NEI-AREDS2 Genetic Repository

Material Transfer Agreement and Assurance Form for DNA Samples

This Material Transfer Agreement and Assurance Form for DNA Samples ("MTA") pertains to the DNA samples ("NEI-AREDS2 Repository Samples") that are part of the NEI-AREDS2 Genetic Repository ("Repository"), and which are administered by the Coriell Institute for Medical Research, Camden, New Jersey ("Coriell"). The "Institutional Official" is the legal representative of the Institution receiving the NEI-AREDS2 Repository Samples ("Institution") who is authorized to make legally binding agreements for the Institution (see Appendix 1).

The Principal Investigator ("Recipient") is the person receiving the NEI Repository Sample(s) and is responsible for the conduct of the Statement of Research Intent, defined below. The Recipient's research team that is under the direct supervision of the Recipient may have access to the NEI Repository Sample(s) only after they have been informed of and agreed to the provisions of this MTA. The Recipient must acknowledge on the signature page of this MTA that the Recipient has read and understands the terms and conditions of this MTA. The Institutional Official must also sign this MTA on behalf of the Institution agreeing to adhere to the terms and conditions of this MTA.

To ensure compliance with the Office for Human Research Protections ("OHRP"), Department of Health and Human Services ("DHHS"), regulations for the protection of human subjects (45 CFR Part 46), before NEI-AREDS2 Repository Samples can be shipped from the Repository, the Recipient must provide the Repository with a written description of the purpose of the research project to be done using the applicable NEI-AREDS2 Repository Samples ("Statement of Research Intent") and this MTA. Both the Recipient and the Institutional Official must sign this MTA agreeing to adhere to the conditions set forth in this MTA. The Recipient remains subject to all applicable local, state, and federal laws and regulations and Institution policies.

The signed Statement of Research Intent and MTA must be returned to Coriell prior to Coriell shipping the applicable NEI-AREDS2 Repository Samples.

A. Warranty and Liability

1. Warranty

NEITHER CORIELL NOR THE REPOSITORY MAKES ANY REPRESENTATIONS OR EXTENDS ANY WARRANTIES OF ANY KIND, EITHER EXPRESSED OR IMPLIED, WITH RESPECT TO THE NEI-AREDS2 REPOSITORY SAMPLES, INCLUDING, WITHOUT LIMITATION, ANY EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR THAT THE USE OF THE NEI-AREDS2 REPOSITORY SAMPLES WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK, OR OTHER PROPRIETARY RIGHTS OF ANY PARTY.

2. Liability Statement

For State Institutions: The Institution agrees to be responsible for any claims, costs, damages, or expenses resulting from any injury (including death), damage, or loss that may arise from the use of the NEI-AREDS2 Repository Samples to the maximum extent permitted under the laws of the state where the Institution is located. This provision shall also apply to any byproducts or derivatives of the NEI-AREDS2 Repository Samples.

For U.S. Government Laboratories: The United States assumes the liability for any claims, costs, damages, injuries, or expenses arising from the use of the NEI-AREDS2 Repository Samples or any byproduct or derivative of the NEI-AREDS2 Repository Samples to the maximum extent permitted under the Federal Tort Claims Act (28 U.S.C. Chapter 171).

For All Other Institutions: The Institution agrees to indemnify and hold harmless the United States Government, Coriell, and the contributor from any claims, costs, damages, or expenses resulting from any injury (including death), damage, or loss that may arise from the use of the NEI-AREDS2 Repository Samples. This provision shall also apply to any byproducts or derivatives of the NEI-AREDS2 Repository Samples.

B. Conditions of Use

1. Protection of Human Subjects

The Recipient acknowledges that the conditions for use of the NEI-AREDS2 Repository Samples are governed by Coriell's Institutional Review Board ("IRB"), in accordance with DHHS regulations (45 CFR Part 46). The Recipient agrees to comply fully with all such conditions and to report promptly to the IRB any unanticipated events involving risks to subjects or others. The Recipient remains subject to all applicable state and local laws and regulations and institutional policies that provide additional protections for human subjects.

2. Changes to Research Project or Recipient's Institution

The Recipient agrees to report promptly to the IRB any proposed changes to the research project. The Recipient also agrees to promptly submit a new Statement of Research Intent and MTA to Coriell if any major changes to the research project are proposed.

The Recipient agrees that if the Recipient changes institutions, then a new Statement of Research Intent and MTA signed by the Institutional Official at the new institution will be provided by the Recipient to Coriell.

3. Non-identification of Subjects

Coriell staff will under no circumstances provide information that will allow recipients to identify subjects. Furthermore, the Recipient agrees not to try to identify or contact the submitter of the sample or the donor subject (or their living relatives) from whom the applicable NEI-AREDS2 Repository Sample(s) was derived. (This condition is not applicable to AREDS2 Principal Investigators who

provided the genetic samples if they have appropriate institutional approval to retain the subject identities or re-contact subjects).

4. Human Experimentation

Human experimentation utilizing NEI-AREDS2 Repository Samples is strictly prohibited.

5. Research Use

Coriell provides biomaterials as a service to the research community. The purpose of the Repository is to stimulate and facilitate research in genetics and related fields, leading to a better understanding of normal genetic and cellular processes, to the identification and function of disease-related genes, and to the diagnosis and treatment of genetic disorders.

It is expressly understood that the NEI-AREDS2 Repository Samples delivered pursuant to this MTA are experimental and are solely for use in research, in teaching and as standards in clinical genetics laboratories. Recipients employing NEI-AREDS2 Repository Samples for use as research standards or controls are responsible for complying with all laws and regulations applicable to the intended use of such samples, including any requirements for FDA approval.

6. Genetic Specimens for Eye Disease Research Only

Some genetic specimens were provided by AREDS2 participants who consented that their specimen only be used for eye disease research. The Recipient agrees to use any genetic information from the specimens from these participants solely to do research in eye disease (age-related macular degeneration and cataract) and no other type of disease.

7. Commercial Use and Intellectual Property

The Recipient and the Institution agree not to distribute, or be party to the distribution of, NEI-AREDS2 Repository Samples (or replicated or subdivided DNA), or products derived from the NEI-AREDS2 Repository Samples, in commercial products or services.

The National Eye Institute ("NEI") recognizes the importance of the later development of intellectual property on downstream discoveries, especially in therapeutics, which will be necessary to support full investment in products that the public needs. As such, there is no restriction on development of commercial products resulting from the knowledge gained from studies using NEI-AREDS2 Repository Samples.

However, in order for the Repository to achieve maximum public benefit, the NEI urges the Recipient and the Institution to adhere to the intellectual property policy outlined below:

- Genetic data and conclusions derived therefrom should remain freely available, without requirement for licensing, for applications such as, but not necessarily limited to, the following: the use of markers in developing assays or diagnostic tools; the use of combinations of markers in multiplex assays; and the use of markers as guides toward identification of new drug targets.
- The NEI recommends that data generated using NEI-AREDS2 Repository Samples be provided

to the NEI Data Commons housed on the NIH Biomedical Research Informatics Computing System ("BRICS") for inclusion with other AREDS2 genetic data at the time that any article using these data is published. Questions on how to upload data on BRICS should be directed to NEIODSHI@nei.NIH.gov.

- The NEI encourages licensing practices consistent with the recommendations cited in NIH's Best Practices for the Licensing of Genomic Inventions and in the NIH Research Tools Policy.

8. Non-transferability

The Recipient agrees to retain control over the NEI-AREDS2 Repository Samples and further agrees not to distribute the NEI-AREDS2 Repository Samples (or replicated or subdivided DNA derived from any NEI-AREDS2 Repository Samples) or products derived from the NEI-AREDS2 Repository Samples, with or without charge, to any entity or individual other than the Recipient's research staff, subject to applicable law, except under special circumstances (see Appendix 2). The Recipient and the Institution acknowledge that it is the responsibility of the Recipient and the Institution to ensure appropriate use of the NEI-AREDS2 Repository Samples and agreement to the terms of this MTA by research staff.

9. Dissemination of Research Results and Acknowledgement of AREDS2

It is the intent of the Repository to promote the dissemination of analyses of NEI-AREDS2 Repository Samples as widely as possible. To further this goal, the Recipient is strongly encouraged to publish the Recipient's research results in peer-reviewed journals.

The Recipient agrees to acknowledge AREDS2 and the AREDS2 Research Group in all oral and written presentations, disclosures, and publications resulting from any analyses of NEI-AREDS2 Repository Samples. The Recipient further agrees that the acknowledgment shall include a citation of the following paper: AREDS2 Research Group; Chew EY, Clemons T, SanGiovanni JP, Danis R, Domalpally A, McBee W, Sperduto R, Ferris FL. The Age-Related Eye Disease Study 2 (AREDS2): study design and baseline characteristics (AREDS2 report number 1). Ophthalmology. 2012 Nov;119(11):2282-9. doi: 10.1016/j.ophtha.2012.05.027. Epub 2012 Jul 26. PMID: 22840421; PMCID: PMC3485447.

An example of a possible acknowledgment for AREDS2 Samples is as follows:

"The DNA samples used for the analyses described in this manuscript were obtained from the National Eye Institute - Age-Related Eye Disease Study 2 (NEI-AREDS2) Genetic Repository. Funding support for AREDS2 was provided by the National Eye Institute (N01-EY-5-0007). We would like to thank the AREDS2 participants and the AREDS2 Research Group for their valuable contribution to this research."

C. Signatures

By signing and dating this MTA, the Recipient and the Institution certify their agreement to the principles, policies and procedures for the use of NEI-AREDS2 Repository Samples as articulated in this MTA. Recipient further acknowledges that Recipient has shared this MTA with any research staff that will participate in the use of NEI-AREDS2 Repository Samples.

The Institution also acknowledges that it has shared this document with the appropriate Institutional organizations, such as the Office of Technology Transfer and the Office for Human Subjects Research or equivalent.

We, the undersigned, have read and understand this MTA and agree to adhere to the terms, conditions, restrictions and warnings stated herein.

Name of Institution: _____

Principal Investigator/Recipient
(typed or printed): _____

Signature: _____

Institutional Official who can make legal
commitments on behalf of the
Institution (typed or printed): _____

Title of Institutional Official _____

Signature of Institutional Official: _____

Date: _____

To contact the CORIELL INSTITUTE FOR MEDICAL RESEARCH:
Write: 403 Haddon Avenue, Camden, New Jersey, 08103 USA
Call: 800-752-3805 in the United States, 856-757-4848 from other countries; OR **Fax**: 856-757-9737
E-mail:ccr@coriell.org

Appendix 1
Signatory Guidelines

With regard to the requirement for the signature of an "Institutional Official" who can make legal commitments on behalf of the Institution receiving NEI-AREDS2 Repository Samples:

The MTA requires that the **Institution** (in addition to the Principal Investigator receiving the NEI-AREDS2 Repository Samples) assure:

1. That the NEI-AREDS2 Repository Samples will be used in compliance with all regulations protecting human subjects.
2. That the NEI-AREDS2 Repository Samples and/or any products derived from them will not be commercialized.
3. That the NEI-AREDS2 Repository Samples will not be distributed to a third party (that the researcher will not "share" with a colleague) without authorization by the Coriell Institute for Medical Research as agent for the National Eye Institute.
4. That the Institution's research laboratory is properly equipped and provides the appropriate training for the handling of potentially hazardous biomaterials.
5. That the Institution does and will assume liability for use of the NEI-AREDS2 Repository Samples, as detailed in the MTA.

These are **legal** commitments by the Institution. If the researcher or end-user (or laboratory technician or other staff) fails to abide by the commitments or misuses the NEI-AREDS2 Repository Samples in any way, the Institution is and shall be liable for failure to fulfill the terms of the MTA.

The individual who can make such commitments on behalf of the Institution is usually a senior Institutional official (e.g., president, vice-president, director) with responsibility for scientific and technological research and development or legal affairs. **This individual is likely to be the person authorized to sign grant applications or contract proposals on behalf of the Institution.**

It is unlikely that staff of a purchasing department would be authorized to make assurances about the scientific use of biomaterials.

We request that sufficient detail be included in the "title" used by the signer of the MTA so that the level and scope of responsibility is clear and unambiguous (the title of "Dr." or "Professor" does not in itself provide sufficient information about the responsibilities of the signer).

Appendix 2
Secondary Distribution and Shared Use of DNA Samples

Principal Investigators who intend to purchase samples that are to be shared should read the statement below and then contact the Order Department of Coriell Cell Repositories by calling 800-752-3805 before proceeding with the order.

Genetic research often involves collaborations among several laboratories that share materials toward a common goal. Also, as a result of new genomic technologies, data are often generated by multi-user core facilities. Many labs often benefit from using common biological standards for research or clinical purposes. Thus, consistent with the mission to facilitate genetic research, the Repository will permit secondary distribution to accommodate certain situations if it can be established that protection of human subjects and quality control can be assured. Examples of situations in which the issue of secondary distribution or shared use might be raised are described below, along with recommendations and the rationale behind the recommendations.

1. **Single purpose collaboration** - Two or more Principal Investigators initiate a collaborative project that requires the use by each laboratory of the same DNA sample. One Principal Investigator purchases a sample and explains in the statement of research intent that the sample will be shared with specific, named collaborators for a common research purpose. Secondary distribution to named collaborators is permitted when the research intent is identical for the collaborators and is thus consistent with the informed consent and quality can be reasonably assured by virtue of the collaboration. *In addition to the Principal Investigator placing the order, all collaborating Principal Investigators must submit a signed MTA (or have a current MTA on file) and also submit a separate Statement of Research Intent.*

2. **Multi-purpose use** - A Principal Investigator working on a particular project purchases a sample and submits a statement of research intent describing that project. At some time after obtaining the sample, the investigator wishes to give a portion of the DNA sample to a colleague who is working on another project. In this case, secondary distribution is prohibited because the Coriell Institute for Medical Research IRB ("CIMR IRB") cannot assure that use of the sample by the original purchaser's colleague is consistent with the informed consent. In addition, errors in identification of DNA samples can occur and could compromise the Repository's reputation.

3. **Multi-user core facility** - A core facility (for high-throughput genotyping, for example) purchases samples for use by the scientists in the facility to perform assays for investigators at that institution or at a consortium of institutions. The statement of research intent describes the range of studies (e.g., the kinds of phenotypes for which genotyping studies would be performed) but explains that the number of users and the exact phenotypes cannot be predicted. In this situation, the use of the samples in the core facility is permitted after the CIMR IRB confirms in writing that it is satisfactorily assured that the use of the samples is consistent with the informed consent. Since the samples will be used in the same facility for multiple investigators, quality can be assured.

4. **Distribution of aliquots or derivatives of samples for use as biological standards** - An organization purchases a sample and describes in the statement of research intent that the sample will be distributed, either with or without modification, for use as standards. The statement may or may not be able to specify the purpose(s) for which the distributed material will be used or the laboratories that would receive the materials. The Repository must decide this type of request on a case-by-case basis.

In cases where the CIMR IRB staff, with the advice of the Repository's project officer, can reasonably expect that the organization would produce high quality control standards (based on the proposed methods of quality control and the expertise and past experience of the organization), and where the CIMR IRB can assure that the uses of distributed samples are limited to those that the CIMR IRB approves, secondary distribution should be permitted. The secondary distribution of aliquots or derivatives of samples of Repository materials for commercial purposes is prohibited under all circumstances. The burden of proof must be on the purchaser of the sample from the Repository. Furthermore, samples that are distributed must be accompanied by a disclaimer, satisfactory to the Repository in form and substance, of the Repository's responsibility regarding safety and quality.