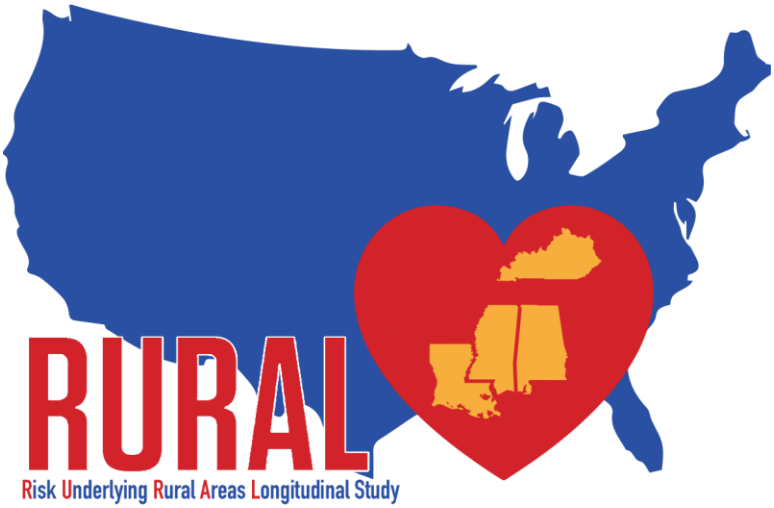

Ancillary Studies Policy

August 2020

Table of Contents

Ancillary Studies Policy

1.0 Ancillary Studies (AS)

1.0.1 List of Terms

Below is a list of commonly used terms throughout the policy and their definitions:

- **RURAL Investigator**: Principal Investigator and Co-PIs named in or funded by the RURAL Cohort Study U01 grant application
- **RURAL-affiliated Investigator**: Investigator, including consultants at a participatory institution, but not specifically named within the grant application
- **Non-RURAL Investigator:** Any Investigator from an institution not named in the RURAL Cohort Study U01 grant application
- **Secondary Analysis:** Analysis involving the use of existing data from the initial funded RURAL Cohort Study
- **ELSI:** The ELSI (Ethical, Legal and Social Implications) is a national team of scientific experts that discusses and helps RURAL Cohort Study Cores think through ELSI of the RURAL Cohort Study, with a specific focus on the reporting of actionable clinical findings including actionable known pathogenic and likely pathogenic genetic variants.

1.1 Definition of an Ancillary Study

An ancillary study (AS) is any study that may request additional data collection from participants or laboratory data from previously collected and stored biospecimens from those enrolled in the RURAL Cohort Study (secondary data analyses are an AS issue as indicated below if funding is sought). Additionally, other forms of AS include analysis of collected data for hypotheses related and unrelated to the central goals and aims of the RURAL Cohort Study. All AS must be reviewed and approved by the RURAL Cohort Study's Ancillary Studies Subcommittee and Steering Committee. AS requiring the use of a third-party data and/or materials transfer agreement require approval from the National Heart, Lung, and Blood Institute (NHLBI). AS are not funded by the current RURAL Cohort Study U01 grant and must seek additional funding. The AS approval process will institute extra layers of review for AS seeking funding from a non-peer-reviewed source. The RURAL Cohort Study Ethics Advisory Board and ELSI panel may contribute additional perspectives. Prior to submission for funding, the RURAL Cohort Study Observational Study Monitoring Board (OSMB) must also approve the AS.

1.2 Types of Ancillary Studies

There are multiple forms of AS that may be performed in conjunction with the RURAL Cohort Study:

- Proposed AS that require additional questionnaires for collection of data at the time of initial mobile examination unit (MEU) visit that were not originally outlined (to be posted on the RURAL Cohort Study website) in the initial funded RURAL Cohort Study U01 grant application.
- Proposed AS that require additional visits to the MEU for additional tests, including additional phenotyping, and/or questionnaires;

- Proposed AS that require access to stored biospecimens collected from the RURAL Cohort Study participants;
- Proposed AS that require additional mHealth measures and equipment;
- Proposed AS that perform secondary analyses of the RURAL Cohort Study data, whose research questions are not a part of the main/central RURAL Cohort Study aims and for which funding is sought (AS that perform secondary analyses but seek no funding are reviewed by the RURAL Cohort Study's Publications and Presentations Committee);
- Proposed AS that require the use of the RURAL Cohort Study data in pooling projects or consortia;
- Proposed AS that involve relatives of the participants (assessed on an individual basis).

Ancillary Studies submitted, as clinical trials will not be considered for review prior to the start of recruitment unless there are exceptional circumstances. If you should have any questions, please contact the RURAL Cohort Study Coordinating Center Administrator at rural@bu.edu

1.3 Local (one-core) vs Multi-Core Studies

In general, proposed AS must be planned as a multi-state study, and must include participants from the RURAL Cohort Study counties in all four constituent states. This provides the AS and member states/counties with an equal opportunity to utilize the large-scale capabilities and resources of the RURAL Cohort Study. Single state single county studies may be considered and approved on a case-by-case basis; feasibility and consistency with the RURAL Cohort Study mission and vision will be weighed in the decision-making process.

AS proposals with similar hypotheses and scientific objectives submitted within the same proposal phase review time period will be collectively assessed based on priority guidelines defined in section 1.7: Application Process. To promote efficient use of resources, funding, and partnership between the RURAL Cohort Study Cores, investigators with similar hypotheses will be encouraged to collaborate on AS proposals.

1.4 Access – Who Can Apply

Applicants of AS may include:

- Any RURAL Cohort Study Principal Investigator (PI) or Co-Investigator may apply with the approval of their Institution's PI or Co-PI.
- RURAL Cohort Study affiliated investigators not named in the initial RURAL Study grant may apply with the sponsorship of the RURAL Study institution's PI or Co-PI. It is not required that the RURAL Cohort Study affiliated investigator's institution be a participating member in a RURAL Cohort Study Core.
- AS should include a PI or Co-PI of the RURAL Study, but RURAL Cohort Study PIs or Co-PIs do not need to be the PI of the AS. AS that do not include a RURAL Cohort Study PI or Co-PI will be examined on a case-by-case basis.

1.5 Non-RURAL Investigators

Applications from non-RURAL Cohort Study investigators will be considered by the RURAL Cohort Study's Ancillary Studies Subcommittee, and Steering Committee. All non-RURAL

Cohort Study investigator applications must involve sponsorship of a RURAL Cohort Study investigator to ensure compliance with the RURAL Cohort Study's policies and procedures. Please see the contact list in the appendix for a list of ancillary study liaisons for each RURAL Cohort Study Core. Non-RURAL Cohort Study Investigators have access to RURAL Cohort Study data either through National Institutes of Health (NIH) repositories or through collaboration with a RURAL Cohort Study sponsor. All AS will have the same review process regardless of the status of affiliation to the RURAL Cohort Study.

1.6 Funding Requirements

AS applicants must be prepared to allocate all funds needed for the AS.
Funds will cover:

1) Costs associated with the integration of AS data with the core RURAL Cohort Study data, including data quality control and return of AS results to participants, where/when applicable;
2) Costs associated with deposition of AS data in NIH/NHLBI-designated public repositories; and
3) For AS requesting biospecimens or new exam components, costs to support one or more RURAL Cohort Study Cores as determined necessary by the RURAL Cohort Study's AS Subcommittee and Steering Committee.

Associated costs with AS involvement with RURAL Cohort Study Cores will be submitted to and reviewed by the RURAL Cohort Study's Ancillary Studies Subcommittee and Steering Committee. A common framework of approximate costs to standardize the process and maintain efficiency is available upon request from the RURAL Cohort Study Coordinating Center (SCC).

Examples of specific costs the AS applicant is responsible for include, but are not limited to:

- RURAL Cohort Study Coordinating Center (SCC)
    - Administrative tasks (MEU coordination, Mobile App integration, recruitment/enrollment summaries, etc.)
    - Integration with core RURAL Cohort Study protocols, including incorporation in annual reports and OSMB review documents
- RURAL Cohort Study's State Core Costs (e.g., Alabama, Kentucky, Louisiana, Mississippi)
    - Contacting and recruiting participants
    - Obtaining IRB and other approvals
    - Participant incentives, transportation, and meals
    - Coordination of data collection, transfer, archiving, distributing
- RURAL Cohort Study's Biorepository and Assay Core
    - Biospecimen aliquoting and shipment costs
- RURAL Cohort Study's Recruitment and Retention Core
    - Contacting and recruiting participants
    - Obtaining IRB and other approvals
- Returning incidental findings and clinically actionable results to the participants
- RURAL Cohort Study's Statistical Data Coordinating Center
    - Assistance with developing a statistical plan, if sought
    - Data management, including the return of data to the core RURAL Cohort Study
    - Biospecimen selection, if applicable

    - Preparation of datasets from the initial funded RURAL Cohort Study
- All RURAL Cohort Study Cores
    - Mailing, photocopies, fax, telephone
    - Other unforeseen costs that may arise
- If the grant is $500k or higher in direct costs, the AS applicant's subcontract budget will include 25-50% of a project manager's time. All grants will require some effort by the project manager regardless of funding.
- Fringe and indirect costs are included, based on BU's negotiated F&A Agreement. These rates typically change on a biannual basis.

The RURAL Cohort Study Ancillary Studies Subcommittee will review AS proposals to assess participant burden and burden to the main RURAL Cohort Study. The RURAL Cohort Study Coordinating Center will facilitate and streamline the process for including the work and efforts of any related RURAL Cohort Study Cores.

1.7 Application Process

Applicants who propose an AS should refer to the RURAL AS process and procedures document and flowchart for detailed instructions of submitting an initial concept proposal and full proposal (See Appendix).

Priority is given to AS *initial* concept proposal based on:

- The initial needs and support of the RURAL Cohort Study's baseline exam;
- The potential to contribute to the health of RURAL Cohort Study Communities;
- Not replicating ongoing or prior RURAL Cohort Study activities;
- Not placing undue burden on RURAL Cohort Study participants, staff, or biospecimen volumes or repositories;
- Relevance to the RURAL Cohort Study specific-aims and NHLBI vision and mission;
- The scientific value it will contribute to the RURAL Cohort Study;
- Alignment with the health needs and preferences of the communities and participants;
- Cultural sensitivity to RURAL Cohort Study Communities; the AS must not adversely impact relations between the RURAL Cohort Study investigators, staff, and the participants.

1.8 Ancillary Study Proposal Components

If the RURAL Cohort Study Ancillary Studies Subcommittee and Steering Committee approve the AS *initial* concept proposal, the applicant may submit an AS *full* proposal using the form in the appendix.

The application form includes:

- Structured abstract
- General research proposal
- Elements of proposed research
- Funding and third-party involvement
- Participant burden
- RURAL Cohort Study staff involvement
- Questionnaire data, if applicable
- Laboratory involvement, if applicable

- DNA specimen and genetic/genomic data request

1.9 Appealing Ancillary Study Proposal Decisions

The RURAL AS review process is extremely rigorous and due care is taken to carefully review each proposal. It is highly unlikely that review decisions will be appealed; however, if an AS investigator would like to appeal their review decision they should contact the RURAL Cohort Study Coordinating Center.

1.10 Contacting and Obtaining Consent from the RURAL Cohort Study Participants

The RURAL Cohort Study's participants have only consented to participation in the core RURAL Cohort Study and can only be contacted by a RURAL Cohort Study PI or their staff. The AS applicant cannot contact the RURAL Cohort Study participants directly to obtain their informed consent. Therefore, a subcontract will be always required for AS requiring participant contact, whereby a RURAL Cohort Study PI or their staff will obtain consent from the RURAL Cohort Study participants. After a RURAL Cohort Study participant has consented to the AS, the AS applicant, or delegated team member consistent with IRB approval, may contact them consistent with the RURAL Cohort Study Recruitment and Retention Manual of Operations (MOP).

1.11 Participant Burden

Proposals that involve RURAL Cohort Study participants in the MEU will be reviewed provisionally by the RURAL Cohort Study's Ancillary Studies Subcommittee at this juncture. Since the RURAL Cohort Study examination in the MEU is still being finalized, it is challenging to develop a framework for what constitutes acceptable participant burden in the MEU. The Ancillary Study Subcommittee will provide the AS investigator clarity around what is acceptable participant burden in RURAL. The Ancillary Study Subcommittee will review such applications because we understand it takes time to obtain grant funding for ancillary studies but there will be a higher threshold for approval until recruitment begins.

1.12 Ancillary Study Requesting Biospecimens and/or DNA

The RURAL Cohort Study aims to provide adequate biospecimens, including DNA, for AS investigators to test their hypotheses, while also considering the importance of preserving the RURAL Cohort Study biospecimens for current and future studies.

AS applicants must provide explanations of the type of material requested, how much they require, why this quantity is needed, and proposed disposal or return to the RURAL Cohort Study of excess material. Sample volume requests should include the necessary 'dead volume' for processing. All applications for biospecimens must be supported by assay performance metrics from the performance laboratory.

The RURAL Cohort Study Ancillary Studies Subcommittee will consider proposals for volumes of samples based on the guidelines below. For approval of higher volume amounts, the AS applicant must provide scientific justification in the proposal.

Biospecimen and amounts available for AS:

Type of Specimen	Volumes per Study Generally Allowable
Serum	
EDTA Plasma	
EDTA Whole Blood	
PaxGene	
Cell Prep Tube	
Saliva	
Urine	
Stool	
Tap Water	
Blood Spots	

After an AS is approved and funded, the RURAL Cohort Study Statistical Data Coordinating Center (SDCC) at The University of Pennsylvania will generate a list of sample IDs. The RURAL Cohort Study Biorepository and Assay (BRAC) Laboratory at The University of Vermont will retrieve the approved specimen aliquots based on the list of IDs prepared by the RURAL Cohort Study's Statistical Data Coordinating Center. AS investigators are responsible for associated costs.

1.13 Ancillary Study Data

AS investigators are required to complete a Data and Materials Distribution Agreement (DMDA) in order to receive study biosamples and/or data (See Appendix). The completed DMDA should be sent to the RURAL Cohort Study Program Officer at NHLBI with a copy to the RURAL Cohort Study Coordinating Center. When signing the DMDA, AS investigators are agreeing to the requirements to send the AS data to the RURAL Cohort Study Coordinating Center to eventually be incorporated into the RURAL Cohort Study database and NHLBI-designated public repositories consistent with NIH data sharing policies.

The AS investigators have exclusive rights to use the non-genetic and -omics data generated from the AS for **one year** after the data set has been cleaned and finalized for analysis or as contemporary NIH data sharing policy mandates. AS Investigators will be given access to the RURAL Cohort Study data only after the AS data has been sent to the RURAL Cohort Study Coordinating Center and the Statistical Data Coordinating Center.

The AS data will be available to RURAL Cohort Study investigators and may be available to external investigators upon request. The RURAL Cohort Study will encourage external investigators requesting access to AS data to collaborate with the PI who generated the data.

The NHLBI Policy for Data Sharing from Clinical Trials and Epidemiological Studies requires the RURAL Cohort Study Coordinating Center to include AS data in the RURAL Cohort Study data set one year after the AS data is cleaned and finalized for analysis by AS investigators. The AS investigators must send relevant information to the RURAL Cohort Study Coordinating Center to ensure the AS data is useful for all eligible external investigators via NHLBI-designated data repositories.

Genome-wide association study (GWAS) data generated in the RURAL Cohort Study must follow the NIH Genomic Data Sharing Policy. AS investigators performing GWAS should understand the policy requirements.

1.14 Study Progress Reports

Once an AS has been funded and started, the AS PI must submit semi-annual progress and quality control reports on the AS to the RURAL Cohort Study Coordinating Center and Statistical Data Coordinating Center. The RURAL Cohort Study Coordinating Center and Statistical Data Coordinating Center will report back to the RURAL Cohort Study's Ancillary Studies Subcommittee and the AS investigator. The RURAL Cohort Study Statistical Data Coordinating Center with the RURAL Cohort Study Coordinating Center will develop an automated system for tracking. There are standardized deadlines across all AS for progress, and quality control reports. If the study starts within 30 days of a standard quarterly deadline, they may skip the quarterly report.

- Progress reports should include:
  - Summary of study activities:
    - Data and/or specimens collected with corresponding quality control
    - Assays and/or analyses in progress or completed with quality control
    - Manuscripts in progress or published
  - For studies collecting DNA or specimens:
    - How DNA/specimen is collected and stored
- AS progress reports will be included in the RURAL Cohort Study Steering Committee semi-annual reports to the NHLBI and the annual report to the NHLBI and the RURAL Cohort Study OSMB.

1.15 Data to be Obtained from the RURAL Cohort Study

The RURAL Study Statistical Data Coordinating Center will provide the RURAL Cohort Study data to the AS PI after manuscript proposals have been approved by the RURAL Cohort Study Publications and Presentations Subcommittee, the Steering Committee, and after the AS PI has submitted cleaned AS data to the RURAL Cohort Study Coordinating Center.

Partial data sets of RURAL Cohort Study data with some deletions and recoding may be released with certain restrictions and conditions upon approval by the RURAL Cohort Study Steering Committee.

The RURAL Cohort Study Statistical Data Coordinating Core will send the AS investigator the partial RURAL Cohort Study dataset after receiving a signed DMDA from the AS investigators, which is also signed by the RURAL Cohort Study NHLBI Project Officer (See Section 1.11 Ancillary Study Data).

1.16 Notification of Clinically Significant Findings to RURAL Cohort Study Participants

The RURAL Cohort Study will inform participants of clinically significant and actionable findings from study activities consistent with contemporary medical standards and guidelines. Some findings may require urgent intervention, while others may need further screening tests, medical follow-up, or counseling (including genetic counseling).

AS investigators must quickly inform the RURAL Cohort Study's Recruitment and Retention Core, at the University of Alabama at Birmingham and the RURAL Study Coordinating Center of these actionable findings. The AS should notify the RURAL Cohort Study of clinically significant findings immediately, as opposed to waiting until the AS is completed or until a batch of data has been analyzed. AS investigators will not inform participants of these findings but must allocate percent effort/salary for the RURAL Cohort Study staff to contact participants

and inform them of the clinically significant actionable findings arising from participation in the AS.

AS proposals must include the following provisions:

- Estimate the number of participants with clinically significant and actionable findings
- Recommendations and plans for the clinically significant and actionable findings
    - Referral to urgent/emergency care
    - Need for further tests to confirm findings
    - Need for treatment and clinical follow-up
    - Genetic counseling
- Anticipated costs for the RURAL Cohort Study staff to contact participants about clinically relevant actionable findings from the AS and administrative costs for this (e.g. mail, phone service)
- Anticipated costs for support or consultant fee for genetic counseling, if necessary

1.17 Manuscripts Arising from the Ancillary Study

Manuscripts and abstracts from the AS must be submitted to the RURAL Cohort Study Publications and Presentations Subcommittee for review and approval. AS investigators must provide the RURAL Cohort Study Coordinating Center the name and qualifications of the lead AS data analyst or statistician.

AS investigators can select authorship for their publications. AS investigators will be encouraged to invite one or more RURAL Cohort Study investigators to serve in writing groups and to provide expertise and knowledge of the RURAL Cohort Study and its data. Appropriate representation of the RURAL Cohort Study investigators will be reviewed by the RURAL Cohort Study Publications and Presentations Subcommittee in consultation with International Medical Committee of Journal Editors (ICJME) guidelines for authorship.

1.18 Feasibility Review

AS applicants must understand that even if grant funding were to be successfully obtained, there will be a feasibility review at the time of funding by the RURAL Cohort Study's Ancillary Studies Subcommittee to determine whether or not to subject RURAL Cohort Study participants to the projected burden as written in the grant application.

If an AS receives final approval, the approval remains effective for **24 months** beginning from the date of notification of approval to the submitting PI. This allows time for submission and resubmission of an application for funding. If an AS receives funding the AS investigator must notify the RURAL Cohort Study Coordinating Center (rural@bu.edu) immediately, who will notify the RURAL Cohort Study Ancillary Studies Subcommittee members.

If an AS proposal is not selected for funding within the 24-month approval timeline, the initial AS proposal approval is no longer active or valid. After this time the RURAL Cohort Study will work with the investigator to renegotiate terms of the AS, which may include a resubmission of a full AS proposal or a slight change in the original proposal.

1.19 Timeline

The investigator should refer to the AS procedure and process documents in the Appendix. Investigators who submit AS proposals should allow for the following timeline:

- The AS Initial Concept Proposal will typically be reviewed and voted on by the RURAL Cohort Study Ancillary Studies Subcommittee, and returned to AS investigators within **7-15 working days of receipt**.
  - The AS Full Proposal will typically be reviewed and returned to AS investigators within **12 weeks of receipt**, which includes review and approval by the Steering Committee and OSMB.
- Review times are an estimate and may vary. Please allow for extra processing time during public holidays.

  Proposals involving biospecimen collections may require a longer time period for completion of the review process, as a review by the RURAL Cohort Study's Laboratory/DNA Review Subcommittees is required. This includes review by RURAL Cohort Study Genomic Core and Biorepository and Assay Core. The RURAL Cohort Study Laboratory/DNA Review Committee will provide recommendations and collaborate with the Ancillary Studies Subcommittee in its initial review and disposition of the AS application.

  Variation in the review timeline may occur contingent on the components and complexity of the AS. Conditional aspects that may impact timelines include the requests for biospecimens or biomaterials, additional mHealth data collection procedures, the nature of proposed data collection procedures, and communications between investigators and oversight and review subcommittees that may lengthen the process.

  Timelines of AS reviews by the RURAL Cohort Study Ancillary Studies Subcommittee will be aligned with NIH grant submission deadlines to allow for proper review of proposals for grant submission. **Please allow for 12 weeks before NIH grant submission deadlines for AS review**. An expedited process for submission may be allowed on a case-by-case deadline based on grants with smaller timelines.

  If the AS proposal is submitted as a grant application to the NIH and requires a budget of greater than $500,000 in direct costs in any funding year, investigators must be aware of the budget approval process from the NIH for such grant applications (see Section 2.3.7.2 of the NIH Grants Policy Statement). Please allow at least 6 weeks for the NIH to review the budget.

1.20 RURAL Cohort Study Contact

RURAL Cohort Study Coordinating Center
Boston University
Email: rural@bu.edu

Ancillary Study liaisons from the RURAL Cohort Study can be provide upon request.

Note: All forms are in the appendices and will eventually be available on the password-protected internal portal on the RURAL Cohort Study website.

1.21 Appendices

A. **Ancillary Study External Framework** (See RURAL Cohort website – password protected)

B. Ancillary Study External Procedures and Process Document

RURAL Cohort Study - Ancillary Study Procedures and Process: EXTERNAL
Version 7: April 2nd, 2020

Procedures

Reviewers of the AS Initial Concept Proposal and Full Proposal

- The three multi-PIs and the Chairs of the AS Subcommittee will review the Initial Concept Proposal. They will provide feedback to the proposer and determine if the proposal is:
    - Approved
    - Disapproved
- A simple majority is required for the Initial Concept Proposal to be accepted, requiring the AS investigator to submit a Full Proposal
- The AS Subcommittee will review the Full Proposal form. They will provide feedback to the proposer and determine if the proposal is:
    - Approved
    - Approved with revisions
    - Disapproved

External Reviewers

- If an AS requires DNA or laboratory samples, the DNA/Laboratory Committee will review the DNA/Laboratory sections of the Full Proposal before it is sent to the AS Subcommittee for their review.
- External reviewers may be added to the review process to ensure balance.

Revisions to Ancillary Study Proposals

- The AS Subcommittee may have no revisions, recommended revisions, or required revisions to the Initial Concept Proposal or Full Proposal.
- It is highly likely that there will be revisions to the Initial Concept Proposal or Full Proposal, which will require additional processing time.

Determining Outcomes for Similar AS Proposals

- If the AS Subcommittee receives two or more AS Initial Concept or Full Proposals that have significant overlap in their aims and/or research design, the AS Subcommittee could recommend one of the following options:
    - Invite the different AS investigators to collaborate and submit a new joint proposal that combines the different proposals into one proposal. This will require communication between the different AS investigators, the AS Chairs, and the SCC Administrator.
    - Suggest that the different AS investigators revise their proposals so there are significant differences between them. This will require communication between the different AS investigators, the AS Chairs, and the SCC Administrator.
    - The SCC Administrator sends the proposals to the Steering Committee for their review. The Steering Committee could:
        - Approve only one proposal
        - Approve more than one proposal. Investigators with approved AS proposals could submit them to peer review, where only the one deemed most meritorious would become an AS.

Budget

- If the AS proposal is submitted as a grant application to the NIH and requires a budget of greater than $500,000 in direct costs in any funding year, investigators must be aware of the budget approval process from the NIH for such grant applications (see Section 2.3.7.2 of the NIH Grants Policy Statement). Please allow at least 6 weeks for the NIH to review the budget.

Participant Burden

- Proposals that involve RURAL participants in the Mobile Examination Unit (MEU), will be reviewed provisionally by the Ancillary Study Subcommittee at this juncture. However, it is unlikely that they can be approved with finality at this early stage in the RURAL study as the RURAL exam is still being finalized, rendering it challenging to develop a framework for what constitutes acceptable participant burden in the MEU. The Ancillary Study Subcommittee will review such applications because we understand it takes time to obtain grant funding for ancillary studies, by which time there may be greater clarity around what is acceptable participant burden in RURAL.

Feasibility Review

- It is critical for ancillary study applicants to understand that even if grant funding were to be successfully obtained, there will be a feasibility review at the time of funding by the Ancillary Studies subcommittee to determine whether or not to subject RURAL participants to the projected burden as written in the grant application.

- If an AS receives final approval, the approval remains effective for **24 months** beginning from the date of notification of approval to the submitting PI. This allows time for submission and resubmission of an application for funding. If an AS receives funding the AS investigator must notify the Study Coordinating Center (rural@bu.edu) immediately, who will notify the AS Subcommittee members.

- If an AS proposal is not selected for funding within the 24-month approval timeline, the initial AS proposal approval is no longer active or valid. After this time the RURAL study will work with the investigator to renegotiate terms of the ancillary study, which may include a resubmission of a full ancillary study proposal or slight change in the original proposal.

Process

A. AS Investigator Contacts Relevant RURAL Cores

- AS investigators must contact the RURAL liaisons from each relevant core prior to submitting an AS proposal to discuss the proposal and obtain Impact Statements from relevant cores, such as BRAC or Genomics Core.
- If the AS investigator does not know who to contact, please email the Study Coordinating Center (SCC) (rural@bu.edu) who can assist in connecting the AS investigator to the relevant RURAL core(s).

B. Submission and Review of AS Initial Concept Proposal

- Investigators will complete the RURAL AS Initial Concept Proposal form and send it to the Study Coordinating Center (SCC) at BU (rural@bu.edu).
- The AS Chairs and three multi-PIs will review the proposal and inform the SCC Administrator of their group decision. They will determine if the proposal is:
  - Approved
  - Approved with revisions
  - Disapproved

- The SCC Administrator will then inform the AS applicant of the review decision, reviewers' feedback, and next steps. If the Initial Concept Proposal was approved, the SCC Administrator will ask them to complete the AS Full Proposal.

C. Submission and Review of AS Full Proposal

- The AS Investigator should submit the AS Full Proposal within **20 working days** of the Initial Concept Proposal being approved by the AS Chairs and three multi-PIs.
- If an AS requires DNA or laboratory samples, the DNA/Laboratory Committee will review the DNA/Laboratory sections of the Full Proposal before being forwarded to the AS Subcommittee for their review.
- The AS Subcommittee discusses the AS proposal and votes on the recommended action:
  - Approved
  - Approved with revisions
  - Disapproved
- The SCC Administrator will send the AS Subcommittee's recommendation to the Steering Committee, who will make the final decision. The AS investigator may address the comments and feedback from the AS Subcommittee and/or the DNA/Lab Committee before it is sent to the Steering Committee. In some cases, the AS Subcommittee and/or DNA/Lab Committee will require AS investigators to make changes before the Full Proposal is sent to the Steering Committee.

D. Steering Committee Review

- The Steering Committee will review the materials for each Full AS proposal and consider the recommended action from the AS Subcommittee. The Steering Committee will determine if the proposal is:
  - Approved
  - Approved with revisions
  - Disapproved

E. Actions after the Steering Committee Meeting

- The SCC Administrator will inform the AS investigator of the Steering Committee's final decision and next steps. If the AS is approved by the Steering Committee, the SCC Administrator will inform the AS investigator that they can only proceed **after** receiving approval from the OSMB. The SCC Administrator will also request a final version of the AS proposal with any incorporated edits.
- If the Steering Committee approves the AS proposal, the AS investigator must contact the SCC Administrator/ Jason Miller (rural@bu.edu) to discuss the budget and fees for the AS.

F. OSMB Provides Approval

- The SCC Administrator will send the final version of the AS proposal and the Steering Committee's final decision to the NHLBI Project Officer and the OSMB Executive Secretary.
- The OSMB and NHLBI will review the AS proposal
- The NHLBI will notify the SCC of the OSMB's decision
- With OSMB approval, the SCC Administrator prepares a final letter on behalf of the Steering Committee stating that all approvals are in place and the AS investigator may apply for funding and develop contractual agreements with external funders or the necessary RURAL Study Cores.

G. Actions after OSMB Approval

- Applicant must inform the Ancillary Studies Subcommittee within 10 working days of receiving Notice of Award (NOA) if they receive funding for the proposed AS.

- AS investigators are required to complete a Data and Materials Distribution Agreement (DMDA) in order to receive study biosamples and/or data

H. Overall Anticipated Review Time

- The AS Initial Concept Proposals will typically be reviewed and returned to AS investigators within **7-15 working days of receipt**.
- The AS Full Proposals will typically be reviewed and returned to AS investigators within **12 weeks of receipt**, which includes review and approval by the Steering Committee and OSMB.
- Review times are an estimate and may vary. Please allow for extra processing time during public holidays.
- **Please submit the AS Initial Concept Form at least 12 weeks before NIH grant submission deadlines**.
    - If an AS proposal requires new participant contact, tests novel technologies or other methods, or requests DNA/Laboratory specimens, please allow for extra processing time for the DNA/Laboratory Committee or additional external reviewers to review the proposal. AS investigators must assess the complexity of their proposal to ensure they submit their proposal with sufficient time for it to be reviewed.
    - An expedited process for submission may be allowed on a case-by-case deadline based on grants with smaller timelines.

C. Ancillary Study Initial Concept Form

RURAL Cohort Study - Ancillary Study Initial Concept Proposal

Version 10: March 20 2020

REVIEW PROCESS: ANCILLARY STUDY (AS) INVESTIGATORS MUST CONTACT RELEVANT CORE(S) IMPACTED BY THE AS PROPOSAL BEFORE COMPLETING THE INITIAL CONCEPT PROPOSAL. PLEASE CONSULT THE ANCILLARY STUDY LIAISON CONTACT LIST TO FIND THE CONTACT INFORMATION FOR EACH CORE. IF YOU DO NOT KNOW WHOM TO CONTACT, PLEASE EMAIL THE STUDY COORDINATING CENTER (SCC) (RURAL@BU.EDU) PRIOR TO SUBMITTING A FULL STUDY PROPOSAL.

ANCILLARY STUDY INVESTIGATORS MUST FIRST SUBMIT A TWO-PAGE INITIAL CONCEPT PROPOSAL TO THE SCC (RURAL@BU.EDU) USING THE FORM BELOW. PLEASE INCLUDE REFERENCES (NOT INCLUDED IN THE PAGE LIMIT). ADDITIONAL FIGURES AND TABLES ARE ACCEPTABLE. THE ANCILLARY STUDIES SUBCOMMITTEE WILL APPROVE OR DISAPPROVE THE INITIAL CONCEPT PROPOSAL. THE SCC WILL INFORM THE APPLICANT OF THE ANCILLARY STUDIES SUBCOMMITTEE DECISION AND WHETHER THEY SHOULD DEVELOP A FULL PROPOSAL.

ANY R01 APPLICATIONS THAT REQUEST $500,000 OR MORE IN DIRECT COSTS IN ANY PROJECT YEAR WILL REQUIRE APPROVAL BY THE RELEVANT NIH INSTITUTE BEFORE SUBMISSION TO THE NIH.
FOR MORE DETAILED INFORMATION ON THE ANCILLARY STUDY PROCESS, PLEASE REVIEW THE FOLLOWING DOCUMENTS:

ANCILLARY STUDY POLICY
ANCILLARY STUDY PROCESS FLOWCHART
ANCILLARY STUDY PROCESS AND PROCEDURES

DATE: CALENDAR	Click or tap to enter a date.

PRINCIPAL INVESTIGATOR AND CO-INVESTIGATORS

PRINCIPAL INVESTIGATOR CONTACT INFORMATION

LAST NAME*	FIRST NAME*	POSITION/TITLE*	INSTITUTION*
TEXT	TEXT	TEXT	AS WRITE TEXT DROP DOWN MENU OFFERS SUGGESTIONS
PHONE NUMBER	**EMAIL ADDRESS**	**INSTITUTIONAL ADDRESS***	
NUMBER	TEXT	TEXT	

ARE YOU AN EARLY STAGE INVESTIGATOR (HELP: THE DEFINITION OF AN EARLY-STAGE INVESTIGATOR IS DEFINED BY THE NIH HERE. A LIST OF NIH GRANTS THAT A PD/PI CAN HOLD AND STILL BE CONSIDERED AN ESI CAN BE FOUND HERE.) **CHECKBOX**	**YES ☐**	**NO☐**

CO-INVESTIGATORS (MUST INCLUDE ONE OR MORE RURAL INVESTIGATORS)

LAST NAME	FIRST NAME	DEGREE	INSTITUTION	EMAIL ADDRESS
TEXT	TEXT	TEXT	TEXT	TEXT

STUDY TITLE, SIGNIFICANCE AND AIMS, METHODS

LONG TITLE OF STUDY*

TEXT
WORD LIMIT: 50 WORDS

SIGNIFICANCE *

BRIEF SUMMARY OF WHAT IS CURRENTLY KNOWN ABOUT THE RESEARCH TOPIC TO BE STUDIED AND HOW THE RESEARCH WILL ADDRESS SPECIFIC KNOWLEDGE GAPS

TEXT
WORD LIMIT: 200 WORDS

IS THERE ANY OVERLAP WITH OTHER RURAL MANUSCRIPTS OR AS PROPOSALS? * (HELP: RURAL INVESTIGATORS MUST CONSULT THE RURAL WEBSITE TO REVIEW THE TITLE OF APPROVED AS PROPOSALS TO ENSURE THERE IS NO OVERLAP. NON-RURAL INVESTIGATORS MUST CONTACT THEIR SPONSORED RURAL INVESTIGATOR TO ENSURE THERE IS NO OVERLAP WITH APPROVED AS PROPOSALS) **CHECKBOX**	YES ☐	NO ☐

SPECIFIC AIMS*

Include how the study builds on the aims of the RURAL Cohort Study

TEXT
CHARACTER LIMIT: 150 WORDS

METHODS*
A. INCLUDE SAMPLE SIZE AND SAMPLE SIZE JUSTIFICATION
B. IF NOT PROPOSING TO USE THE FULL RURAL COHORT, A JUSTIFICATION FOR WHY ONLY A SUBSET WOULD BE USED

TEXT
WORD LIMIT: 200 WORDS

IMPACT ON RURAL

RURAL STAFF INVOLVEMENT* CHECKBOX
PLEASE CHECK ALL CORES BELOW THAT WILL BE INVOLVED OR IMPACTED BY YOUR ANCILLARY STUDY:

STUDY COORDINATING CENTER	☐	BIOREPOSITORY AND ASSAY CORE	☐
COMMUNITY COLLABORATIONS CORE	☐	ECG READING CORE	☐
GENOMICS CORE	☐	IMAGING CORE	☐
MHEALTH CORE	☐	PULMONARY CORE	☐
RECRUITMENT AND RETENTION CORE	☐	SAMPLING CORE	☐
SOCIAL DETERMINANTS CORE	☐	STATISTICAL DATA COORDINATING CORE	☐
ALABAMA	☐	KENTUCKY	☐
LOUISIANA	☐	MISSISSIPPI	☐
MOBILE EXAMINATION UNIT (MEU) TECHNICIANS	☐		

BRIEFLY DESCRIBE STAFF INVOLVEMENT*

TEXT
WORD LIMIT: 100 WORDS

BRIEFLY DESCRIBE PARTICIPANT BURDEN*

TEXT
WORD LIMIT: 100 WORDS

DESCRIBE ALIGNMENT AND INVOLVEMENT WITH OTHER COHORT STUDIES*
State if you are involving other cohort studies (if you are not involving other cohorts, write does not apply)

TEXT
WORD LIMIT: 50 WORDS

DATA COLLECTION

ARE YOU REQUESTING GENETIC DATA, DNA SPECIMENS, OR BIOSPECIMENS? * CHECKBOX. **IF ANSWER "YES" THEY MUST ANSWER QUESTIONS A-D**	YES ☐	NO ☐

A. RURAL DNA OR BIOSPECIMEN(S) REQUESTED
PLEASE REVIEW THE RURAL ANCILLARY STUDY POLICY FOR INFORMATION ABOUT AVAILABLE BIOSPECIMENS AND ALLOWABLE VOLUMES

TEXT
WORD LIMIT: 75 WORDS

B. STUDY YEAR(S) FOR WHICH SAMPLES ARE TO BE USED

NUMBER
SELECT FROM 1-5 (CAN SELECT MORE THAN ONE NUMBER)

C. SAMPLE TYPE(S)

TEXT
WORD LIMIT: 75 WORDS

D. SAMPLE VOLUMES TO BE USED

TEXT
WORD LIMIT: 50 WORDS

DESCRIBE USE OF QUESTIONNAIRES (QUESTIONNAIRE INSTRUMENT(S) – INDICATE IF VALIDATED); DEVICE (E.G. ZIO PATCH, GLUCOSE MONITOR, HOME AIR QUALITY MONITOR); IMAGING (E.G., BRAIN MRI); MHEALTH (E.G. NEW FEATURE OF RURAL APP, PHONE-SYNCED BLOOD PRESSURE MONITORS); GENOMIC/OMIC PROFILING (E.G. NASAL MICROBIOME); OR OTHER TECHNOLOGIES*
TEXT WORD LIMIT: 75 WORDS

D. Ancillary Study Full Proposal Form

RURAL Cohort Study - ANCILLARY STUDY FULL PROPOSAL FORM

Version 15: April 8 2020

REVIEW PROCESS: ONE OR MORE RURAL COMMITTEES WILL REVIEW THE RESEARCH PROPOSAL DEPENDING ON WHICH ELEMENTS ARE CHECKED. IF THE PROPOSAL INVOLVES NEW PARTICIPANT CONTACT OR ADDITIONAL SPECIMEN COLLECTION, THE OBSERVATIONAL STUDIES MONITORING BOARD (EXTERNAL TO RURAL) WILL ALSO REVIEW THE PROPOSAL. PROPOSALS MAY BE ELIGIBLE FOR EXPEDITED REVIEW ON A CASE-BY-CASE DEADLINE BASED ON GRANTS WITH SMALLER TIMELINES.

FOR MORE DETAILED INFORMATION ON THE ANCILLARY STUDY PROCESS PLEASE REVIEW THE FOLLOWING DOCUMENTS:

ANCILLARY STUDY POLICY
ANCILLARY STUDY PROCESS FLOWCHART
ANCILLARY STUDY PROCESS AND PROCEDURES
ANCILLARY STUDY LIAISON CONTACT LIST
PLEASE REVIEW YOUR APPLICATION CAREFULLY BEFORE SUBMITTING IT. ONCE AN APPLICATION HAS BEEN REFERRED TO THE REVIEW COMMITTEE(S), A RETRACTED AND RESUBMITTED APPLICATION MAY BE DELAYED.

Ancillary Studies Subcommittee Review: ALL APPLICANTS MUST COMPLETE THIS SECTION

DATE:	Click or tap to enter a date.	
IS THIS A RESUBMISSION?*	YES ☐	NO☐

PRINCIPAL INVESTIGATOR AND CO-INVESTIGATORS

PRINCIPAL INVESTIGATOR CONTACT INFORMATION

LAST NAME*	FIRST NAME*	POSITION/TITLE*	INSTITUTION*

PHONE NUMBER	EMAIL	INSTITUTIONAL ADDRESS*

ARE YOU AN EARLY STAGE INVESTIGATOR (HELP: AN EARLY-STAGE INVESTIGATOR IS A PROGRAM DIRECTOR / PRINCIPAL INVESTIGATOR (PD/PI) WHO HAS COMPLETED THEIR TERMINAL RESEARCH DEGREE OR END OF POST-GRADUATE CLINICAL TRAINING, WHICHEVER DATE IS LATER, WITHIN THE PAST 10 YEARS AND WHO HAS NOT PREVIOUSLY COMPETED SUCCESSFULLY AS PD/PI FOR A SUBSTANTIAL NIH INDEPENDENT RESEARCH AWARD. A LIST OF NIH GRANTS THAT A PD/PI CAN HOLD AND STILL BE CONSIDERED AN ESI CAN BE FOUND HERE.)	YES ☐	NO☐

CO-INVESTIGATORS

LAST NAME	FIRST NAME	DEGREE	INSTITUTION	EMAIL ADDRESS

RURAL SPONSOR (IF YOU ARE NOT A RURAL INVESTIGATOR)

NAME OF RURAL SPONSOR(S): (HELP: A RURAL SPONSOR IS A RURAL INVESTIGATOR(S) FROM ONE OR MORE OF THE CORES. THIS IS THE PERSON/PEOPLE YOU CONTACTED BEFORE YOU SUBMITTED THE INITIAL CONCEPT FORM. IF YOU ARE A RURAL INVESTIGATOR TYPE YOUR OWN NAME)	

RURAL SPONSOR(S) TICK ALL THAT APPLY:

STUDY COORDINATING CENTER	☐	BIOREPOSITORY AND ASSAY CORE	☐
COMMUNITY COLLABORATIONS CORE	☐	ECG READING CORE	☐
GENOMICS CORE	☐	IMAGING CORE	☐
MHEALTH CORE	☐	PULMONARY CORE	☐
RECRUITMENT AND RETENTION CORE	☐	SAMPLING CORE	☐
SOCIAL DETERMINANTS CORE	☐	STATISTICAL DATA COORDINATING CORE	☐
ALABAMA	☐	KENTUCKY	☐
LOUISIANA	☐	MISSISSIPPI	☐

STUDY TITLE AND STRUCTURED ABSTRACT ALL APPLICANTS MUST COMPLETE THIS SECTION

LONG TITLE OF STUDY*

TEXT 50 WORDS LIMIT

SHORT TITLE OF STUDY

TEXT 25 WORDS LIMIT

STRUCTURED ABSTRACT* TEXT 500 WORDS LIMIT

BACKGROUND:

AIM:

METHODS:

GENERAL RESEARCH PROPOSAL ALL APPLICANTS MUST COMPLETE THIS SECTION

BACKGROUND AND PURPOSE OF THE PROPOSAL*

TEXT 500 WORDS LIMIT

SPECIFIC AIMS *

TEXT 250 WORDS LIMIT

HYPOTHESIS *

TEXT 100 WORDS LIMIT

METHODS* TEXT 1000 WORDS LIMIT

STUDY DESIGN:

SAMPLE SIZE JUSTIFICATION (INCLUDE ROBUST CALCULATIONS):

METHODS OF ANALYSIS (E.G. STATISTICAL MODELS):

DATA TO BE COLLECTED (E.G. QUESTIONNAIRES, OUTCOMES, EXPOSURES, COVARIATES)

LITERATURE REFERENCES (UP TO 20)

TEXT 500 WORDS LIMIT

IF YOU ARE USING NEW QUESTIONNAIRES PLEASE UPLOAD THEM IN THE ATTACHMENTS SECTION AT THE END OF THE APPLICATION FORM. IF YOU WOULD LIKE TO INCLUDE TABLES OR FIGURES, PLEASE REFER TO THEM IN YOUR ANSWERS AND UPLOAD THE DOCUMENTS IN THE ATTACHMENTS SECTION AT THE END OF THE APPLICATION FORM. PLEASE DO NOT USE THE ATTACHMENTS SECTION TO REPLICATE INFORMATION THAT HAS ALREADY BEEN PROVIDED WITHIN THIS FORM.

Ancillary Studies Subcommittee Review:

ELEMENTS OF PROPOSED RESEARCH ALL APPLICANTS MUST COMPLETE THIS SECTION		
WILL YOU USE EXISTING PHENOTYPIC (NON-GENETIC) DATA?*	YES ☐	NO ☐
WILL YOU COLLECT NEW PHENOTYPIC (NON-GENETIC) DATA WITHOUT PARTICIPANT CONTACT?*	YES ☐	NO ☐
WILL YOU USE GENETIC/GENOMIC DATA IN dbGaP? (HELP GENETIC/GENOMIC DATA INCLUDES BUT IS NOT LIMITED TO GENOTYPING, SEQUENCING, METABOLOMICS, PROTEOMICS, TRANSCRIPTOMICS, EXPRESSION DATA (RNA TRANSCRIPTS, MICRORNA, EXTRA-CELLULAR RNA), AND EPIGENOMICS)*	YES ☐	NO ☐
WILL YOU USE GENETIC/GENOMIC DATA NOT AVAILABLE IN dbGaP?*	YES ☐	NO ☐
WILL YOU USE DNA SPECIMENS?* IF "YES" MUST ANSWER SECTION ON DNA SPECIMEN AND GENETIC/GENOMIC DATA REQUEST	YES ☐	NO ☐
WILL YOU USE OTHER BIOLOGICAL SPECIMENS FOR GENETIC/GENOMIC/OMIC RESEARCH?* IF "YES" MUST ANSWER SECTION ON DNA SPECIMEN AND GENETIC/GENOMIC DATA REQUEST	YES ☐	NO ☐
WILL YOU USE BIOLOGICAL SPECIMENS FOR NON-GENETIC RESEARCH?* IF "YES" MUST ANSWER SECTION ON LABORATORY INVOLVEMENT	YES ☐	NO ☐
WILL YOU USE RURAL'S QUESTIONNAIRE DATA?* IF "YES" MUST ANSWER SECTION ON QUESTIONNAIRE DATA	YES ☐	NO ☐
WILL YOU ASK NEW QUESTIONNAIRES? * IF "YES" MUST ANSWER SECTION ON QUESTIONNAIRE DATA	YES ☐	NO ☐
WILL THERE BE NEW PARTICIPANT CONTACT?* IF "YES" MUST ANSWER SECTION ON PARTICIPANT CONTACT (HELP IF THE PROPOSAL INVOLVES NEW PARTICIPANT CONTACT OR ADDITIONAL SPECIMEN COLLECTION, THE OBSERVATIONAL STUDIES MONITORING BOARD (EXTERNAL TO RURAL) WILL ALSO NEED TO REVIEW THE PROPOSAL)	YES ☐	NO ☐
WILL THERE BE NEW EXAMINATION COMPONENT(S)?*	YES ☐	NO ☐
WILL THERE BE THIRD PARTY INVOLVEMENT?* IF ANSWER "YES" THEY MUST ANSWER THE QUESTION BELOW ON THIRD PARTY INVOLVEMENT (HELP :"THIRD PARTY INVOLVEMENT MAY ENTAIL PROVIDING FINANCIAL SUPPORT; PARTICIPATING DIRECTLY IN A STUDY; SUPPLYING STUDY RESOURCES; OR RECEIVING SPECIAL ACCESS TO STUDY RESULTS, DATA, FINDINGS, OR INTELLECTUAL PROPERTY. "SEE NHLBI'S DEFINITION AND POLICY OF THIRD-PARTY INVOLVEMENT.)	YES ☐	NO ☐
IF YOU HAVE THIRD PARTY INVOLVEMENT PLEASE NAME THE PARTY AND DESCRIBE THE NATURE OF THEIR INVOLVEMENT		
TEXT WORD LIMIT: 50 WORDS		
WILL THE PROJECT GENERATE NEW INDIVIDUAL LEVEL DATA ON RURAL PARTICIPANTS?* (HELP: FOR EXAMPLE, SETS OF ANALYZABLE DATA FROM INDIVIDUAL LEVEL MEASUREMENTS, IMAGES, OR LAB SPECIMENS.)	YES ☐	NO ☐
WILL YOU INCLUDE OTHER COHORT STUDIES IN YOUR STUDY?* IF ANSWER "YES" THEY MUST ANSWER THE QUESTION BELOW ON INVOLVEMENT WITH OTHER COHORT STUDIES	YES ☐	NO ☐
IF YES, PLEASE STATE THE NAME OF OTHER COHORT STUDIES INVOLVED:		
TEXT WORD LIMIT: 50 WORDS		

REVIEW PROCESS: ONE OR MORE RURAL COMMITTEES WILL REVIEW THE RESEARCH PROPOSAL DEPENDING ON WHICH ELEMENTS ARE CHECKED. IF THE PROPOSAL INVOLVES NEW PARTICIPANT CONTACT OR ADDITIONAL SPECIMEN COLLECTION, THE OBSERVATIONAL STUDIES MONITORING BOARD (EXTERNAL TO RURAL) WILL ALSO REVIEW THE PROPOSAL. PROPOSALS MAY BE ELIGIBLE FOR EXPEDITED REVIEW ON A CASE-BY-CASE DEADLINE BASED ON GRANTS WITH SMALLER TIMELINES.

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ANCILLARY STUDY PROCESS FLOWCHART
ANCILLARY STUDY PROCESS AND PROCEDURES

Ancillary Studies Subcommittee Review:

FUNDING ALL APPLICANTS MUST COMPLETE THIS SECTION				
WHAT IS YOUR FUNDING SOURCE? (HELP: GRANT AWARDING AGENCY (E.G. NIH))				
TEXT WORD LIMIT: 10 WORDS				
IF FUNDED THROUGH NIH, WHAT IS THE FUNDING MECHANISM? (HELP: A 3-CHARACTER CODE IDENTIFYING THE GRANT, CONTRACT, OR INTRAMURAL ACTIVITY THROUGH WHICH A PROJECT IS SUPPORTED. WITHIN EACH FUNDING MECHANISM, NIH USES 3-CHARACTER ACTIVITY CODES (E.G., F32, K08, P01, R01, T32, ETC.) TO DIFFERENTIATE THE WIDE VARIETY OF RESEARCH-RELATED PROGRAMS NIH SUPPORTS. A COMPREHENSIVE LIST OF ACTIVITY CODES FOR GRANTS AND COOPERATIVE AGREEMENTS MAY BE FOUND ON THE TYPES OF GRANT PROGRAMS WEB PAGE. THE CODE ZIA MAY BE USED TO INDICATE INTRAMURAL FUNDING.)			**WHAT IS THE GRANT NUMBER (WHEN FUNDED)** (HELP: IF YOU DO NOT HAVE A GRANT NUMBER YET PLEASE LEAVE BLANK)	
WORD LIMIT: 10 WORDS				
WHAT IS THE GRANT APPLICATION DUE DATE?	**WHAT IS THE PROPOSED GRANT START DATE?**		**WHAT IS THE PROPOSED GRANT END DATE?**	
MM/DD/YYYY	MM/DD/YYYY		MM/DD/YYYY	
WHAT IS THE GRANT TITLE (IF DIFFERENT FROM THE STUDY TITLE)?				
TEXT WORD LIMIT: 10 WORDS				
ESTIMATED DIRECT COSTS PER YEAR				
FY01: $	**FY02: $**	**FY03: $**	**FY04: $**	**FY05: $**

RURAL SERVICE FEES:

PROVIDING DATA, MATERIALS (INCLUDING DNA) OR OTHER RESEARCH AND ADMINISTRATION SERVICES TO ANCILLARY STUDIES INVOLVES COSTS THAT CAN VARY WIDELY AND MAY INDIVIDUALLY BE QUITE MODEST, BUT NONE OF THESE COSTS ARE COVERED BY THE RURAL GRANT.

THE COST TO RURAL TO SERVICE ANCILLARY STUDIES NEEDS TO BE REIMBURSED BY THE PRINCIPAL INVESTIGATORS (PI) OF ANCILLARY STUDIES; THEREFORE, IT IS IMPORTANT FOR YOU TO CONSIDER INCLUDING RURAL FEES IN YOUR PROJECT BUDGET.

Ancillary Studies Subcommittee Review:

PARTICIPANT BURDEN APPLICANT COMPLETES THIS SECTION IF ANSWERED "YES" TO QUESTION ON NEW PARTICIPANT CONTACT IN "ELEMENTS OF PROPOSED RESEARCH"		
DOES THIS PROPOSED STUDY INVOLVE NEW CONTACT WITH PARTICIPANTS FOR THE COLLECTION OF DATA OR SPECIMENS?* IF "YES" MUST ANSWER ALL QUESTIONS UNDER PARTICIPANT BURDEN	YES ☐	NO ☐ **PROCEED TO RURAL STAFF INVOLVEMENT**
WHAT ARE THE INCLUSION AND EXCLUSION CRITERIA FOR THE PROPOSED STUDY?		
WORD LIMIT: 100 WORDS		
WILL PARTICIPANTS BE INTERVIEWED?	YES ☐	NO ☐
WILL PARTICIPANTS HAVE A NON-INVASIVE TEST OR MEASUREMENT?	YES ☐	NO ☐
WILL PARTICIPANTS HAVE AN INVASIVE TEST OR MEASUREMENT?	YES ☐	NO ☐
DO YOU REQUIRE NEW SPECIMENS (BIOLOGICAL AND/OR NON-BIOLOGICAL)	YES ☐	NO ☐
WILL THE STUDY INVOLVE ACQUISITION OF NEW IMAGING, APPLICATION OF RADIATION, OR ADMINISTRATION OF A DRUG OR CONTRAST DYE?	YES ☐	NO ☐

IF YES, INDICATE AMOUNT OF RADIATION EXPOSURE EACH PARTICIPANT WILL RECEIVE	____ MSV	
WILL READS OF EXISTING IMAGES BE DONE?	YES ☐	NO ☐
WILL THE STUDY PROVIDE REIMBURSEMENT/COMPENSATION TO PARTICIPANTS?	YES ☐	NO ☐
WHAT IS THE FORMAT OF REIMBURSEMENT (I.E. GIFT CARD, MONEY ETC.)?	**WORD LIMIT: 20 WORDS**	
WHAT IS THE MONETARY VALUE OF COMPENSATION	**WORD LIMIT: 20 WORDS**	
WHERE WILL PARTICIPANTS BE CONTACTED? (SELECT ALL THAT APPLY)	ALABAMA ☐ KENTUCKY ☐ LOUISIANA ☐ MISSISSIPPI ☐ OTHER, PLEASE SPECIFY: _____	
WHAT IS THE NATURE OF CONTACT? (SELECT ALL THAT APPLY)	MEU EXAM ☐ HOME VISIT ☐ CALL-BACK VISIT ☐ PHONE CALL ☐ MOBILE APP ☐ MAIL TO HOME ☐	
WHAT IS THE EXPECTED TOTAL TIME REQUIRED OF EACH PARTICIPANT DURING THE CONDUCT OF THIS PROPOSED ANCILLARY STUDY?	_____:_____ (HH:MM)	
DO YOU BELIEVE THAT YOUR PROPOSED STUDY MIGHT IDENTIFY A CLINICALLY SIGNIFICANT AND ACTIONABLE FINDING(S) WHICH IF NOT REPORTED TO THE RURAL PARTICIPANT (OR PARTICIPANT'S HEALTH CARE PROVIDER) MIGHT HAVE POTENTIALLY SERIOUS CONSEQUENCES FOR THIS INDIVIDUAL'S HEALTH?	YES ☐	NO ☐
ESTIMATED NUMBER OF PARTICIPANTS WITH CLINICALLY SIGNIFICANT AND ACTIONABLE FINDINGS		
TYPE OF CLINICALLY SIGNIFICANT AND ACTIONABLE FINDING(S)	WORD LIMIT: 50 WORDS	
PROVIDE A DETAILED DESCRIPTION OF THE ACTION TO BE TAKEN, INCLUDING HOW TO INFORM THE PARTICIPANT OF THE ABNORMAL RESULT AND ACTION RECOMMENDED (REFERRAL TO URGENT/EMERGENCY CARE, NEED FOR FURTHER TESTS TO CONFIRM FINDINGS, NEED FOR TREATMENT AND CLINICAL FOLLOW-UP, GENETIC COUNSELLING, OR OTHER ACTIONS)		
WORD LIMIT: 300 WORDS		
WHAT ARE THE ANTICIPATED COSTS OF RETURNING CLINICALLY SIGNIFICANT AND ACTIONABLE FINDINGS TO PARTICIPANTS? (INCLUDE COSTS FOR A CONSULTANT FEE FOR GENETIC COUNSELING, IF NECESSARY)		
WORD LIMIT: 200 WORDS		
DESCRIBE PARTICIPANT INVOLVEMENT AND SAFETY MONITORING		
WORD LIMIT: 300 WORDS		
DESCRIBE HOW INCIDENTAL FINDINGS WILL BE HANDLED		

WORD LIMIT: 300 WORDS

DESCRIBE THE POTENTIAL RISKS OF PARTICIPATION TO RURAL PARTICIPANTS

WORD LIMIT: 300 WORDS

DESCRIBE THE BENEFITS OF PARTICIPATION TO RURAL PARTICIPANTS

WORD LIMIT: 300 WORDS

Ancillary Studies Subcommittee Review:

RURAL STAFF INVOLVEMENT ALL APPLICANTS MUST COMPLETE THIS SECTION

PLEASE CHECK ALL CORES BELOW THAT WILL BE INVOLVED OR IMPACTED BY YOUR ANCILLARY STUDY: *

STUDY COORDINATING CENTER	☐	BIOREPOSITORY AND ASSAY CORE	☐
COMMUNITY COLLABORATIONS CORE	☐	ECG READING CORE	☐
GENOMICS CORE	☐	IMAGING CORE	☐
MHEALTH CORE	☐	PULMONARY CORE	☐
RECRUITMENT AND RETENTION CORE	☐	SAMPLING CORE	☐
SOCIAL DETERMINANTS CORE	☐	STATISTICAL DATA COORDINATING CORE	☐
ALABAMA	☐	KENTUCKY	☐
LOUISIANA	☐	MISSISSIPPI	☐
MOBILE EXAMINATION UNIT (MEU) TECHNICIANS	☐		

A. RURAL STATE CORE(S) (ALABAMA, KENTUCKY, LOUISIANA, MISSISSIPPI):

DESCRIBE RURAL STATE CORES' INVOLVEMENT

WORD LIMIT: 200 WORDS

DESCRIBE EFFORT REQUIRED FOR STAFF AT EACH STATE CORE

WORD LIMIT: 200 WORDS

B. RURAL STUDY COORDINATING CENTER (SCC):

DESCRIBE EFFORT REQUIRED FOR STAFF AT THE SCC

WORD LIMIT: 200 WORDS

C. RURAL STATISTICAL DATA COORDINATING CORE (SDCC):

DESCRIBE EFFORT REQUIRED FOR STAFF AT THE SDCC

WORD LIMIT: 200 WORDS

WILL THE SDCC BE INVOLVED IN DATA COLLECTION AND TRACKING?	**YES ☐**	**NO ☐**
WILL THE SDCC BE INVOLVED WITH CREATING FORMS OR SOFTWARE?	**YES ☐**	**NO ☐**
WILL THE SDCC BE INVOLVED IN DATA ANALYSES? IF "NO" MUST ANSWER QUESTION: "IF ANALYSES ARE NOT DONE BY SDCC, PLEASE INDICATE…"	**YES ☐**	**NO ☐**
WILL YOU REQUEST VERIFICATION OF ANALYSES FROM THE SDCC?	**YES ☐**	**NO ☐**

IF ANALYSES ARE NOT DONE BY SDCC, PLEASE INDICATE THE NAME AND INSTITUTION OF THE LEAD STATISTICIAN/ DATA ANALYST

WORD LIMIT: 100 WORDS

WHAT VARIABLES WILL BE NEEDED FROM THE RURAL CENTRAL DATABASE?

WORD LIMIT: 150 WORDS

D. RECRUITMENT AND RETENTION CORE:

DESCRIBE EFFORT REQUIRED FOR STAFF AT THE RECRUITMENT AND RETENTION CORE (INCLUDING RETURNING CLINICALLY SIGNIFICANT AND ACTIONABLE FINDINGS)

WORD LIMIT: 200 WORDS

E. BIOREPOSITORY AND ASSAY CORE:

DESCRIBE EFFORT REQUIRED FOR STAFF AT THE BIOREPOSITORY AND ASSAY CORE

WORD LIMIT: 200 WORDS

F. OTHER CORE(S)

PLEASE COMPLETE THIS SECTION IF THE RELEVANT CORE IS NOT INCLUDED IN SECTION A-E

NAME OF CORE(S)

WORD LIMIT: 20 WORDS

DESCRIBE EFFORT REQUIRED FOR STAFF AT OTHER CORE(S)

WORD LIMIT: 200 WORDS

ESTIMATED TIME REQUIRED OF STAFF AT OTHER CORE(S)

WORD LIMIT: 200 WORDS

Ancillary Studies Subcommittee Review:

QUESTIONNAIRE DATA

APPLICANT COMPLETES THIS SECTION IF ANSWERED "YES" TO QUESTIONNAIRE QUESTIONS IN "ELEMENTS OF PROPOSED RESEARCH"

PLEASE CHECK THE QUESTIONNAIRE DATA REQUESTED FROM THE RURAL MAIN DATABASE (CHECK ALL THAT APPLY):

MEU QUESTIONNAIRES

PERSONAL/REGISTRATION INFORMATION:		MEDICAL INFORMATION:		SOCIAL DETERMINANTS INFORMATION:	
HEALTHCARE ACCESS (INSURANCE)	☐	CARDIOVASCULAR HISTORY	☐	STRESS IN ADULTHOOD	☐
	☐	HYPERTENSION HISTORY	☐	STRESS IN CHILDHOOD	☐
MARITAL STATUS	☐	HIGH CHOLESTEROL HISTORY	☐	FINANCIAL STRAIN	☐
LENGTH OF TIME IN COUNTY	☐	DIABETIC HISTORY	☐	FOOD INSECURITY	☐
SEX ASSIGNED AT BIRTH	☐	CHEST PAIN	☐	HOUSING STABILITY	☐
GENDER IDENTITY	☐	CEREBROVASCULAR DISEASE	☐	DEPRESSION	☐
SEXUAL ORIENTATION	☐	VENOUS AND PERIPHERAL ARTERIAL DISEASE	☐	RESILIENCE	☐
RACE/ETHNICITY	☐	HEART FAILURE	☐	RESIDENTIAL HISTORY	☐
EDUCATION	☐	MEDICATION LIST	☐	HEALTHCARE UTILIZATION	☐
INCOME	☐	RESPIRATORY HEALTH	☐		
		ENVIRONMENTAL ALLERGIES	☐		
		OCCUPATIONAL HAZARDS	☐		
		SLEEP	☐		
		ALCOHOL USE	☐		
		TOBACCO USE	☐		
		PHYSICAL ACTIVITY	☐		
		DIETARY SCREENER	☐		

MOBILE APP QUESTIONNAIRES

PERSONAL/ REGISTRATION INFORMATION:		MEDICAL INFORMATION:		SOCIAL DETERMINANTS INFORMATION:	
OCCUPATION AND WORK HISTORY	☐	ALCOHOL USE	☐	SOCIAL SUPPORT AND NETWORKS	☐
		TOBACCO USE	☐	RELIGIOSITY AND SPIRITUALITY	☐
		RECREATIONAL DRUG USE	☐	SELF-EFFICACY AND LOCUS OF CONTROL	☐
		SLEEP	☐	ACCULTURATION	☐
		GENERAL HEALTH STATUS	☐	NEIGHBORHOOD SAFETY	☐
		CANCER SCREENING	☐	SOCIAL COHESION	☐
		SINO-NASAL	☐	AESTHETIC QUALITY	☐
		BIOLOGICAL PARENT MEDICAL HISTORY	☐	WALKABILITY	☐
		PAST SURGICAL HISTORY	☐	ACTIVITIES WITH NEIGHBORS	☐
		WEIGHT HISTORY	☐	RESIDENTIAL HISTORY	☐
				OCCUPATION-WORKPLACE STRESS	☐
				ACCESS TO HEALTHY FOOD	☐

WILL YOU COLLECT ANY ADDITIONAL NEW QUESTIONNAIRE DATA?*		YES ☐ IF "YES" MUST FILL OUT TABLE BELOW	NO ☐
WHAT DATA WILL YOU COLLECT? PLEASE UPLOAD QUESTIONNAIRES AT THE END OF APPLICATION FORM	**WHEN WILL THE DATA BE COLLECTED?**	**TIME TO ADMINISTER QUESTIONNAIRE**	**WILL IT BE INTERVIEWER OR SELF-ADMINISTERED?**
WORD LIMIT: 20 WORDS	MM/YY	(MINS)	WORD LIMIT: 10 WORDS
WORD LIMIT: 20 WORDS	MM/YY	(MINS)	WORD LIMIT: 10 WORDS
WORD LIMIT: 20 WORDS	MM/YY	(MINS)	WORD LIMIT: 10 WORDS
WORD LIMIT: 20 WORDS	MM/YY	(MINS)	WORD LIMIT: 10 WORDS
WORD LIMIT: 20 WORDS	MM/YY	(MINS)	WORD LIMIT: 10 WORDS
WORD LIMIT: 20 WORDS	MM/YY	(MINS)	WORD LIMIT: 10 WORDS

Genetics/Laboratory Subcommittee Review:

LABORATORY INVOLVEMENT APPLICANT COMPLETES THIS SECTION IF ANSWERED "YES" TO BIOSPECIMEN QUESTIONS IN "ELEMENTS OF PROPOSED RESEARCH"	
A. ASSAY NAME	
ASSAY NAME*	**EXPLAIN THE PURPOSE OF THIS ASSAY IN ONE SENTENCE***
WORD LIMIT: 10 WORDS	WORD LIMIT: 50 WORDS
B. PREVIOUS WORK WITH THIS ASSAY: PROVIDE A BRIEF SUMMARY OF PREVIOUS WORK WITH THIS ASSAY (CITATIONS ALONE ARE INSUFFICIENT)	
EXPLAIN WHY THE ASSAY IS UNIQUE AND NOT DUPLICATIVE OF OTHER EXISTING ASSAYS	
WORD LIMIT: 150 WORDS	
PROVIDE EVIDENCE (PREVIOUS CROSS-SECTIONAL STUDIES, PRELIMINARY DATA OR PILOT STUDIES) THAT THE ASSAY CORRELATES WITH SOME MEASURE OF DISEASE	
WORD LIMIT: 150 WORDS	
PROVIDE EVIDENCE (PREVIOUS CROSS-SECTIONAL STUDIES, PRELIMINARY DATA OR PILOT STUDIES) THAT THE ASSAY WILL LIKELY YIELD DATA TO SUPPORT THE AIMS OF THE STUDY	
WORD LIMIT: 150 WORDS	
PROVIDE EVIDENCE (PRELIMINARY DATA OR PILOT STUDIES) OF FEASIBILITY OF THIS ASSAY (INTER- ASSAY PRECISION CV < 10%) WITH SPECIMEN TYPE REQUESTED AND WITH A COMMUNITY-BASED COHORT (E.G., DISEASE MARKER ASSAY WILL PERFORM WELL IN LOW RANGE)	
WORD LIMIT: 150 WORDS	
PROVIDE A DATA ANALYSIS TO DETERMINE IF PROPOSED SAMPLE NUMBERS ARE SUFFICIENT TO REVEAL STATISTICAL SIGNIFICANT RESULTS (I.E., A POWER-ANALYSIS):	
WORD LIMIT: 150 WORDS	

WHAT ARE THE LIMITATIONS OF THE PROPOSED ASSAY, AND HOW DO YOU PROPOSE TO ADDRESS THEM?
WORD LIMIT: 150 WORDS

C. ASSAY DESCRIPTION AND PERFORMANCE CHARACTERISTICS

IS THIS A NOVEL OR NON-ROUTINE ASSAY?	NOVEL ☐	NON-ROUTINE ASSAY ☐ (HELP: I.E. NON-CLINICALLY ACTIONABLE)
PROVIDE A BRIEF TECHNICAL DESCRIPTION OF ASSAY (PROVIDE MORE DETAIL IF THE ASSAY IS NOVEL)		
WORD LIMIT: 150 WORDS		
PROVIDE BRAND AND CATALOG NUMBER AND/OR REFERENCE CITATION(S)		
WORD LIMIT: 100 WORDS		

REPRODUCIBILITY - INTRA-ASSAY (PROVIDE CV):	REPRODUCIBILITY - INTER-ASSAY (PROVIDE CV):
WORD LIMIT: 50 WORDS	WORD LIMIT: 50 WORDS

ANALYTICAL RANGE (DISCUSS ASSAY PERFORMANCE AT LOW, MIDDLE, AND HIGH END OF EXPECTED RANGE)
WORD LIMIT: 50 WORDS

CAN THE ASSAY CAN BE PERFORMED WITH ACCEPTABLE INTER-ASSAY PRECISION (CV<10%) ON PREVIOUSLY FROZEN SPECIMENS?	YES ☐	NO ☐	UNKNOWN ☐

WHAT IS THE PROPOSED LABORATORY FOR ANALYSES (IF NOT RURAL, PROVIDE DIRECTOR, ADDRESS, CONTACT NUMBER)
WORD LIMIT: 150 WORDS

D. BIOSPECIMEN REQUEST INFORMATION

BIOSPECIMEN REQUESTED	VOLUME REQUESTED*	JUSTIFICATION OF REQUESTED VOLUME	DESCRIBE HOW EXCESS BIOSPECIMENS WILL BE HANDLED (I.E. DISPOSAL OR RETURN TO RURAL)	NUMBER OF PARTICIPANTS
WORD LIMIT: 50 WORDS	WORD LIMIT: 20 WORDS	WORD LIMIT: 150 WORDS	WORD LIMIT: 50 WORDS	
WORD LIMIT: 50 WORDS	WORD LIMIT: 20 WORDS	WORD LIMIT: 150 WORDS	WORD LIMIT: 50 WORDS	
WORD LIMIT: 50 WORDS	WORD LIMIT: 20 WORDS	WORD LIMIT: 150 WORDS	WORD LIMIT: 50 WORDS	
WORD LIMIT: 50 WORDS	WORD LIMIT: 20 WORDS	WORD LIMIT: 150 WORDS	WORD LIMIT: 50 WORDS	
WORD LIMIT: 50 WORDS	WORD LIMIT: 20 WORDS	WORD LIMIT: 150 WORDS	WORD LIMIT: 50 WORDS	
WORD LIMIT: 50 WORDS	WORD LIMIT: 20 WORDS	WORD LIMIT: 150 WORDS	WORD LIMIT: 50 WORDS	

**SEE ANCILLARY STUDY POLICY FOR GENERALLY ALLOWABLE SPECIMEN VOLUMES. REQUESTS FOR VOLUMES OVER THIS AMOUNT WILL BE REVIEWED ON A CASE-BY-CASE BASIS AND REQUIRE STRONG SCIENTIFIC JUSTIFICATION.*

ARE SAMPLES REQUIRED TO BE FASTING OR NON-FASTING?	FASTING ☐	NON-FASTING ☐

WHAT ARE YOUR SHIPPING REQUIREMENTS?
WORD LIMIT: 100 WORDS

IS THERE A BAR CODE READER AVAILABLE AT YOUR LABORATORY FOR THIS ANALYTE?	YES ☐	NO ☐

CAN THIS SAMPLE BE USED FOR OTHER ANALYTES; IF SO WHICH ONES?
WORD LIMIT: 100 WORDS

DO YOU HAVE ANY RURAL SPECIMENS (NUMBER AND TYPE) IN YOUR POSSESSION FROM A PREVIOUSLY APPROVED APPLICATION?	YES ☐	NO ☐

INVESTIGATOR AGREES TO NOTIFY THE RURAL LABORATORY SUBCOMMITTEE OF ANY SUBSTITUTION, ADDITION, OR DELETION OF AN APPROVED ASSAY	AGREED ☐

Genetics/Laboratory Subcommittee Review:

DNA SPECIMEN AND GENETIC/GENOMIC DATA REQUEST APPLICANT

COMPLETES THIS SECTION IF ANSWERED "YES" TO DNA QUESTIONS IN "ELEMENTS OF PROPOSED RESEARCH"

A. DNA SPECIMEN REQUEST

ARE YOU REQUESTING CELL LINE DNA?	YES ☐	NO ☐
ARE YOU REQUESTING GENOMIC DNA?	YES ☐	NO ☐
ARE YOU REQUESTING CUSTOM SET OF SAMPLES?	YES ☐	NO ☐

IF YES, PLEASE DESCRIBE THE CUSTOM DNA REQUEST WITH A JUSTIFICATION

WORD LIMIT: 150 WORDS

CONCENTRATION (NG/UL)		AMOUNT OF DNA (NG)	
DO YOU HAVE ANOTHER SPECIMEN REQUEST IF YES, MUST ANSWER QUESTION BELOW "PLEASE DESCRIBE THE SPECIMEN REQUEST"		YES ☐	NO ☐

PLEASE DESCRIBE THE SPECIMEN REQUEST

WORD LIMIT: 200 WORDS

B. DESCRIBE THE ASSAY

DESCRIBE THE LABORATORY THAT WILL CONDUCT THE ASSAY, THE LABORATORY METHODS, AND QUALITY CONTROL. PROVIDE EVIDENCE THE ASSAY WILL LIKELY YIELD DATA TO SUPPORT THE AIMS OF THE STUDY, INCLUDING PUBLICATIONS OF THE METHOD

WORD LIMIT: 300 WORDS

C. GENETIC/GENOMIC DATA REQUEST

WILL YOU REQUEST DATA FROM RURAL SDCC?	YES ☐	NO ☐
WILL YOU REQUEST DATA FROM DBGAP?	YES ☐	NO ☐

DESCRIBE THE GENETIC/GENOMIC DATA REQUEST AS THOROUGHLY AS POSSIBLE

WORD LIMIT: 500 WORDS

DESCRIBE THE PHENOTYPIC DATA REQUEST AS THOROUGHLY AS POSSIBLE

WORD LIMIT: 500 WORDS

INVESTIGATOR AGREES TO NOTIFY THE RURAL GENETICS COMMITTEE OF ANY SUBSTITUTION, ADDITION, OR DELETION OF AN APPROVED ASSAY	AGREED ☐

Ancillary Studies Subcommittee Review:

PLEASE READ CAREFULLY: ANCILLARY STUDY INVESTIGATORS ARE REQUIRED TO COMPLETE A DATA AND MATERIALS DISTRIBUTION AGREEMENT (DMDA) IN ORDER TO RECEIVE STUDY SAMPLES AND/OR DATA. THE COMPLETED DMDA SHOULD BE SENT TO THE RURAL STUDY PROJECT OFFICER AT NHLBI WITH A COPY TO THE RURAL STUDY COORDINATING CORE. WHEN SIGNING THE DMDA, ANCILLARY STUDY INVESTIGATORS ARE AGREEING TO THE REQUIREMENTS TO SEND THE ANCILLARY STUDY DATA TO THE STUDY COORDINATING CORE TO EVENTUALLY BE INCORPORATED INTO THE RURAL STUDY DATABASE AND NHLBI-DESIGNATED PUBLIC REPOSITORIES CONSISTENT WITH NIH DATA SHARING POLICIES.

THE ANCILLARY STUDY INVESTIGATORS HAVE EXCLUSIVE RIGHTS TO USE THE GENETIC AND OMICS DATA GENERATED FROM THE ANCILLARY STUDY FOR ONE YEAR AFTER THE DATA SET HAS BEEN CLEANED AND FINALIZED FOR ANALYSIS OR AS CONTEMPORARY NIH DATA SHARING POLICY MANDATES. ANCILLARY STUDY INVESTIGATORS WILL BE GIVEN ACCESS TO THE RURAL STUDY DATA ONLY AFTER THE AS DATA HAS BEEN SENT TO THE STUDY COORDINATING CORE AND THE STATISTICAL AND DATA COORDINATING CORE.

THE ANCILLARY STUDY DATA WILL BE AVAILABLE TO RURAL STUDY INVESTIGATORS AND MAY BE AVAILABLE TO EXTERNAL INVESTIGATORS UPON REQUEST. THE RURAL STUDY WILL ENCOURAGE EXTERNAL INVESTIGATORS REQUESTING ACCESS TO ANCILLARY STUDY DATA TO COLLABORATE WITH THE PI WHO GENERATED THE DATA.

THE NHLBI POLICY FOR DATA SHARING FROM CLINICAL TRIALS AND EPIDEMIOLOGICAL STUDIES REQUIRES THE RURAL STUDY COORDINATING CORE TO INCLUDE ANCILLARY STUDY DATA IN THE RURAL STUDY DATA SET ONE YEAR AFTER THE ANCILLARY STUDY DATA IS CLEANED AND FINALIZED FOR ANALYSIS BY ANCILLARY STUDY INVESTIGATORS. THE ANCILLARY STUDY INVESTIGATORS MUST SEND RELEVANT INFORMATION TO THE RURAL STUDY COORDINATING CORE TO ENSURE THE ANCILLARY STUDY DATA IS USEFUL FOR ALL ELIGIBLE EXTERNAL INVESTIGATORS VIA NHLBI-DESIGNATED DATA REPOSITORIES.

GENOMIC AND OMIC DATA GENERATED IN THE RURAL STUDY MUST FOLLOW THE NIH GENOMIC DATA SHARING POLICY. ANCILLARY STUDY INVESTIGATORS PERFORMING GENOMIC AND OMIC STUDIES SHOULD UNDERSTAND THE POLICY REQUIREMENTS.

I AGREE TO THE ABOVE TERMS REGARDING DATA SHARING:	**AGREED ☐**	***TYPE NAME (TEXT BOX)***
I AGREE TO PROVIDING SEMIANNUAL UPDATE REPORTS:	**AGREED ☐**	***TYPE NAME (TEXT BOX)***
I AGREE TO FOLLOW ALL POLICIES AND PROCEDURES SET FORTH BY THE RURAL COHORT STUDY. THESE POLICIES ARE REVIEWED AND UPDATED REGULARLY BY RURAL LEADERSHIP.	**AGREED ☐**	***TYPE NAME (TEXT BOX)***
I AGREE TO ENTIRELY SUPPORT THE ANCILLARY PROGRAM'S COSTS INVOLVED IN CONDUCTING THEIR STUDY WITH THE RURAL COHORT STUDY. INCLUDING, BUT NOT LIMITED TO, SUBCONTRACTS, RURAL COHORT STUDY SERVICE CENTER FEES, ETC.	**AGREED ☐**	***TYPE NAME (TEXT BOX)***
I CONFIRM THAT ALL NAMED CO-INVESTIGATORS HAVE BEEN MADE AWARE OF THEIR APPOINTMENT IN THE CO-INVESTIGATORS ROLE FOR THIS STUDY.	**AGREED ☐**	***TYPE NAME (TEXT BOX)***
I AGREE TO CITE THE RURAL CORE CONTRACT (NHLBI AWARD U01HL146382) AND ANY RURAL COHORT STUDY GRANT NUMBERS THAT HAVE FUNDED THEIR RESEARCH ACTIVITIES IN PUBLICATIONS THAT RESULT FROM SUCH WORK.	**AGREED ☐**	***TYPE NAME (TEXT BOX)***

ATTACHMENTS: IF YOU WOULD LIKE TO INCLUDE TABLES OR FIGURES, PLEASE REFER TO THEM IN YOUR ANSWERS AND UPLOAD THE DOCUMENTS IN THE ATTACHMENTS SECTION AT THE END OF THE APPLICATION FORM. PLEASE DO NOT USE THE ATTACHMENTS SECTION TO REPLICATE INFORMATION THAT HAS ALREADY BEEN PROVIDED WITHIN THIS FORM PLEASE ATTACH QUESTIONNAIRE AT END OF APPLICATION

FOR STUDY COORDINATING CENTER USE ONLY

APPROVED BY GENETICS/ LABORATORY COMMITTEE? (IF APPLICABLE)	**YES ☐**	**NO ☐**	**DATE:** Click or tap to enter a date.
IF NO, PLEASE STATE WHY			
APPROVED BY ETHICS ADVISORY BOARD? (IF APPLICABLE)	**YES ☐**	**NO ☐**	**DATE:** Click or tap to enter a date.
IF NO, PLEASE STATE WHY			

APPROVED BY ANCILLARY STUDIES COMMITTEE?	**YES ☐**	**NO ☐**	**DATE:** Click or tap to enter a date.
IF NO, PLEASE STATE WHY			
APPROVED BY STEERING COMMITTEE?	**YES ☐**	**NO ☐**	**DATE:** Click or tap to enter a date.
IF NO, PLEASE STATE WHY			
IF APPROVED, ANCILLARY STUDY ID			
DMDA ON FILE?	**YES ☐**	**NO ☐**	**DATE:** Click or tap to enter a date.
OSMB APPROVAL?	**YES ☐**	**NO ☐**	**DATE:** Click or tap to enter a date.
NHLBI APPROVAL?	**YES ☐**	**NO ☐**	**DATE:** Click or tap to enter a date.

PLEASE CHECK ALL CORES BELOW THAT WILL REQUIRE SUBCONTRACTS:

STUDY COORDINATING CENTER	☐	**BIOREPOSITORY AND ASSAY CORE**	☐
COMMUNITY COLLABORATIONS CORE	☐	**ECG READING CORE**	☐
GENOMICS CORE	☐	**IMAGING CORE**	☐
MHEALTH CORE	☐	**PULMONARY CORE**	☐
RECRUITMENT AND RETENTION CORE	☐	**SAMPLING CORE**	☐
SOCIAL DETERMINANTS CORE	☐	**STATISTICAL DATA COORDINATING CORE**	☐
ALABAMA	☐	**KENTUCKY**	☐
LOUISIANA	☐	**MISSISSIPPI**	☐

E. Data and Materials Distribution Agreement (DMDA)

The undersigned parties hereby enter into this Data and Materials Distribution Agreement (DMDA) as of the date specified on the final page hereof.

INTRODUCTION

The **R**isk **U**nderlying **R**ural **A**reas **L**ongitudinal (RURAL) Cohort Study is a multicenter prospective epidemiology cohort study that seeks to address gaps in our knowledge of heart and lung disorders as well as to understand the health concerns of rural communities in the southeastern regions of the United States. Focusing on ten counties in Alabama, Kentucky, Louisiana, and Mississippi, the multi-investigator team will examine 4,600 rural residents to study their heart, lung, and overall health. The RURAL Cohort Study will have a mobile examination vehicle (MEU) that will be staffed with trained technicians and will travel to the target counties to perform the RURAL Cohort Study. The RURAL Cohort Study will collect biological specimens and clinical data from participants, which will serve as valuable scientific resources for the population and scientific community. This repository will be maintained under the joint stewardship of Boston University and the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH). As part of the RURAL Cohort Study, participants will receive their results and general Study information will be shared with the communities.

To ensure the confidentiality and privacy of RURAL Cohort Study participants and their families, the approved investigator requesting access to RURAL Cohort Study Data and Materials must follow the requirements detailed in this DMDA. The failure to adhere with this DMDA could result in its termination, denial of further access to the RURAL Cohort Study and other NHLBI resources, and may leave violators liable to legal action on the part of the RURAL Cohort Study participants, their families, Boston University, or the U.S. Government.

The undersigned parties entering into this DMDA include: the Recipient and Recipient's Principal Investigator (defined in the next section), the NHLBI, and Boston University, on behalf of the RURAL Cohort Study and under the direction of the RURAL Cohort Study Steering Committee.

DEFINITIONS

For purposes of this agreement,

"Genetic Analysis Data" refers to any and all information derived from genetic materials, and any and all data derived from statistical analyses linking data from genetic materials with other study data.

"Data" refers to any and all study data, including laboratory, examination, and questionnaire results, and
Analysis Data, images (e.g., computed tomography scans), or primary signal data (e.g., ECG, spirometry tracings, or pulse wave velocity forms) and associated records either obtained directly from RURAL Cohort Study participants or obtained from third parties as authorized by the participants pursuant to the contracts with the NHLBI, as well as data provided to the RURAL Cohort Study by ancillary studies.

"Resultant Data" refers to data derived in whole or in part by Recipient from Data and/or Materials provided under this DMDA.

"Materials" refers to bio-samples, including but not limited to, urine and blood samples and products thereof, including but not limited to, immortalized lymphocytes and extracted DNA from said bio-samples pursuant to the contracts with the NHLBI, as well as Materials provided to the RURAL Cohort Study by ancillary studies.

"RURAL Study Investigator" is a research investigator who works with the RURAL Cohort Study either as an employee of Boston University, as an employee of a RURAL Cohort Study associated institution, or the NHLBI or through a current and active contract or consulting agreement with Boston University, the NHLBI, or one of their contractors.

"Research Project" refers to the project described in the attached research application.

"Recipient" refers to the institution or other entity receiving access to the RURAL Cohort Study Data and/or Materials requested for the Research Project identified in Section 3 below as described in the attached research application.

"Principal Investigator (PI)" refers to the Research Project Director for the Recipient.

TERMS and CONDITIONS

It is mutually agreed as follows:

1. Materials. Boston University and NHLBI agree to transfer to Recipient the Materials described below, including the types of samples, amount per sample, the number of individuals from whom samples are to be provided, and whether samples are nonrenewable or from a renewable resource (e.g., DNA from immortalized cell lines) for use by the Recipient's PI to conduct the Research Project as summarized in Section 3 below.

2. Data. Boston University agrees to provide Recipient with Data described as follows:

_____

_____

The RURAL Cohort Study will provide Recipient with the name and contact information of Study Investigators and all other investigator(s) who generated such Data.

3. Research Project.

3.1 These Materials and Data will be used by Recipient's PI solely in connection with the Research Project, as named and described in the attached research application (insert Research Project name below):

_____

_____

3.2 If any aspect of the Research Project, e.g., biological assays and/or genetic analyses, is to be performed by an entity other than Recipient as permitted by Section 4.2, such entity is to be named below:

_____

_____

3.3 This DMDA covers only the Research Project cited in Section 3.1 of this DMDA. Recipient must submit a separate DMDA for each Research Project for which Data and/or Materials are requested.

4. Non-transferability. This DMDA is not transferable.

4.1 Recipient and Recipient's PI agree that substantive changes made to the Research Project, and/or appointment by Recipient of another Principal Investigator and/or transfer of Recipient's PI to another institution or other entity to complete the Research Project, require execution of a separate DMDA. Except as provided in Section 4.2 below, Recipient may not distribute Data or Materials to any other individual or entity, regardless of the intended use of such Data or Materials. However, nothing in this section precludes Recipient from publishing results of the Research Project through the usual channels of scientific publication.

4.2 Recipient and Recipient's PI may transfer or cause to be transferred Materials to an institution or institutions or other entities not affiliated with Recipient but with which Recipient either has a fee-for or subcontract agreement or specific authorization from the NHLBI for the performance of assays and/or genetic analyses for the Research Project as identified in Section 3.2. A separate DMDA is not required if the derived data are either returned to the Recipient and Recipient's PI or are deposited for Recipient and Recipient's PI in a publicly accessible database authorized by the NHLBI upon completion of the assays. No Data are to be provided to such institutions or other entities unless a separate DMDA has been approved by Boston University and NHLBI.

5. Conduct of Research Project. Recipient's PI is responsible for the conduct of the Research Project and shall be responsible for assuring that any Co-Investigator(s) comply with the terms of this DMDA.

6. Publication. Prompt publication of the results of the Research Project is encouraged. Boston University and NHLBI request that the Recipient's PI provides to the contact representative for the RURAL Cohort Study (named below) a copy of any abstract ten (10) days in advance of submission for publication and any manuscript or other disclosure document thirty (30) days in advance of submission for publication, in order to permit review and comment and ensure compliance with the confidentiality requirements of this DMDA.

7. Acknowledgments. Recipient and Recipient's PI agree to acknowledge the contribution of the RURAL Cohort Study staff in any and all oral and written presentations, disclosures, and publications resulting from any and all analyses of Data or Materials.

7.1 Collaborations. If a manuscript resulting from the Research Project has Study Investigators as
co-authors, then the manuscript will be reviewed by the RURAL Cohort Study Publications and Policy Committee.

7.1.a If the manuscript is approved by the RURAL Cohort Study Publications and Policy Committee, the Recipient and Recipient's PI agree to include the following language in an acknowledgment:

"The RURAL Cohort Study is supported by Contract No. U01HL146382 from the National Heart, Lung, and Blood Institute (NHLBI) with additional support from other sources."

"This manuscript has been reviewed by the RURAL Cohort Study for scientific content and consistency of data interpretation with previous RURAL Cohort Study publications."

7.1.b If the manuscript is not approved by the RURAL Cohort Study Publications and Policy Committee, and the Recipient and Recipient's PI wish to proceed to publish without the inclusion of Study Investigators as co-authors, the Recipient and Recipient's PI agree to include the following language in an acknowledgment:

"The RURAL Cohort Study is supported by Contract No. U01HL146382 from the National Heart, Lung, and Blood Institute (NHLBI) with additional support from other sources."

"This manuscript was not approved by the RURAL Cohort Study. The opinions and conclusions contained in this publication are solely those of the authors, and are not endorsed by the RURAL Cohort Study or the NHLBI and should not be assumed to reflect the opinions or conclusions of either."

7.2 Other Studies. If the Research Project does not involve collaboration with Study Investigators, then the Recipient and Recipient's PI agree to include the following language in an acknowledgment.

"The RURAL Cohort Study is supported by Contract No. U01HL146382 from the National Heart, Lung, and Blood Institute (NHLBI) with additional support from other sources."
"This manuscript was not prepared in collaboration with investigators of the RURAL Cohort Study and does not necessarily reflect the opinions or conclusions of the RURAL Cohort Study or the NHLBI."

7.3 Ancillary Study Investigator Acknowledgments. If Data include data provided to the RURAL Cohort Study by ancillary study investigators, Recipient and Recipient's PI also agree to acknowledge their contribution in any and all oral and written presentations, disclosures, and publications resulting from any and all analyses of such Data.

8. Non-Identification. Recipient and Recipient's PI agree that Materials and/or Data will not be used, either alone or in conjunction with any other information, in any effort to determine the individual identities of any of the participants from whom Data and/or Materials were obtained or derived.

9. Use Limited to Research Project. Recipient and Recipient's PI agree that Data, Materials, their progeny, or derivatives thereof will not be used in any experiments or procedures unless said experiments or procedures are disclosed and approved as part of the Research Project.

10. Use in Human Experimentation Prohibited. Recipient and Recipient's PI agree that Materials, their progeny, and derivatives thereof will not be used in human experimentation of any kind.

11. Compliance with Participants' Informed Consent. Recipient and Recipient's PI agree that Data and/or Materials, their progeny, and derivatives thereof will not be used for any purpose contrary to a participant's applicable signed informed consent document(s). Recipient and Recipient's PI agree to consult with Study Investigators and ascertain, specifically and in detail, the terms and conditions of applicable RURAL Cohort Study informed consent documents.

12. No Distribution; Avoidance of Waste. Recipient and Recipient's PI agree to retain control over Data, Materials and their progeny, and derivatives thereof. Recipient and Recipient's PI further agree not to transfer Data, Materials and their progeny, and derivatives thereof, with or without charge, to any other entity or individual, except for Data and/or Materials as provided for in Section 4.2 above. Recipient and Recipient's PI agree to make reasonable efforts to avoid contamination or waste of Materials.

13. Resultant Data to be Provided to Boston University and NHLBI. Recipient and Recipient's PI agree to provide the RURAL Cohort Study with a report every twelve (12) months during the term of this DMDA. The report shall include a description of the activities performed and Resultant Data obtained during the twelve (12) months before the reporting date. Recipient and Recipient's PI agree that Boston University and NHLBI, in accordance with the NIH Data Sharing Policy and NHLBI Policy for Data Sharing from Clinical Trials and Epidemiologic Studies, may distribute all such Resultant Data through established NHLBI procedures to all institutions requesting access for their identified qualified scientific investigators to such Resultant Data, and that submit to NHLBI and Boston University a signed DMDA comparable to this DMDA. Recipient and Recipient's PI will provide all Resultant Data in the precise electronic format specified by NHLBI or Boston University. If errors in family structure, especially paternity, are identified, Recipient and Recipient's PI agree to contact the RURAL Cohort Study contact representative (named below), at the time such errors are identified, to receive detailed instructions as to how to provide such information and to whom. Recipient and Recipient's PI further agree to refrain from any disclosure of such identified errors to anyone other than the individual(s) specifically identified and authorized by Boston University and NHLBI.

14. Costs/No Warranties. Cost for Materials distribution will be determined on a case by case basis. Costs are subject to change following written notification from Boston University with the approval of NHLBI. NO WARRANTIES, EXPRESS OR IMPLIED, ARE OFFERED AS TO THE MERCHANTABILITY OR FITNESS FOR ANY PURPOSE OF THE MATERIALS AND/OR DATA PROVIDED TO RECIPIENT UNDER THIS AGREEMENT, OR THAT THE MATERIALS AND/OR DATA MAY BE EXPLOITED WITHOUT INFRINGING THE INTELLECTUAL PROPERTY OR PROPRIETARY RIGHTS OF ANY THIRD PARTIES.

15. Recipient's Responsibility for Handling Materials. Recipient and Recipient's PI acknowledge that Materials may carry viruses, latent viral genomes, and other infectious agents. Recipient and Recipient's PI agree to treat Materials as if they were not free of contamination, and affirm that Materials will be handled by trained persons under laboratory conditions that afford adequate biohazard containment. By accepting Materials, Recipient assumes full responsibility for their safe and appropriate handling.

16. Non-Endorsement, Indemnification. Recipient and Recipient's PI agree not to claim, infer, or imply United States Government endorsement of the Research Project, the entity, or personnel conducting the Research Project, or any resulting commercial product(s) except as described in Section 7.

Recipient and Recipient's PI agree to release the United States Government, Boston University, and all investigator(s) who generated Data and Materials, and the agents and employees of each of them from all liabilities, demands, damages, expenses, and losses arising out of Recipient's use for any purpose.

Except where prohibited by law, Recipient agrees to defend and indemnify the United States Government, Boston University, and all investigator(s) who generated Data and Materials, and the agents and employees of each of them for all liabilities, demands, damages, expenses, and losses arising out of Recipient's use for any purpose.

17. Accuracy of Data. Recipient agrees that the United States Government and Boston University are not responsible for the accuracy of Data or the provenance or integrity of Materials provided.

18. Recipient's Compliance with Recipient IRB's Requirements. Recipient certifies that the conditions for use of the Data and/or Materials in conjunction with the Research Project have been reviewed by the Recipient's Institutional Review Board (IRB) or similar human subjects oversight body in accordance with the Department of Health and Human Services (HHS) regulations at 45 CFR Part 46. Recipient agrees to comply fully with all such conditions and with the participants' informed consent documents, and any additional conditions that may be imposed by the University of Alabama Birmingham's IRB, which serves as the single IRB governing the RURAL Cohort Study. Recipient agrees to report promptly to Boston University and the NHLBI any unanticipated problems or proposed changes in the Research Project. Recipient also agrees to report to Recipient's IRB any unanticipated problems or changes in the Research Project that involve additional risks to participants or others. Recipient remains subject to applicable state and local laws and regulations and institutional policies that provide additional protections for human subjects.

19. Recipient's Responsibility to follow Data Security Best Practices. Recipient is aware of computer and data security best practices and will follow them for receipt, storage, and use of Data and Resultant Data. An example of best practice guidelines can be found in https://osp.od.nih.gov/wp-content/uploads/NIH_Best_Practices_for_Controlled-Access_Data_Subject_to_the_NIH_GDS_Policy.pdf

20. Amendments. Amendments to this DMDA must be made in writing and signed by authorized representatives of all parties.

21. Termination. This DMDA shall terminate at the earliest of: the completion of the Research Project; five (5) years after the effective date of this DMDA; abandonment of the Research Project; or violation by Recipient of any provisions of this DMDA not remedied within 30 days after the date of written notice by NHLBI or Boston University of such violation.

Upon termination of this DMDA:

(a) If Data provided to Recipient include Center for Medicare and Medicaid Services (CMS) data, Recipient agrees to destroy all copies of all Data received from the RURAL Cohort Study and consult with the Boston University and the NHLBI regarding the disposition of all remaining Materials. Recipient will verify that the RURAL Cohort Study data have been destroyed in a written or electronic communication to the RURAL Cohort Study contact representative (named below).

(b) If Data provided to Recipient do not include Center for Medicare and Medicaid Services (CMS) data, Recipient agrees to consult with Boston University and the NHLBI regarding the disposition of all remaining Data and/or Materials.

22. Disqualification, Enforcement. Failure to comply with any of the terms of this DMDA may result in the disqualification of Recipient from receiving additional Data and/or Materials. The United States

Government and/or Boston University may have the right to institute and prosecute appropriate proceedings at law or in equity against the Recipient for violating or threatening to violate the confidentiality requirements of this DMDA, the limitations on the use of the Data or Materials provided, or both. Proceedings may be initiated against the violating party, or legal representatives, and assigns, for a restraining injunction, compensatory and punitive damages, mandamus, and/or any other proceeding at law or in equity, including obtaining the proceeds from any intellectual property or other rights that are derived in whole or in part from the breach of the confidentiality requirements or use limitations of this agreement. In addition, Recipient and Recipient's PI acknowledges that a breach or threatened breach of the confidentiality requirements or use limitations of this DMDA may subject Recipient and Recipient's PI to legal action on the part of RURAL Cohort Study participants, their families, or both.

23. Representations. Recipient and Recipient's PI expressly certify that the contents of any statements made or reflected in this document are truthful and accurate.

24. Prior Distribution Agreements. By execution of this DMDA, Recipient certifies its good faith belief that it is in compliance with the terms and conditions of all its existing DMDAs with Boston University and/or the NHLBI.

25. RURAL Cohort Study Coordinating Center Contact Representative:

Jason Miller
Administrative Director
Telephone: 617-358-1315
Email: jasonjmi@bu.edu

AUTHORIZED SIGNATURES

Required signatures begin on the next page.

RECIPIENT'S PRINCIPAL INVESTIGATOR AND RECIPIENT'S AUTHORIZED REPRESENTATIVE:

_____

Name and Title of Recipient's Principal Investigator

_____

Surface Mail Address of Recipient's Principal Investigator

_____

Email Address of Recipient's Principal Investigator

_____

Telephone and Fax Number of Recipient's Principal Investigator

_____

Signature of Recipient's Principal Investigator and Date

_____ *(a [non-profit ☐] OR [for-profit ☐] corporation/institution)*

Name of Recipient (Corporation/Institution)

organized under the laws of (State/Country): _____

with a principal address at: _____

_____

and Title of Recipient's Authorized Representative

_____

Signature and Date of Recipient's Authorized Representative

COORDINATING CENTER FOR THE RISK UNDERLYING RURAL AREAS LONGITUDINAL (RURAL) COHORT STUDY

_____

Name and Title of RURAL Coordinating Center Authorized Representative

_____

Signature and Date of RURAL Coordinating Center Authorized Representative

NHLBI (for Materials only):

_____

Name and Title of NHLBI's Authorized Representative

_____

Signature and Date of NHLBI Authorized Representative

This Distribution Agreement is entered into as of:_____(effective date)(DD/MM/YYYY)