The Sister Study Data Sharing Policy

General Policy

To promote research on breast cancer and other women's health topics, the Sister Study welcomes proposals for collaborative studies from within NIEHS and the wider scientific community. All proposals will be reviewed by the Sister Study to ensure scientific merit and to protect the integrity of the study and the confidentiality of its participants. Acceptable study topics will take advantage of the unique characteristics of the Sister Study cohort, and must not have been previously planned or be under consideration by Sister Study investigators. Proposed studies may involve the analysis of routinely collected data or entail analysis of samples or new data collection from study participants. Proposals involving the use of limited biological or environmental samples or participant burden will require more extensive review. For proposals involving the use of biological or environmental samples, the threshold for approval will be proportional to the amount of sample requested and the availability of remaining samples. In general, study samples will not be shared for pilot studies and documentation of successful implementation of assays in the laboratories of proposed collaborators will be required before samples are shared. Projects require and will benefit from the active collaboration of a Sister Study investigator. Prior to submitting a full proposal, applicants must establish appropriate collaborations with at least one Sister Study investigator based on the proposed study topic and investigator interests.

Collaborative studies may require outside (non-Sister Study) funding, including reimbursement to the Sister Study or its contractors for tasks such as sample selection, preparation and documentation of analysis files, and laboratory costs incurred in handling and shipping samples. Sister Study approval must be obtained before grant applications are submitted to support collaborative studies using Sister Study data. Proposals involving biological or environmental samples or collection of new data may require additional scientific peer review (e.g., via review by an established NIH Study Section) or be subject to external review coordinated through the Sister Study.

At least one-third of the biological samples collected from Sister Study participants are reserved for breast cancer research. Requests for the use of final remaining aliquots of any sample will be subject to additional levels of review by the Sister Study Steering Committee and/or Scientific Advisory Board. Policies related to sample use, storage, and analysis will be revisited in consultation with the Sister Study Scientific Advisory Board as the study progresses to accommodate anticipated advances in sample storage and testing technologies. The Sister Study's compact with study participants precludes the use of Sister Study data or biological samples for the development of commercial products.

Requirements for Approval

Key criteria for approval of collaborative studies are scientific merit and the potential impact on the main study. Preference will be given to proposals that address questions the Sister Study is uniquely positioned to address. In addition, the collaborative study should

not interfere with the main objectives of the Sister Study, hamper continued participation in the study, place inappropriate demands on study resources (personnel, equipment or study samples), use Sister Study contract resources without reimbursement, or jeopardize the public image of the Sister Study.

If contact of participants is planned, it should take place during regularly scheduled cohort follow-ups when possible, and should place minimal burden on participants and be acceptable to them in terms of their time, comfort and privacy.

Application Procedure

The application procedure is a two-part process that can be completed using Sister Study Tracking and Review System (STaRs; www.sisterstudystars.org). For initial inquiries, applicants should submit a study concept to determine if the proposed study is suitable for full application. Applicants may contact the Sister Study Principal Investigator or Lead Investigator to discuss the feasibility of the project before submitting the study concept. If the study has scientific merit, is appropriate for the unique characteristics of the Sister Study cohort, is feasible given Sister Study resources (outcomes, approximate numbers of subjects, and available study samples), and is not currently under consideration by another investigator, the applicant will be invited to submit a full proposal for further consideration. It is recommended that applicants work with a Sister Study collaborator to vet the full proposal prior to submission.

Review Process

Study proposals will be distributed to at least two members of the Sister Study Steering Committee for review. All projects involving the use of biological or environmental specimens or new data collection will undergo additional scientific review by independent experts. Such review will focus on scientific merit, feasibility, and suitability for the Sister Study cohort. Independent reviewers may include members of the Sister Study Scientific Advisory Board or *ad hoc* reviewers as needed, depending on the study topic, and will be selected in consultation with the Chair of the Scientific Advisory Board. For proposals funded through an extramural grant, scientific review by an established or *ad hoc* study section or review panel may take the place of NIEHS coordinated external review, although in some instances, additional review may be requested. Proposals will be "accepted," "accepted pending revisions," or "rejected" based on the advice of the reviewers. An "accept pending revisions" decision will be given if the proposal has scientific merit, but one or more issues need to be addressed before the project can be approved. An expedited review will then be accommodated for revised proposals that have addressed reviewers' concerns. The final decision to accept or reject a proposal will rest with Dr. Dale Sandler, Sister Study Principal Investigator.

Conducting Studies Using Sister Study Data

Each data user must agree to accept and abide by the policies established by the Sister Study Steering Committee and the NIEHS for access to and use of Sister Study data

and/or samples. Collaborators will be asked to sign a confidentiality agreement that is available through STaRS. In signing the agreement, collaborators will be confirming that they have read the guidelines and both understand and agree to comply with them. Use of Sister Study data will be limited to the nature and scope of the collaborative study as outlined in the full proposal application. Any changes to the nature or scope of the project will require additional review and approval.

Prior to the release of data or samples, investigators must demonstrate approval from their institute's IRB, or the NIEHS IRB, or both, depending on the nature of the study and institutional requirements. For proposals involving only de-identified data, documentation that the work has been deemed not to be Human Subjects Research may suffice. A formal NIH Material or Data Transfer Agreement (or similar, as required by a collaborating institution) must be completed before data or samples are transferred. Data will be released as time-limited, restricted-use datasets with no identifying information. Use of data or samples from the Sister Study cohort is limited to the specific project for which approval was obtained. If further research or analysis becomes relevant, the applicant must obtain additional approval for such activities by submitting an addendum application to an existing project. In some cases, requests for the conduct of additional data or laboratory analyses may require the submission of a new project application. Data and samples may not be transferred to other parties unless prior authorization by the Sister Study Steering Committee has been granted.

Special considerations for requests involving biological or environmental samples, identifiable data, or cohort contact

The Sister Study will release the minimum amount of sample required to complete assays. Depending on the amount of sample needed, the Sister Study and its contractors may do the aliquoting, batching, and inserting of quality control samples prior to sending the samples to the testing laboratories or may require the requester to complete these tasks. The release of samples will be contingent upon the requester's demonstration that the proposed assay is feasible. Samples for specific subgroups may be withheld if there is not adequate statistical power for subgroup analysis (and where combined analysis would not be publishable – e.g., for racial subgroups in GWAS analysis).

The Sister Study will allow tumor blocks to be used only in rare circumstances and then will make arrangements for slices/slides to be made at cost to collaborators, as appropriate. As there is sample waste each time a block is cut, the approval threshold will be high, and investigators will be encouraged to focus on subgroups of participants, including those with larger tumors or for whom more than one block was sent. Investigators should consult with the Sister Study early in the application process to determine the feasibility and costs of using tumor blocks.

Unless otherwise negotiated beforehand, the Sister Study will be the owner of data resulting from laboratory assays of biological or environmental samples to facilitate other research and avoid reusing samples to generate data already available from other projects. To ensure the return of laboratory data to the Sister Study, samples will be shared with

only minimal individual data. After laboratory analysis, all results and any remaining sample must be returned to the Sister Study to be linked with the corresponding individual data before the release of the analysis file to collaborative researchers. For collaborative studies involving contact with participants, the Sister Study will initiate contact with potential participants to obtain active or passive consent, as appropriate, prior to the release of any identifying information to the collaborating researcher.

Due to privacy concerns, restrictions may be placed on the number and/or types of variables released to collaborators. Release of potentially identifiable data will require special justification and safety precautions. Data will be released to collaborators using pseudo IDs, with links retained only by the Sister Study contractor. Information such as addresses or geocodes or other data required for linkage with external databases may be shared with qualified collaborators. Such data will be shared initially without accompanying individual data. De-identified analytic datasets will be created by the Sister Study once the linked exposure and/or outcome data are returned to the Sister Study.

Data/specimen users are required to release all laboratory data and/or data analysis results generated by the collaborative study, along with corresponding documentation, to the Sister Study for potential use in other studies, unless otherwise negotiated during the review and approval process.

Tracking the progress of collaborative studies

The Sister Study Steering Committee will monitor the development of collaborative studies, receipt of funding, initiation dates, and progress. A written progress report summarizing on-going work on data analyses, analytes measured, and/or data collected is to be submitted annually to the Steering Committee. Before publication or presentation, manuscripts and abstracts resulting from Sister Study collaborative studies must be reviewed by one or more members of the Sister Study Steering Committee. The Sister Study may check statistical analyses for accuracy before the publication of findings.