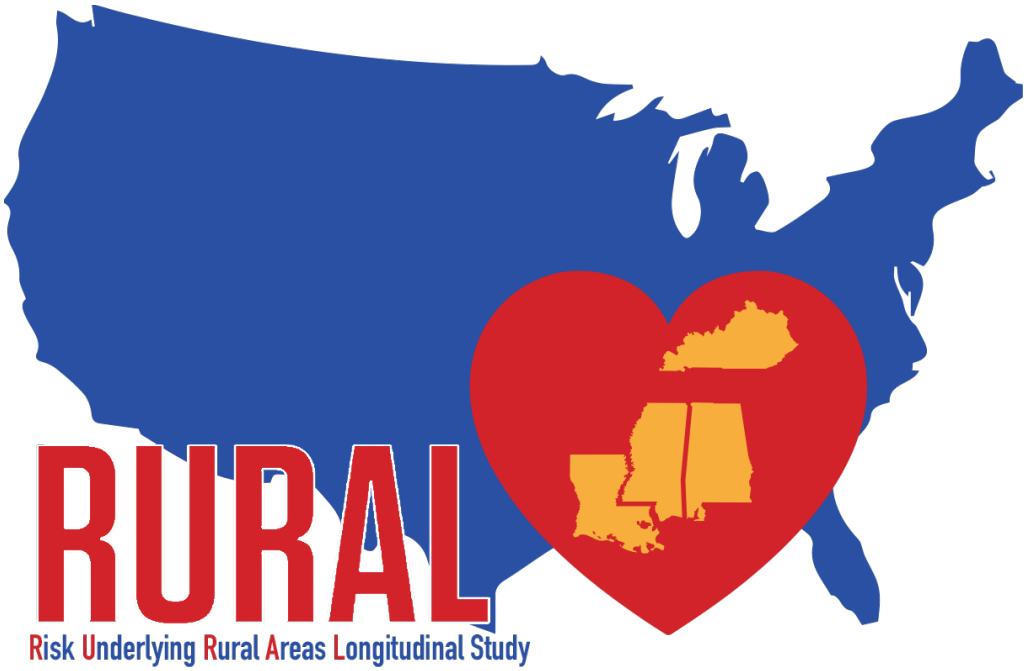

Ancillary Studies Policy

Version 22: April 2nd 2020

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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 is a national team of scientific experts that discusses and helps RURAL cores think through Ethical, Legal and Social Implications of RURAL, 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 RURAL. All AS must be reviewed and approved by RURAL's Ancillary Studies Subcommittee and Steering Committee. AS requiring the use of a third-party data and/or materials transfer agreement require approval from NHLBI. AS are not funded by the current RURAL 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 Study Ethics Advisory Board and ELSI panel may contribute additional perspectives. Prior to submission for funding, the AS must also be approved by the RURAL Study OSMB.

1.2 Types of Ancillary Studies

There are multiple forms of AS that may be performed in conjunction with the RURAL 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 Study website) in the initial funded RURAL 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 Study participants
- Proposed AS that require additional mHealth measures and equipment
- Proposed AS that perform secondary analyses of the RURAL Study data, whose research questions are not a part of the main/central RURAL Study aims and for which funding is sought (AS that perform secondary analyses but seek no funding are reviewed by the RURAL Study Publications and Presentations committee).

- Proposed AS that require the use of the RURAL Study data in pooling projects or consortia
- Proposed AS that involve relatives of the participants (assessed on an individual basis)

Statement on Clinical Trials is being developed

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

In general, proposed AS must be planned as a multi-state study, including participants from the RURAL 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 Study. Single state single county studies may be considered and approved on a case-by-case basis; feasibility and consistency with the RURAL 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 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 Study Principal Investigator (PI) or Co-Investigator may apply with the approval of their Institution's PI or Co-PI.
- RURAL 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 Study affiliated investigator's institution be a participating member in a RURAL Study Core.
- AS should include a PI or Co-PI of the RURAL Study, but RURAL Study PIs or Co-PIs do not need to be the PI of the AS. Ancillary Studies that do not include a RURAL Study PI or Co-PI will be examined on a case-by-case basis.

1.5 Non-RURAL Investigators

Applications from non-RURAL Study investigators will be considered by the Ancillary Studies Subcommittee, and Steering Committee. All non-RURAL Study investigator applications must involve sponsorship of a RURAL Study investigator to ensure compliance with RURAL Study policies and procedures. Non-RURAL Investigators have access to RURAL data either through NIH repositories or through collaboration with a RURAL sponsor. All AS will have the same review process regardless of status of affiliation to the RURAL 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 integration of AS data with the core RURAL 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 Study cores as determined necessary by the Ancillary Studies Subcommittee and Steering Committee. Associated costs with AS involvement with study cores will be submitted to and reviewed by the Ancillary Studies Subcommittee and Steering Committee. We will be developing a common framework of approximate costs to standardize the process and maintain efficiency.

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

- Study Coordinating Center (SCC)
    - Administrative tasks (MEU coordination, Mobile App integration, recruitment/enrollment summaries, etc.)
    - Integration with core RURAL Study protocols, including incorporation in annual reports and OSMB review documents
- RURAL State Core Costs (e.g., Alabama, Kentucky, Louisiana, Mississippi)
    - Contacting and recruiting participants
    - Obtaining IRB and other approvals
    - Participant incentives, transportation, meals
    - Coordination of data collection, transfer, archiving, distributing
- Biorepository and Assay Core
    - Biospecimen aliquoting and shipment costs
- Recruitment and Retention Core
    - Contacting and recruiting participants
    - Obtaining IRB and other approvals
- Returning incidental findings and clinically actionable results back to participants
- Statistical Data Coordinating Core
    - Assistance with developing a statistical plan, if sought
    - Data management, including return of data to the core RURAL Study
    - Biospecimen selection, if applicable
    - Preparation of datasets from the initial funded RURAL Study
- All Cores
    - Mailing, photocopies, fax, telephone
    - Other unforeseen costs that may arise
- If grant is $500k or higher in direct costs, 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 Ancillary Studies Subcommittee will review AS proposals to assess participant burden and burden to the main RURAL study. The Study Coordinating Center will facilitate and streamline the process for including the work and effort of any related RURAL cores. .

1.7 Application Process

Applicants who propose an AS should refer to the RURAL Ancillary Study Process and Procedures Document and Flowchart for detailed instructions of submitting a Concept Proposals and Full Proposal.

Priority is given to AS Concept Proposals based on:

- The initial needs and support of the RURAL Study baseline exam
- The potential to contribute to the health of RURAL Study communities.

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

1.8 Ancillary Study Proposal Components

If the 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 or proposed research
- Funding and third-party involvement
- Participant burden
- RURAL 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 Ancillary Studies 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 Ancillary Studies Investigator would like to appeal their review decision they should contact the RURAL Study Coordinating Center.

1.10 Contacting and Obtaining Consent from the RURAL Study Participants

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

1.11 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.

1.12 Ancillary Study Requesting Biospecimens and/or DNA

The RURAL Study aims to provide adequate biospecimens, including DNA, for ancillary investigators to test their hypotheses, while also considering the importance of preserving the RURAL 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 Study of excess material. Sample volume requests should include necessary 'dead volume' for processing. All applications for biospecimens must be supported by assay performance metrics from the performance laboratory.

The 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	
Hair (head)	
Urine	
Stool	
Tap Water	
Nails	
Blood Spots	

After an AS is approved and funded, the RURAL Study Statistical Data Coordinating Core will generate a list of sample IDs. The RURAL Study Biorepository and Assay Laboratory at The University of Vermont will retrieve the approved specimen aliquots based on the list of IDs prepared by the RURAL Study Statistical Data Coordinating Core. AS investigators are responsible for associated costs. Costs will be posted on the RURAL Study website.

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 Study Project Officer at NHLBI with a copy to the RURAL Study Coordinating Center. When signing the DMDA, AS investigators are agreeing to the requirements to send the AS data to the Study Coordinating Center to eventually be incorporated into the RURAL Study database and NHLBI-designated public repositories consistent with NIH data sharing policies.

The AS investigators have exclusive rights to use the nongenetic 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 Study data only after the AS data has been sent to the Study Coordinating Center and the Statistical and Data Coordinating Core.

The AS 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 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 Study Coordinating Center to include AS data in the RURAL 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 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 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 Study Coordinating Center and Statistical and Data Coordinating Core. The Study Coordinating Center and Data Coordinating Core would will report back to the AS and develop and automated system for tracking. There are standardized deadlines across all AS for progress and quality control reports. If the study starts 30 days before 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 Study Steering Committee semi-annual reports to the NHLBI and the annual report to the NHLBI and the RURAL Study OSMB.

1.15 Data to be Obtained from the RURAL Study

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

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

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

1.16 Notification of Clinically Significant Findings to RURAL Study Participants

The RURAL 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 Recruitment and Retention Core and the RURAL Study Coordinating Center of these actionable findings. The AS should notify the RURAL 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 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 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 Study Publications and Presentations Subcommittee for review and approval. AS investigators must provide the RURAL 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 Study investigators to serve in writing groups and to provide expertise and knowledge of the RURAL Study and its data. Appropriate representation of the RURAL Study investigators will be reviewed by the Publications and Presentations Subcommittee in consultation with ICJME guidelines for authorship.

1.18 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

1.19 Timeline

Investigators who submit AS proposals should allow for the following timeline:

- 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.

Proposals involving biospecimen collections may require a longer time period for completion of the review process, as a review by the Laboratory/ DNA Review Subcommittees is required. The 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 Ancillary Study Subcommittee will be aligned with NIH grant submission deadlines to allow for proper review of proposals for grant submission. Graphic will show standard NIH review dates and align AS review with NIH submission dates. **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.

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

1.20 Appendices

1.20.1 Ancillary Study Initial Concept Form

1.20.2 Ancillary Study Full Proposal Form

1.20.3 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 4,000 rural residents to study their heart, lung and overall health. The Study will have a mobile examination vehicle that will be staffed with trained technicians and will travel to the target counties to perform the Study. The 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 of the NIH (NHLBI). As part of the 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 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 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 provide 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 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 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 Department of Health and Human Services 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 Boston University Medical Campus IRB(s). 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 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 acknowledge 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 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)

1.20.4 Ancillary Study Process and Procedures Document

1.20.5 Ancillary Study Process Flowchart