should be notified of all such communications, before they appear or are presented.

Manuscript Review:

Manuscripts should be submitted to the DIAN Administration Core at least 4 weeks prior to submission to a journal in order to allow time for review and response to recommendations.

Authorship:

Publication Authorship: The overarching considerations for DIAN publications are collaboration and inclusiveness. When studies use DIAN data and/or tissue processed by the DIAN Coordinating Center Cores, an invitation to collaborate (meriting authorship) on the manuscript should be issued to respective Core Leaders and Steering Committee members. DIAN Steering Committee members may also communicate their desire to collaborate when a study is reviewed. Authorship is determined by current standards of authorship responsibilities (e.g. contribute significantly to the conception, design, execution, and/or analysis and interpretation of data; participate in drafting, reviewing, and/or revising the manuscript for intellectual content). If included, it is permissible to have the masthead read “First Author, Other Authors” and the DIAN Steering Committee” with the individual Steering Committee members listed in an appropriate section of the presentation or manuscript. **All publications based on DIAN data must include “for the Dominantly Inherited Alzheimer Network (DIAN)” as an author.** If the DIAN group author cannot be used because of journal policies, then all DIAN Steering Committee members should be listed in the acknowledgments and a link to the web page where lists of personnel can be found should be also be included. A grievance process (beginning with notification of the DIAN Principal Investigator) will hear any authorship issues that arise.

Abstract Authorship: The categories and authorship rules for abstracts accompanying presentations are as stated above but may have limitations on the number of authors permitted. If authorship is limited

or impractical to include all authors then "The DIAN Study Group" would be listed as an author. A full list of members is not included.

Other Personnel as Authors: The writing group for a manuscript may include trainees, study coordinators, and other personnel as authors, providing that each author was involved in the analysis and writing of the paper.

Arbitration: When conflicts exist regarding DIAN publications, written summaries of the conflict submitted by those involved will be reviewed by the DIAN Administration Core. The DIAN PI will adjudicate the resolution. Any DIAN investigator who wishes to opt out of any automatic authorship listing may do so in writing to the DIAN Administration Core.

Press releases, interviews, and presentations (without published abstracts) usually do not have authors. When presentations are accompanied by published abstracts, the authorship rules for the abstracts are the same as for other types of publications, as described in this document

Designation of DIAN Study Members in Supplements to Publications: Supplemental material can accompany manuscripts when space is limited. Supplemental material for DIAN publications should recognize non-author DIAN members and their contribution to the study. All professional members who have the approval of the Principal Investigators and have served in a substantial capacity with the study are listed. Every clinical site and all collaborating entities are listed as participating centers. The Administration Core will be responsible for maintaining the list of all current DIAN investigators for inclusion in publications and will update this list as needed on the DIAN investigator website. Those scientific, federal, or commercial organizations providing funding are also recognized.

Required language to appear in acknowledgments of all publications using DIAN resources:

"Data collection and sharing for this project was supported by The Dominantly Inherited Alzheimer's Network (DIAN, U19AG032438) funded by the National Institute on Aging (NIA). This manuscript has been reviewed by DIAN Study investigators for scientific content and consistency of data interpretation with previous DIAN Study publications. We acknowledge the altruism of the participants and their families and contributions of the DIAN research and support staff at each of the participating sites for their contributions to this study."

If the publication includes Data Freeze 6 or later, then the following paragraph should be used:

"Data collection and sharing for this project was supported by The Dominantly Inherited Alzheimer's Network (DIAN, U19AG032438) funded by the National Institute on Aging (NIA), the German Center for Neurodegenerative Diseases (DZNE), Raul Carrea Institute for Neurological Research (FLENI), Partial support by the Research and Development Grants for Dementia from Japan Agency for Medical Research and Development, AMED, and the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI).This manuscript has been reviewed by DIAN Study investigators for scientific content and consistency of data interpretation with previous DIAN Study publications. We acknowledge the altruism of the participants and their families and contributions of the DIAN research and support staff at each of the participating sites for their contributions to this study."

For a listing of current DIAN sites, please see the DIAN website (www.DIAN-info.org)

IN SUPPORT OF THESE POLICIES THE DIAN PI AND ADMINISTRATION CORE WILL:

- Organize the submission, review and approval processes for data requests and manuscripts (to include a statistical review if necessary).
- Receive and track notifications of interviews and press releases, abstracts, presentations and publications of unpublished DIAN data.

- Ensure that all publications and presentations acknowledge the funding agency: National Institute on Aging, NIH, U19AG032438, meet current public access requirements, and report to DIAN productivity to NIA.
- Maintain a website that will:
    - Inform the research community at large of the procedures to utilize data from the study through a project website.
    - Provide information about the data that are available, a detailed description of the cohort, and an overview of the methods by which data have been collected, and a data dictionary
    - Provide an electronic data request form
    - Provide a list of all Steering Committee members, current DIAN investigators, language for acknowledgment of DIAN and its source of funding
    - Maintain a list of DIAN study presentations and publications and routinely review the progress of DIAN proposals for data analyses to support future publications and presentations
    - Post all approved DIAN data requests/proposals for transparency and documentation of intention to pursue specific projects. Investigators wishing to initiate a project with DIAN data or tissue can search previous or existing DIAN projects to avoid duplication or competition and to invite collaboration.