Blood and Saliva Sample Collection and Submission to the Age-Related Eye Disease Study 2 (AREDS2) Genetic Repository

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INVESTIGATOR STATEMENT OF APPROVAL

Blood and Saliva Sample Collection and Submission to the Age-Related Eye Disease Study 2 (AREDS2) Genetic Repository

I have read the Protocol and agree to follow the procedures as outlined in this Protocol.

I will not start the study until I have obtained written approval by the governing Institutional Review Board/Ethics Committee. I will obtain written informed consent from all study participants prior to conducting any study procedures.

I understand that my electronic or handwritten signature, or that of a co-investigator, on a case report form indicates that the data contained on that form have been reviewed and accepted as accurate by the signatory.

I agree to conduct this study in compliance with the applicable local regulations, FDA regulations (21 CFR 50, 54, 56, 312), Good Clinical Practices, and the Declaration of Helsinki.

I understand and am aware of my responsibilities as an Investigator as described in the applicable Good Clinical Practices regulations.

I understand that this protocol and related information is subject to the confidentiality terms found in my signed Confidentiality or Clinical Services Agreement. I agree to protect the confidentiality of my patients when allowing the Sponsor of this clinical trial and/or relevant regulatory authorities access to my medical records for AREDS2 participants.

________________________________________________________________________
Principal Investigator, Printed Name

________________________________________________________________________
Address: Telephone #

________________________________________________________________________
Principal Investigator, Signature Date

Upon signing, send this page to The EMMES Corporation for their files and keep a copy for your Regulatory Binder.

AREDS2 Coordinating Center
401 N. Washington Street, Suite 700
Rockville, MD 20850-1785
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### List of Abbreviations

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<thead>
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<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>AMD</td>
<td>Age-related macular degeneration</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
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<tr>
<td>GR</td>
<td>Genetic repository</td>
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<tr>
<td>IRB</td>
<td>Institutional Review Board</td>
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<tr>
<td>NEI</td>
<td>National Eye Institute</td>
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<td>NIH</td>
<td>National Institutes of Health</td>
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Protocol Summary

Title: Blood and Saliva Sample Collection and Submission to the AREDS2 Genetic Repository

Phase: NA

Project Type: Genetic Repository

Population: Participants enrolled in the Age-related Eye Disease Study 2 (AREDS2).

Number of Sites: Up to 82

Project Duration: Present -- December 2012

Description of Agent or Intervention: NA

Objective: Submit blood and saliva specimens to the AREDS2 Genetic Repository.

Description of Project Design: AREDS2 participants who have signed the informed consent document will have two 10 mL tubes of blood and 1 saliva sample (using an Oragene kit) collected. One tube of blood will be processed by the AREDS2 Genetic Repository into DNA and plasma. The saliva sample will be processed into DNA if needed. The other tube of blood will be processed by the AREDS2 clinical site into serum which will later be shipped frozen to the AREDS2 Genetic Repository. AREDS2 clinical sites not able to process blood into serum will only draw one 10 mL tube of blood from their AREDS2 participants.
1 OBJECTIVE

To successfully submit blood and saliva samples to the AREDS2 Genetic Repository.
2 PROJECT DESIGN

AREDS2 participants will be requested to provide a blood draw and a saliva sample to the AREDS2 Genetic Repository. This Genetic Repository will serve as a public resource providing materials for the study of the genetic and biochemical bases for eye disease.

AREDS2 participants will be provided with the option to consent to participate in the project. Study staff will answer any questions the prospective participant has about the study or participation before the prospective participant is asked to sign the consent. After the informed consent is signed, a participant will have two 10 mL tubes of blood drawn and one saliva sample collected. The blood samples and saliva sample will be labeled with a unique identifier (Specimen Number) in order to prevent identification of the participant. The AREDS2 Genetic Repository will retain a paper and electronic “sample record” file of each sample submitted to the Repository. The paper record will consist of the AREDS2 Participant ID and the Specimen Number provided with the sample by the submitter; the electronic record will contain Specimen Number but not the AREDS2 Participant ID. Both paper and electronic files are only accessible to authorized Repository staff. The Specimen Number, not the AREDS2 Participant ID, will be used for display of the phenotypic data in the catalog. See Figure 1 below for a flow diagram of the sample submission process.

The AREDS2 Genetic Repository will have a process in place to satisfy withdrawal requests from participants who wish to have their samples withdrawn from further distribution to researchers.

Figure 1. Sample Submission Process:

- Collect samples and label with a unique identifier (Specimen Number)
- Submit samples with Specimen Shipping Manifest to AREDS2 GR with Specimen Number and AREDS2 Participant ID
- AREDS2 GR receives and processes the samples
- AREDS2 GR displays information on the processed material with phenotype in the Repository’s catalog using Specimen Number as the sole identifier
3 PROJECT POPULATION

AREDS2 participants are eligible to participate in this study.
4 PROJECT PROCEDURES

4.1 Eligibility

AREDS2 participants will be approached by physicians or authorized representatives familiar with the protocol for contribution to the repository. Prospective participants will be given information about the repository and the risks and benefits of participating in the project. Prior to enrollment, a signed informed consent will be collected.

Once a participant or a participant’s legal guardian has signed the informed consent document, the following materials will be collected for submission to the Repository:

1. One blood sample in a 10 mL lavender top (EDTA) blood tube.
2. One saliva sample in an Oragene collection tube.
3. One blood sample in a 10 mL red/black, tiger top serum separator tube. This sample will be collected only at AREDS2 Clinical Centers with the capacity to process serum.

4.2 Phenotypic Information

Phenotypic information for each specimen will be provided to the AREDS2 Genetic Repository by the AREDS2 Coordinating Center for display in the Repository’s Catalog after sample processing has been completed. This will include basic demographic information such as age, gender, race, and ethnicity as well as eye-disease specific information.

4.3 Sample Labeling

Samples should be labeled with a unique Specimen ID. The AREDS2 Participant ID will be shown on the shipping manifest but not on the label on the sample tubes. The Specimen ID will be used for display of phenotypic data in the catalog, not AREDS2 Participant ID.

4.4 Sample Materials and Shipping

The AREDS2 Genetic Repository will provide lavender top blood tubes and red/black, tiger top serum separator tubes, Oragene kits, packing material, boxes, shipping labels, and FedEx US air bills for the shipment of samples. These kits must be ordered in advance of the first blood draw after the AREDS2 Clinical Center receives IRB approval for the study.
4.5 Guidelines for Collecting and Shipping Samples to the Repository

1. Draw one tube of blood in a 10 mL lavender top tube from each participant. Clinical sites that are able to process blood into serum will also draw one tube of blood in a 10 mL red/black, tiger top tube. Use the tubes provided by the AREDS2 Genetic Repository.

2. Obtain a saliva sample in the Oragene collection tube. Make sure that the participant puts enough saliva into the tube so that it reaches the fill line.

3. Package the blood and saliva tubes using the materials provided by the AREDS2 Genetic Repository. Clinical sites able to process blood into serum will package and ship vials of frozen serum on dry ice using the materials provided by the AREDS2 Genetic Repository. Serum may be shipped in batches that contain samples from more than one AREDS2 participant. All shipments are to include a paper copy of the Specimen Shipping Manifest.

4. Samples should be shipped FedEx Standard Overnight to arrive at the AREDS2 Genetics Repository Monday through Saturday. If you are planning to ship specimens on a Friday, please notify the Genetic Repository Project Manager via e-mail one week in advance.

5. Mail submission prepaid via overnight delivery service to:
Fisher BioServices
14665 Rothgeb Drive
Rockville, MD 20850

6. Notify the Genetic Repository Project Manager the day samples are sent. Please provide him/her with the number of samples to be shipped and the FedEx tracking number.

For the Genetic Repository Project Manager’s contact information as well as additional details regarding the collection, storage, and shipment of samples, please refer to the AREDS2 Manual of Operations.

AREDS2 Genetic Repository Staff contact information can also be found on the AREDS2 Roster at www.areds2.org.
5 ETHICS/PROTECTION OF PARTICIPANTS

Individually signed informed consent documents must be secured for each participant and stored with their research record. There are no requirements for sending these documents to the AREDS2 Genetic Repository. The Repository will take measures to protect participant privacy. Each blood specimen will be given a code number upon arrival at the AREDS2 Genetic Repository. Identifiable information will not be used or retained by Fisher BioServices for any samples distributed. Some participant data that may facilitate identification (e.g. age, gender, eye disease diagnosis, and race) will be made available to the Repository and scientists; however, these data will not be traceable to any individuals and will be HIPAA compliant. The Privacy Rule is a federal regulation under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 that governs the protection of individually identifiable health information. The Repository does not accept or store any personally identifying information on samples submitted, and therefore, both submitters and withdrawers of samples are HIPAA compliant during repository usage. Note that Fisher BioServices and the AREDS2 Coordinating Center are not covered entities, and therefore, are not subject to HIPAA regulations. DNA obtained by researchers using the specimens in the Repository will allow them to analyze unique genetic information. We believe the risks of this information being used for unique identification of participants are minimal; however they are unknown.
6 DATA HANDLING AND RECORD KEEPING

All research records should be maintained at all times in a manner that protects the confidentiality of the participant. Keep the original signed informed consent document with the research records on site in a locked file cabinet with restricted access. Informed consent documents may be reviewed by auditors in the future.

Adverse Event Reporting: Adverse events (any unexpected problem resulting from the study procedures that involve risk to the participant or others) may occur during the blood draw. In some instances, participants may report problems that may have developed after the procedure (infection, rash, excessive bruising, etc). Reporting begins when the blood draw procedure is initiated and ends upon discharge from the visit unless the participant contacts the site about a delayed reaction, in which case a report would be filed beyond the time period of the clinic visit. A breach of participant confidentiality may also be considered an unexpected problem that involves a risk to the participant or others. If the participant experiences an adverse event as a result of the study procedures, the incident must be reported to the local/central IRB according to their reporting procedures and to the AREDS2 Coordinating Center. The adverse event report and each page of any attached materials must describe the study participant only by their coded study identifier(s). Any personally identifying information (e.g., name, telephone number, address, etc.) must be removed or obscured before delivery to the Coordinating Center. Transmission may be done electronically via the AdvantageEDC™ system or by facsimile transmission to 877-804-9618. Any information that cannot be submitted via the AdvantageEDC™ system to the Coordinating Center must be sent by facsimile transmission and then subsequently entered into AdvantageEDC™. A copy of the adverse event report must be saved with the participant’s research records stored in a secure location.

An adverse event that meets one of the criteria below is considered serious and must be reported to the AREDS2 Coordinating Center and to the local/central IRB within 24 hours of recognizing the event. A serious adverse event is one that meets any one of the following criteria:

1. Results in death or is life-threatening.
2. Results in persistent or significant disability/incapacity.
3. Requires inpatient hospitalization or prolongation of existing hospitalization.
4. Is medically significant; i.e., an event that jeopardizes the participant or may require medical or surgical intervention to prevent one of the outcomes listed above.

Each clinical site is assigned a Protocol Monitor from the AREDS2 Coordinating Center. Be sure to indicate clearly the study name and the site number when contacting the Coordinating Center. Back-up personnel and procedures exist to assure that personnel at the Coordinating Center can adequately handle urgent requests or address issues related to adverse event reporting requirements.
Sample Removal: If you wish to have a sample removed from the project, please notify the AREDS2 Coordinating Center and provide the AREDS2 Participant ID. The AREDS2 Coordinating Center will locate the requested sample information and provide it to the AREDS2 Genetic Repository so it will be destroyed.
7 DISTRIBUTION OF SAMPLES AND DATA

Samples and associated phenotypic data will be made available to researchers. Researcher requests will be reviewed by a committee of scientists selected by the National Eye Institute. Each researcher must submit: 1) an assurance form signed by an official of their organization; and, 2) a statement of research intent to assure that the samples are being used for appropriate scientific research purposes only.

In the event that the AREDS2 biospecimens yield products of proprietary value, neither AREDS2 investigators nor participants will receive financial benefits.

There may be costs in storing and sharing samples as well as associated de-identified data; the Repository may charge a fee to help offset these costs. However, money from these charges will be used only to offset costs of the AREDS2 Genetic Repository itself.

Results will not be reported to AREDS2 investigators or participants. This project is not designed for screening, diagnostic, or prognostic purposes for individual participants.