

## **GUIDELINES FOR INVESTIGATORS CONDUCTING ANCILLARY STUDIES USING GENETIC MATERIAL**

The CARDIA Study was initiated to examine the evolution of cardiovascular disease risk factors in a biracial cohort of young men and women. As such, CARDIA represents a public resource with data and specimens available for collaborative research by clinical, public health and basic research investigators to further our understanding of the development of cardiovascular disease. The CARDIA investigators are committed to maintaining the stored biologic specimens collected at each cohort visit, including DAN and immortalized cell lines. General ancillary guidelines exist for collaboration that does not involve CARDIA genetic material. Approval for use of genetic material will be based upon availability of specimens, the clarity of the proposal, its plausibility, and its potential impact on cardiovascular disease epidemiology.

### Responsibilities of Ancillary Study Investigators

1. A member of the CARDIA Steering Committee must be identified as a liaison between the ancillary study investigator and the CARDIA Study investigators. Ideally, that member would be a participating investigator in the ancillary study itself.
2. Proposals requesting use of CARDIA participants' DNA, cryopreserved cells or immortalized cell lines must have a specific research hypothesis, including a rationale and review of existing literature, and a testable research hypothesis with appropriate comparison groups. Both the CARDIA Steering Committee and the CARDIA Review Board will review these proposals.
3. The investigators must specify the DNA polymorphisms to be examined in candidate genes, the variants to be genotyped, and the methods to type them, the phenotypic expression, if known, and the endpoint of interest. These details are to be submitted to the CARDIA Steering Committee as part of the ancillary study proposal and will be reviewed by the Committee and the Genetics Working Group. The proposal must also clearly state the significance of the proposal research.
4. The amount of genetic material must be specified and justified based upon the number of assays to be performed and the number of participants involved. The Steering Committee and the DNA Laboratory will review the amount for appropriateness.
5. Phenotypic data required for associations must be specified in the ancillary study proposal. With the help of the designated CARDIA investigator contact, a list of variables should be included in the proposal; these data will be sent to the ancillary study investigator, if requested, upon approval by the CARDIA Steering Committee. Any extant CARDIA data transmitted as part of collaborative research is subject to the more general Ancillary Study Guidelines.
6. The proposals should be based upon research rather than clinical criteria. Genotypes that are associated with a condition without strong evidence of clinical relevance will not be considered. The goals of the ancillary study concerning participant contact and safety

must be specified a priori. If a genotype is found to be causally related to a treatable condition/phenotype, the ancillary study investigator must contact the CARDIA Steering committee, who will review these findings on a case-by-case basis and evaluate how to proceed. Under no circumstances will the ancillary study investigator be permitted to contact CARDIA participants or their family members; this responsibility lies with the Field Center Principal Investigators, if warranted.

7. The ancillary study investigators will respect the confidentiality of the CARDIA participant and will not attempt to contact the participant in any case where the data results obtained about the participant could lead to the identification of a specific participant. In accordance with this, the ancillary study investigator must have IRB approval at the time the study is initiated.
8. Any risks and/or benefits to the participants must be clearly spelled out in the ancillary study proposal.
9. Once the investigator has the genetic material, it may be sued for the approved proposal. Any changes in the research hypothesis or protocol must be resubmitted to the Steering Committee for approval.
10. Ancillary study proposals with potential commercial use will be subject to the same review process as noncommercial studies; however, these proposals must explicitly enumerate how the data will be used, as well as detailing how the protection of the CARDIA participants will be ensured.

## Procedures

1. After the ancillary study proposal has been approved, the CARDIA Coordinating Center will generate a list of IDs, consistent with the study's agreed upon design and objectives. The Genetics Working Group will approve the quantity of DNA requested and the methods involved.
2. This list will be sent to the CARDIA DNA Laboratory, where these samples will be taken from archive, stripped of any identifiers, and sent to the investigator. The investigator will cover all costs associated with sample retrieval and shipping.
3. Biological samples will be shipped to ancillary study investigators with only a CARDIA identification number as a descriptor. As a population-based observational study, we do not provide treatment for our participants. If a potentially dangerous condition is identified through the ancillary data, either as a phenotype or a genotype, the ancillary study investigator will report these findings immediately to the CARDIA Coordinating Center. Each Field Center PI will be responsible for deciding if the participant already knows about the condition or if she/he needs to be informed. Often, this will require human subjects' approval and obtaining new consent from the participant.

4. Upon completion of the study, the samples will either be returned to the DNA Laboratory under appropriate shipping conditions, or destroyed, depending upon the CARDIA Steering Committee's recommendation. The DNA may not be used for other purposes without the approval of the CARDIA Steering Committee and its review board.

5. Details of any subcontractual arrangements between ancillary study investigators and the Field Center investigators will need to be made in coordination with NHLBI staff and the participating institutions.

6. Resulting data from the ancillary study must be made available to the CARDIA Coordinating Center prior to publication or within one year of completion of the analyses. This allows the CARDIA Study resource to grow and become a database for future investigations. However, this transfer of data will not affect the originating investigator's proprietary ideas or publication rights. Refer to the general CARDIA ancillary study guidelines for further detail.

7. The ancillary study investigator will be responsible for keeping the CARDIA Steering Committee informed as to the status of their grant submission, the submission and acceptance of any manuscripts for publication, and for ultimately returning the data to CARDIA. The ancillary study investigator will also provide the CARDIA Steering Committee with periodic updates during the conduct of the ancillary study.