The Mediators of Atherosclerosis in South Asians Living in America (MASALA)
Ancillary Studies Policies and Procedures

MASALA Ancillary Study Policy

Definition of an ancillary study: A MASALA ancillary study is one that uses MASALA resources and derives funding from other than MASALA contract funds. Examples include studies funded by investigator-initiated NIH research awards (R01s), grants from academic institutions, private sources (e.g., drug companies), or those performed at no cost (generally because of the special interest of a researcher). A study that involves the collection of new data, either directly from participants or from previously collected samples, images, or other sources (e.g., medical records), is an ancillary study, regardless of the method of funding. A study that provides external funding for the Coordinating Center, one or more Clinic Centers, or a Reading Center, is an ancillary study. Each ancillary study must include a MASALA Principal Investigator or Co-investigator on the proposal.

When an ancillary study proposal is not needed: If an investigator is seeking funding to support analysis of existing MASALA data, and the project does not involve new data collection, new readings of imaging data, new lab/genotyping assays, or the preparation of a complex data set by the Coordinating Center, then an Ancillary Study application is not needed, but one or more Manuscript Proposals must be submitted and approved before grant submission. The investigator may submit the Manuscript Proposal approval to the funding agency as evidence of MASALA study approval.

Philosophy: MASALA investigators are encouraged to consider ancillary studies and to involve other investigators, within and outside of MASALA, in this process.

Necessary approvals: The MASALA Steering Committee must approve ancillary study proposals prior to submission for funding and prior to implementation at the MASALA sites to ensure that the proposed ancillary study does not impose an unacceptable burden on MASALA staff or participants, interfere with successful recruitment or follow-up, or conflict with the aims of MASALA.

Members of the MASALA Steering Committee will review proposals for scientific merit, feasibility, and impact on the main MASALA protocol. Ancillary studies will also be prioritized to maximize use of limited participant and staff time and biological specimens. To maximize efficiency, the Steering Committee may recommend that several similar and potentially competing proposals be combined.

Review criteria: At each level of review, highest priority will be given to studies that:

1. Do not interfere with the main MASALA objectives
2. Have the highest scientific merit
3. Produce the smallest burden on MASALA participants and the least demand on MASALA resources, such as blood samples
4. Require the unique characteristics of the MASALA cohort

In addition, priority for studies requesting biological samples will be highest if they:

1. Do not make use of samples from those participants with the fewest samples;
2. Use thawed samples whenever possible;

3. Involve assays that may be done on more than one sample type to allow selection of the most abundant type available (e.g. serum or EDTA plasma);
4. Use the smallest sample volume possible;
5. Can be integrated with other studies to conserve sample or limit freeze-thaw cycles.

Responsibilities of Ancillary Study Investigators

1. Costs. The investigator applying for an ancillary study must supply all additional funds required to conduct the study. The Steering Committee will be concerned with both the obvious and the hidden costs to MASALA entailed by an ancillary study (such as costs to the Coordinating Center for coordinating the additional data collection, costs to Clinic Centers for notification of alert values, costs to laboratory for retrieving samples, etc).

   It is important to note that the MASALA Coordinating Center (CC) at the University of California, San Francisco nearly always incurs expenses on behalf of ancillary studies by providing support in data collection, data management, quality control, data analysis, study coordination and communications, events ascertainment, and other functions. These services can be of critical value to an ancillary study. PIs who plan to propose an ancillary study with the intention of seeking grant funding should first consult with the MASALA CC Principal Investigator to determine what level of involvement will be required of the CC and the associated costs. In general, this will result in a subcontract proposal from the CC to be included in the PI's grant application.

2. Confidentiality and identification of MASALA participants. Confidentiality of individually identifiable data about MASALA participants must be assured. As a general rule, no personal identification of participants will be provided to ancillary studies staff. There are no assurances that participants will be able to be identified and contacted in the future for the purposes of an ancillary study, particularly after MASALA ends.

3. Clinical implications of findings. The proposing investigator must clearly delineate any findings of clinical significance that may result from the study, including genetic findings, and propose how these will be handled, including reporting to participants and their physicians and providing recommendations for follow up. This includes incidental findings, such as pathology identified from an imaging study that is not the focus of the study.

4. Genetic studies. Genetics studies may include only participants who provided appropriate informed consent. Investigators should consult the Coordinating Center to determine the number of participant samples eligible for analysis based on responses from the appropriate informed consent. Medical and other (ethical, legal and social) implications of the findings and reporting of results must be addressed in the proposal.

5. Inclusion of Sponsoring MASALA investigator(s). A MASALA-affiliated investigator must be included as a co-investigator on an ancillary study. This individual is responsible for presenting the study to the Steering Committee, monitoring the study to assure continuing compatibility with MASALA and serving as a liaison to the MASALA Steering Committee. In addition, each manuscript and abstract is generally expected to include a MASALA investigator.

6. Early communication with MASALA Centers. The proposing investigator and/or his/her

liaison should consult with PIs of pertinent Clinic Centers, Reading Centers, and/or the Coordinating Center, depending on the anticipated involvement of Clinic Center staff and oversight, blood or urine analysis, and data management and analysis. Such discussions should focus on feasibility and provision of necessary resources and do not constitute formal approval of the study.

7. Timeline. All proposed ancillary studies must be submitted to the MASALA Coordinating Center for subsequent circulation and review. Studies must be submitted **8 weeks** prior to a funding application. Studies submitted after these deadlines may not receive timely approval. In addition, studies that involve a subcontract to the Coordinating Center must have their final budget negotiated and approved for internal University of California, San Francisco review no later than **5 weeks** prior to a funding application.

8. Final application or proposal. A copy of the final proposal as submitted for funding should be submitted to the Coordinating Center.

9. Industry participation. Proposals for industry sponsorship or collaboration will be evaluated in accordance with the procedures described above. In addition, it will be the responsibility of the PI to obtain agreement through an appropriate contractual mechanism that all data relevant to the MASALA ancillary study will be shared with the Coordinating Center. As an initial step in study planning, the PI should contact the MASALA Project Officer to determine if an agreement between NHLBI and industry should be developed and implemented or to approve the agreement between industry and the investigator's institution. Industry-sponsored ancillary studies shall include only participants who provided appropriate informed consent and must comply with current NHLBI guidelines, which are available from the Coordinating Center or Project Office upon request.

10. Status reports. The ancillary study PI should keep the MASALA Coordinating Center apprised of major developments in the life of the application or proposal, including success of funding, start date, changes in protocol, and any resulting publications or presentations. The MASALA Coordinating Center will query PIs twice per year, or as needed, for a status update of their ancillary studies, the results of which will be included in the Steering Committee report.

11. Revising and resubmitting proposals. Ancillary Studies that are not approved or not funded become inactive. If the PI wishes to resubmit the proposal for funding, s/he must communicate this to the Coordinating Center. A summary of the main points of the critique, plus a summary of the PI's response to the critique should be provided. A statement about changes to participant burden must be included. If either the science, scope, or burden has changed, the revised proposal must be approved by the Steering Committees.

12. Review of publications and presentations. Manuscript proposals based on ancillary study data require approval of the MASALA Steering Committee. All the publications, presentations and abstracts from an ancillary study must be reviewed and approved by the MASALA the Steering Committee prior to submission or presentation, in accordance with the general rules for publications and presentations.

Incorporation of ancillary study data into MASALA database

The data collected by the ancillary study are first to be provided to the MASALA Coordinating Center for integration into the main database, after which the ancillary investigators will receive the integrated file containing necessary data from the main study. The ancillary study PI will be given the exclusive opportunity to analyze, present and publish data collected under the auspices of the ancillary study. After a reasonable time (in general, 12 months after data collection and cleaning are complete) the ancillary study data will be made available for additional uses by other MASALA investigators in collaboration with the ancillary investigators. It is the responsibility of the ancillary study PI to state in writing to the Steering Committee any special circumstances that would militate against these guidelines for data sharing.

MASALA Ancillary Study Review Procedures

1. Investigators wishing to propose studies that pose participant, clinic, or Blood Lab burden are encouraged to discuss their studies with the MASALA coordinating center Project Assistant before submitting a proposal to the Steering Committee.

2. Principal Investigator submits ancillary study proposal using the template provided on the MASALA website via an email to the MASALA Coordinating Center (CC) Project Assistant (see Appendix 1).

3. MASALA CC Project Assistant reviews proposal for administrative compliance (assures that all questions have been answered) and to determine involvement of other MASALA labs and/or reading centers. If the proposal is not complete, it will be returned by email to the investigator for revision and resubmission.

4. MASALA CC Project Assistant forwards the proposal by email to the MASALA Coordinating Center PI for review. The CC PI will decide whether to convene a Steering Committee conference call or handle the review by email. Each SC member's review and recommendation for approval are communicated to all SC members.

5. For a proposal that poses burden, after it is reviewed and approved by Steering Committee, the Project Office will weigh the participant/clinic burden against the scientific enthusiasm and participant appeal. Studies without a favorable balance will not be approved.

6. Proposals will be discussed by the SC, generally during conference calls. In some cases, as determined by the chair of the SC, email reviews will be conducted. The SC may also invite the PI to present the proposal and answer questions and absent him/herself during discussion and voting.

7. If the proposal requires revisions, the comments of the SC are sent to the PI by the CC Project Assistant (with cc to SC chair). The PI must address these comments in a separate letter that accompanies the revised proposal and send these to the CC Project Assistant who forwards them to the Steering Committee.

8. Proposals that are approved by the SC but involve no participant burden (though they may use scans or repository samples), and minimal clinical implications are sent by the CC PI who sends the formal letter of approval to the PI.

Appendix 1 **Committee Members Lists and Relevant Staff**

MASALA Steering Committee
Alka M. Kanaya, MD, Coordinating Center and Clinical Site Principal Investigator
University of California, San Francisco
Steering Committee Chair

Namratha Kandula, MD, Clinical Site Principal Investigator
Northwestern University

Kiang Liu, MD, Clinical Site Co-Investigator
Northwestern University

David Herrington, MD, MHS, Ultrasound Reading Center Principal Investigator
Wake Forest University Medical Center

Nadia Islam, PhD
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Adapted From: The Multi-Ethnic Study of Atherosclerosis (MESA) Study