

POLICIES AND GUIDANCE FOR SHARING OF RESOURCES AND DATA FROM STUDIES ON THE GENETICS OF ALZHEIMER'S DISEASE

Policies

Background

The National Institutes of Health (NIH) advocates making available to the public the results and accomplishments of the activities that it funds. NIH assures that research resources developed with public funds become readily available to the broader research community in a timely manner for further research, development, application, and secondary data analysis in the expectation that this will lead to products and knowledge of benefit to the public health. Resources expected to be shared include data and biological materials collected and pertinent methods of analysis. The National Institute on Aging (NIA) supports the NIH policy that whenever possible research resources be made available to qualified investigators. Compliance with these policies is an important requirement of an NIH award.

While NIH policy (http://www.grants.nih.gov/grants/policy/data_sharing/) applies only to awards exceeding \$500,000 in any one year, NIA is instituting a sharing policy in the area of human Alzheimer's disease genetics that applies to all NIA funded research in the area of Alzheimer's disease genetics regardless of cost. Principal Investigators should discuss with their program official their data sharing plan or possible reasons why they cannot share final research data prior to application or proposal submission. Program officials will be responsible for assessing the appropriateness and adequacy of any proposed data sharing plan prior to award, and may allow a study to waive a data sharing plan under exceptional circumstances. Documentation of agreement to comply with the terms and conditions for this award must be sent to the NIA program official within 15 calendar days of receipt from the NIA of the Guidance for Sharing in Studies on the Genetics of Alzheimer's Disease document (see below).

Implementation

NIA has in place a Genetics Initiative to assist in the identification of the risk factor genes for Alzheimer's disease. To this end, NIA supports a National Cell Repository for Alzheimer's Disease (NCRAD) at Indiana University <http://ncrad.iu.edu/> and invites investigators to utilize this resource. More information can be obtained from the website or through an NIA Neuroscience and Neuropsychology of Aging program official. A Cell Bank Advisory Committee (CBAC) to NCRAD; the coordinator of the NIA Genetics Initiative; NCRAD staff; and NIA staff have jointly established 1]. eligibility criteria, 2]. guidance on protection of human subjects, confidentiality, and compliance with relevant laws and regulations, and 3]. operating procedures for the sharing of biological samples and Associated Phenotypic Data.

Associated Phenotypic Data is defined as deidentified data on family structure, age, sex, vital status, psychopathology, diagnosis, and other clinically relevant associated phenotypic information, stripped of all personal identifiers and thus unlinkable to the individuals from whom they were obtained.

NIA has established NCRAD as a national repository in order to facilitate access by qualified investigators to samples and Associated Phenotypic Data for the study of the genetics of late onset Alzheimer's disease. Therefore it is the policy of the NIA that useful specimens and Associated Phenotypic Data for the genetics of late onset Alzheimer's disease be deposited at NCRAD whenever possible. Qualified investigators will be able to use biological samples and

Associated Phenotypic Data supplied by NCRAD. Application for use will be made directly to NCRAD.

Genetic Data is defined as de-identified data derived from genotyping, mutation analysis, single nucleotide polymorphisms (SNPs) and other genetic analyses of Biomaterials and Associated Phenotypic Data conducted by Submitters and other scientists, stripped of all personal identifiers and thus unlinkable to the individuals from whom they were obtained.

NIA has established the National Institute on Aging Genetics of Alzheimer's Disease Data Storage Site (NIAGADS) (<http://www.niageneticsdata.org/>) at Washington University, funded by NIA, as a national genetics data repository in order to facilitate access by qualified investigators to genotypic data for the study of the genetics of late onset Alzheimer's disease. It is the policy of the NIA that all Genetic Data derived from NIA funded studies for the genetics of late onset Alzheimer's disease be deposited at NIAGADS or another NIA approved site or both whenever possible. Such Genetic Data shall be made available as soon as possible, but no later than upon acceptance of a subset of data for publication or public disclosure of a submitted patent application, whichever is earlier. For example, after publication of preliminary reports of the work, a subset of phenotypic data and Genetic Data is to be shared with other investigators for secondary analysis. Generally, this will be a subset of data, or data that are made public and will not typically include the full range of Associated Phenotypic Data being collected in genetic studies. NIAGADS along with other NIA approved sites will make these Genetic Data and Associated Phenotypic Data available to qualified investigators in the scientific community for secondary analysis in accordance with standards established by the NIA.

Exemptions to providing a sharing plan will be considered by NIA staff with proper justification. The reason for requesting that samples and Associated Phenotypic Data not be deposited at NCRAD or that Genetic Data not be deposited at NIAGADS or other NIA approved sites must be clearly stated in writing. Guidance for Sharing Resources and Data from Studies on the Genetics of Alzheimer's Disease is provided later in this document.

Sharing of biological samples and Associated Phenotypic Data between the Principal Investigator and other qualified investigators (other than through NCRAD) should be accomplished via a simple letter of agreement (SLA). An SLA should be used for the transfer of samples and Associated Phenotypic Data to for-profit entities as described at: http://ott.od.nih.gov/NewPages/RTguide_final.html. NIA requests a copy of any pre-existing SLAs that apply to the samples associated with this award. Existing SLAs should be mailed to your NIA program official along with your signed sharing plan agreement.

Sharing of biological samples, Associated Phenotypic Data, and resources through NCRAD should be accomplished through the NIH approved Material Transfer Agreement (MTA) for transferring biological samples to NCRAD. The NIH approved template MTA is available from the program official responsible for your award.

NIA requests a copy of any pre-existing MTAs that apply to the samples associated with this award. Existing MTAs should be mailed to your NIA program official along with your signed sharing plan agreement.

Subjects consenting to participation in a specific study must be informed of the purpose of the study, including the measures developed for protecting confidentiality; must have given appropriate consent to participate in the study; and must have provided authorization for the sharing and archiving of de-identified samples and Associated Phenotypic and Genetic Data for use by qualified investigators. For DNA samples and phenotypic information stored at the parent Institution, the consent process should document permission for sharing of samples and selected Associated Phenotypic Data with qualified investigators, as determined by a local advisory board. A copy of the Institutional Review Board (IRB) approved consent form must be sent to the

program official responsible for this award within 15 calendar days of approval. Please see the appendix for additional information on IRB consent forms.

Whether stored at NCRAD or at the grantee Institution, biological samples along with relevant subsets of Associated Phenotypic Data, as well as Genetic Data resulting from the research should be released to qualified investigators as soon as possible but no later than within one year of the completion of the funded project period for the parent award or upon acceptance of a subset of data for publication, or public disclosure of a submitted patent application, whichever is earlier, even if a competing renewal application is submitted. For biological samples and for Associated Phenotypic Data, a record of requests for data and biological specimens including relevant names and Institutions, and the action taken on them must be documented and retained by the investigator and reported with the annual progress report for the non-competitive renewal of the funded award.

Please consult the web pages cited below for information related to sharing policies and patent issues:

- http://grants2.nih.gov/grants/policy/data_sharing/ The sharing of data for awards that exceed \$500,000 direct costs in any one year of funding.
- http://grants2.nih.gov/grants/policy/nihgps_2001/ The sharing of research resources and intellectual property for research purposes to qualified individuals within the scientific community in accordance with the NIH Grants Policy Statement (2001).
- <http://grants2.nih.gov/grants/guide/notice-files/not96-184.html>. "Public Health Service Policy Relating to Distribution of Unique Research Resources Produced with PHS Funding" was published in the NIH GUIDE, Volume 25, Number 23 (1996).
- http://ott.od.nih.gov/NewPages/RTguide_final.html. "Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources," and <http://ott.od.nih.gov/NewPages/64FR72090.pdf> [pdf file of this document]. These documents define terms, parties, responsibilities for sharing; prescribe the order of disposition of rights; prescribe a chronology of reporting requirements; and delineate the basis for and extent of government actions to retain rights (1999).
- <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html>. NIH has reaffirmed its support for the concept of data sharing with the release of NOT-OD-03-032. The latest policy statement on the sharing of unique research resources can be found at this site (2003).
- http://ott.od.nih.gov/NewPages/RTguide_final.html. Please refer to the "Principles and Guidelines for Recipients of NIH Research Grants and Contracts" where a simple letter of agreement (SLA) template is available from the Office of Technology Transfer (NIHOTT@od.nih.gov). The SLA may be expanded for use in transferring tools to for-profit entities.
- <http://www.iedison.gov>. Patent rights clauses may be found at 37 CFR Part 401.14 and are accessible from the Interagency Edison web page.
- <http://www.nia.nih.gov/>. The NIA home page.
- <http://ncrad.iu.edu/>. The NCRAD website at Indiana University.
- <http://www.niageneticsdata.org/>. The National Institute on Aging Genetics of Alzheimer's Disease Data Storage Site (NIAGADS) at Washington University.

The document below constitutes the requirements for a sharing plan in which NIA invites you to participate in order to fulfill the terms and conditions placed on your Notice of Grant Award. The program official responsible for this project at NIA will work with the Principal Investigator during the process of instituting the sharing plan. Please return a signed copy of this document to the NIA program official within 15 calendar days of receipt of this communication.

**Guidance for Sharing of Resources and Data from
Studies on the Genetics of Alzheimer's Disease**

Grant/Contract number _____
Grant/Contract Title _____
Principal Investigator _____
Date of Notice of Grant Award _____
Program Official _____

1.a. I agree to maintain biological samples, including DNA and/or cell lines, and Associated Phenotypic Data at my parent Institution. I agree that the names and Institutions of persons either given or denied access to the biological materials and Associated Phenotypic Data, and the basis for decisions will be summarized in the annual progress report of the non-competitive renewal for each year of award. If the NIA or my colleagues determine at some time in the future that there is scientific benefit to do so, I agree that following review of protocols and acceptance by NCRAD, I will deposit biological samples and Associated Phenotypic Data at NCRAD. I agree to place Genetic Data in NIAGADS or another NIA approved site or both. I understand that qualified investigators will have access to these data.

1.b. I agree that biological samples along with relevant subsets of Associated Phenotypic Data, as well as Genetic Data resulting from the research will be released to qualified investigators as soon as possible but no later than within one year of the completion of the funded project period for the parent award or upon acceptance of a subset of data for publication, or public disclosure of a submitted patent application, whichever is earlier, even if a competing renewal application is submitted.

2. I agree that in the case of DNA samples that are in limited supply, a local advisory committee will help to determine which investigators have access to these samples and Associated Phenotypic Data. I further agree that the board will be established through my Institution and will include *ex officio* NIA representative(s). I further agree that in the case of DNA samples, the local advisory committee will weigh several factors including the amount of the sample remaining, the amount that the PI will need to complete ongoing work, and the significance of the research question.

3.a. In the event that only DNA is being used, but cell lines are not being prepared, I agree that the DNA will be stored at my Institution or research site and made available to other qualified investigators as summarized in items 1 and 2. I understand that if I, my colleagues, or the NIA determine that there is scientific need for cell lines to be made from my samples at a later time, then the Institution, the investigator, and the NIA may develop a plan to prepare the cell lines.

3.b. I agree that in the event that my study involves the preparation of cell lines that are not to be deposited at NCRAD, the cell lines and Associated Phenotypic Data derived in the present study will be stored at my Institution or Institutionally approved study site and made available to other qualified investigators as summarized in item 1.

3.c. In the event that my study involves the preparation of cell lines that are not initially deposited at NCRAD I understand that at a later time, I may be requested to arrange with NCRAD for the cell lines to be considered by the advisory committee to NCRAD for deposit in the Repository. I understand that, if so requested, then the expense for this undertaking will be incurred by NCRAD and the NIA.

4. I agree that sample sharing and sharing of the subset of phenotypic data with other

investigators can be accomplished via a simple letter of agreement (SLA) that will be provided to NIA. I agree to send pre-existing SLAs to the program official responsible for this award. The SLA should state that recipients of samples that have been obtained through NIA funding agree to place genetic outcome data in NIAGADS or another NIA approved site or both to which qualified investigators will have access; Genetic Data resulting from the research should be released to NIAGADS or another NIA approved site or both as soon as possible but no later than within one year of the completion of the funded project period for the parent award or upon acceptance of a subset of data for publication, or public disclosure of a submitted patent application, whichever is earlier, even if a competing renewal application is submitted.

5. I agree to use the NIH approved MTA if I am transferring my samples to NCRAD. I agree to send pre-existing MTAs to the program official responsible for this award.

6. I agree to obtain appropriate consent from subjects participating in the study as described in the policy statement of this document and in the appendix. I agree to send a copy of the IRB approved consent form to the program official responsible for this award within 15 calendar days of approval.

By signing below, the signee acknowledges that the information in this document has been read and agrees to the terms and conditions prescribed herein.

Signature of the Principal Investigator

Date

Printed name of the Principal Investigator

Signature of Institutional Official

Date

Printed name of the Institutional Official

Appendix:

I. Consent forms: Regardless of whether samples and data are initially to be kept at the awardee Institution, or also to be sent to the National Cell Repository for Alzheimer's Disease (NCRAD), the points outlined below should be addressed in the consent form. A sample Institutional Review Board consent form will be available at the NCRAD website. If current consent forms do not permit the type of sharing outlined in this document, then they must be amended and approved by the IRB. Language in the consent form must be geared toward an eighth grade educational level.

A. HIPAA: Samples, phenotypic and family information are to be redacted of all personal identifiers and will be identifiable solely by a unique number generated at the study site. No information that identifies the subject will be distributed. De-identification of samples and data must conform to the guidelines set forth by the Privacy Act 5 USC 552a; HIPAA Privacy Rule 45 CFR § 160.103; and the HIPAA Privacy Rule 45 CFR § 164.514.

B. De-identification of samples: The recipient of de-identified samples and accompanying phenotypic data must agree that neither the de-identified samples nor accompanying data will be used either alone or in conjunction with any other information, in any effort whatsoever to establish the individual identities of any subjects from whom the research material was derived. A statement with a reasonable facsimile of this language must appear in the related MTAs.

C. Storage of DNA or cell lines at the grantee Institution: When de-identified samples and accompanying phenotypic data are to be stored at the grantee Institution, the consent form must include an explanation that at some time in the future the subject may be re-contacted in order to obtain an additional blood sample. In this case, the subject's identity will be protected according to HIPAA regulations. The consent form should also indicate that the sample and accompanying de-identified phenotypic data may also be stored at NCRAD (see D. below).

D. NCRAD: The consent form must include an explanation of NCRAD. Suggested language is: "Participants in this study are being asked to agree to the possibility that their de-identified samples may be stored at NCRAD, a research facility at Indiana University that is supported by the National Institute on Aging to facilitate genetic research on Alzheimer's disease and related disorders. NCRAD is a national resource that prepares and stores cell lines and DNA samples and makes them available to investigators who would otherwise have no access to them to determine whether certain differences in a gene or genes within the population correlate with clinical symptoms and/or brain changes at autopsy."

E. Content: Whether stored at the grantee Institution or at NCRAD, consent forms must contain statements on:

1]. Purpose of the study: Samples and related phenotypic information will be used to find genes that may play a role in the occurrence of late onset Alzheimer's disease, related disorders, and aging.

2]. Subject identification: There is always a small possibility that the subject may be identified. The subject's identity will not be shared with other researchers. Samples, phenotypic data, and Genetic Data will be coded to minimize the risk of identification. De-identified phenotypic data will be kept on a secure computer at the investigator's study site that can be accessed only by qualified investigators. De-identified Genetic Data will be kept separate from de-identified phenotypic data on a secure computer that can be accessed only by authorized investigators. De-identified Genetic Data may be stored on a secure website through an NIA supported genetic data repository that is separate from NCRAD and may be shared for secondary analysis by other investigators.

3]. Samples and Associated Phenotypic Data: A blood sample will be drawn; a portion of the subject's sample may be made into a cell line (a family of cells grown in the laboratory) and stored at the grantee Institution. The de-identified sample, along with phenotypic data (such as demographics, family history of dementia, and diagnosis) may be shared with qualified investigators and could be used for secondary study purposes such as finding genes that contribute to the aging process. An extra blood sample along with de-identified phenotypic data may be sent to NCRAD to enable the subject's DNA to be made available indefinitely for use by other qualified investigators. All stored biological samples will be kept indefinitely except when the subject requests they be destroyed or when the resource has been exhausted.

4]. Commercial entities: Sharing of de-identified samples and phenotypic data may occur with commercial entities. Research done with biological materials may be used to develop new products. Subjects will receive no financial remuneration for the development of new products derived from the use of their biological samples, phenotypic or Genetic Data.

5]. Autopsy tissue: If the only appropriate tissue available to do for these studies is from an autopsy, then a small amount of frozen tissue (3-5 grams) may be stored at the grantee Institution and may be shared with qualified investigators. A portion of the sample may be sent to NCRAD to enable the subject's DNA to be made available indefinitely for use by other qualified investigators.

6]. Withdrawal from the study: If a subject withdraws from the study, then the subject can request that any unused sample(s) be destroyed immediately upon request. Suggested language is: "You may decide to withdraw consent from the study at any time. In this event, the Principal Investigator will notify the storage site that consent has been withdrawn and that the sample(s) are to be destroyed. The storage site will, in turn, notify all recipients of your research material and Associated Phenotypic Data and

request that the recipients destroy the samples.” Note that samples that have already been used or disseminated prior to the request for withdrawal may continue to be used in order to protect the integrity of ongoing research.

7]. Risks and benefits: There are no additional risks to the subject from participating in this study. There is no financial cost of the study to the subject. There are no additional benefits, including financial benefits, to the subject from participating in this study.

8]. Follow-up: There is the possibility of follow-up interview / testing.

II. Simple Letter of Agreement (SLA). Sharing of biological samples and phenotypic data between the Principal Investigator and other qualified investigators (other than NCRAD) should be accomplished via an SLA. An SLA should be used for the transfer of samples and accompanying phenotypic data to for-profit entities as described at: http://ott.od.nih.gov/NewPages/RTguide_final.html.

III. Material Transfer Agreement (MTA): For samples sent to NCRAD, de-identified samples and phenotypic data will be transferred to NCRAD by means of the NIH approved MTA and will be made available to qualified investigators.