Data and Biospecimen Use and Publications Committee

GUIDELINES GOVERNING THE USE AND PUBLICATION OF SCCS DATA

Updated May 26, 2005

Table of Contents

Summary

The SCCS is a landmark study of racial disparities in cancer incidence and mortality, as well as of disparities in the occurrence of other chronic diseases such as diabetes, hypertension and heart disease. The data collected in this study are available for use to both SCCS investigators and their non-SCCS investigator collaborators. As with all carefully conducted studies, quality control measures applied to the raw data, to the analytic procedures performed on the data, to the use of stored biosamples, and to the resulting scientific manuscripts are essential in order to maintain the integrity of the study. In addition, the collection of ancillary data using study participants is an activity that is encouraged, but must be done in close coordination with SCCS investigators to ensure the validity and success of such an ancillary study, and to minimize the burden on these participants.

The Data and Biospecimen Use and Publications Committee was thus assembled as the body to have primary responsibility for these quality control issues. The main objectives of the Committee are to assure the protection of SCCS research subjects, to assure the integrity of the main goals of the SCCS, and to assure the scientific validity of all reports and results generated from SCCS data and biospecimens. The Committee will carry out these responsibilities, and respond to requests regarding data and biospecimen use and publications, as detailed on the following pages.

Data and Biospecimen Use and Publications Committee members

Co-Chairs of the Committee

William J. Blot, Ph.D.
Address: International Epidemiology Institute
1455 Research Blvd., Suite 550
Rockville, MD 20850
Telephone: (301)517-4062
Fax: (301)517-4063
Email: BlotW@cs.com

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1005 D.B. Todd Blvd., PO Box A120
Nashville, TN 37208
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Committee Members

The Committee co-chairs will establish sub-committees for the review of specific applications from among the following members:

Ray DuBois, M.D.
Vanderbilt University

Richard Hayes, Ph.D.
National Institutes of Health / National Cancer Institute

Clark Heath, M.D.

Brian Henderson, M.D.
University of Southern California

Joseph McLaughlin, Ph.D.
Vanderbilt University
International Epidemiology Institute

Rubens Pamies, M.D.
Meharry Medical College

Lisa Signorello, Sc.D.
Vanderbilt University
International Epidemiology Institute

David Williams, M.D.
Southside Medical Center

Wei Zheng, Ph.D.
Vanderbilt University

1.00 General guidelines for submitting an Application for Data and Biospecimen Use (ADBU).

Anyone requesting access to existing SCCS data or biospecimens, or access to the SCCS study population for the proposed collection of new data or biospecimens must submit an Application for Data and Biospecimen Use (ADBU). This includes:

- Investigators who would like to submit a grant proposal to a funding agency, and the proposed study requires either the use of existing SCCS data/biospecimens or access to the SCCS population for the collection of new data/biospecimens (an *ancillary study*).

- Investigators who would like to use existing SCCS data/biospecimens to perform analyses leading to a scientific manuscript.

- Investigators who would like to have basic data analyses performed for them, which they will use, for example, to support a grant application or a presentation.

In certain respects, the guidelines for submitting an ADBU are different for individuals who are SCCS Investigators and those who are not. Where there are such differences, they are noted.

All ADBUs should be mailed or emailed to:
SCCS Data Use and Publications Committee
c/o International Epidemiology Institute
1455 Research Blvd., Suite 550
Rockville, MD 20850
datause@southerncommunitystudy.org

For SCCS Investigator Applicants, the ADBU may be submitted at any time. For Non-SCCS Investigator Applicants, the ADBU may be submitted on January 1st, April 1st, July 1st, and October 1st of each year. Non-SCCS Investigator Applicants must have an SCCS Investigator listed on their ADBU as a co-applicant.

All Applicants must provide an email address, and receipt of the ADBU will be acknowledged via email. ADBUs will be circulated to the members of the Data and Biospecimen Use and Publications Committee (the "Committee"), and potentially to outside scientific consultants as deemed necessary by the Co-Chairs of the Committee. The Applicant may not suggest consultants to participate in the review process. The Committee will judge whether the research duplicates existing SCCS research, whether it is feasible, whether the impact of the proposed research on SCCS operations and resources is justified by its scientific merit, and whether it is in line with the main goals of the SCCS. As a general rule, ADBUs that are focused on one hypothesis will have a greater chance of being accepted than ADBUs which have broader objectives and/or seek to utilize large portions of the SCCS dataset, biospecimens or population. The Applicant will typically receive notification of the Committee's decision within eight weeks after the Committee's receipt of the ADBU.

Incomplete or incorrectly completed ADBUs will be returned to the Applicant, and not reviewed.

If an Applicant's ADBU is denied, the Applicant may submit a revised ADBU. For this resubmission, the entire application needs to be submitted, with all changes highlighted in the text, accompanied by one sheet describing and justifying the changes. If, in the Chair's opinion, the re-submitted ADBU has not been revised to such an extent that it might affect a change in the Committee's decision, the Chair has the authority to deny the re-submitted ADBU without a Committee review. If, in the Chair's opinion, the re-submitted ADBU does merit a new review, it will be distributed to the same Committee members who reviewed the original ADBU. An ADBU may only be submitted twice (an original submission and one re-submission).

2.00 Requesting use of SCCS data for analyses leading to the preparation of scientific manuscript(s).

As noted on the ADBU, Applicants who request to use existing SCCS data must submit both a Data Analysis Proposal and a Data Request Form along with the ADBU.

If an Applicant's request for data use is approved, the Data Request Form will automatically be forwarded to an SCCS data manager, who will prepare the appropriate analytic dataset. The native format for SCCS datasets will be SAS version 8 (PC format). Other dataset formats can be provided (e.g., STATA, Access, Delimited ASCII, etc.), however, additional time may be required to prepare these types of files. Analytic datasets will be de-identified for the purposes of confidentiality. Prior to receiving SCCS data, the Applicant and all co-applicants must agree in writing not to share the data with individuals other than those listed on the approved application.

If the Applicant does not submit a Manuscript Proposal (see section 7.00) for the Committee's review within six months after receipt of the analytic dataset, the Committee has the right to revoke the Applicant's ADBU and make the data available for other Applicants to use for the same analyses.

The Applicant should have funds to cover SCCS personnel effort (and other costs) associated with preparing analytic datasets.

3.00 Requesting use of SCCS biospecimens for analyses leading to the preparation of scientific manuscript(s).

As noted on the ADBU, Applicants who request use of existing SCCS biospecimens (whether to perform the analyses themselves or to request biospecimen analyses be done for them) must submit a Biospecimen Request Form along with the ADBU. In most cases where an Applicant would request use of biosamples, the Applicant would likely be requesting use of some SCCS data as well. If the Applicant is requesting simultaneous use of existing SCCS data and biospecimens, the Applicant must also follow the guidelines listed in section 2.00.

If an Applicant's request for biospecimen use is approved, the Biospecimen Request Form will automatically be forwarded to an SCCS laboratory investigator, who will coordinate either the transfer of the necessary biospecimens or the conduct of the necessary biospecimen analyses on-site or at a collaborating laboratory. If biospecimens are transferred to the Applicant, they will be de-identified for the purposes of confidentiality. Prior to receiving SCCS biospecimens, the Applicant and all co-

applicants must agree in writing not to share the biospecimens with individuals other than those listed on the approved application.

The Applicant must submit a Manuscript Proposal (see section 7.00) for the Committee's review within six months after receipt of the biospecimens or assay results. The Applicant should have funds to cover SCCS personnel effort (and other costs) associated with preparing biospecimens and/or performing assays.

3.01 Types of biospecimens available (and collection details)

A 20ml venous blood sample (10ml drawn into a heparin vacutainer tube, and 10ml drawn into a serum vacutainer tube) was collected from a subset (approx. 50-60%) of SCCS participants. After collection, the blood samples were kept refrigerated, and then at the end of each day packed in a styrofoam box with ice packs and sent via Federal Express for next day early morning delivery to the Molecular Epidemiologic Laboratory at Vanderbilt-Ingram Cancer Center for processing. The blood samples were typically processed within 4 hours of arriving at the laboratory.

(Note: At the time of blood collection, SCCS participants were asked to report on specific factors that could affect laboratory analyses. For a complete listing of these variables, see the official SCCS codebook).

An exfoliated buccal cell sample was collected from a subset (approx. 30-40%) of SCCS participants. These cells were collected using the "swishing" method, where a participant swished about one ounce of Scope mouthwash in their mouth for 45 seconds and then spit the mouthwash into a sterilized collection cup. After collection, the buccal cell sample cups were kept refrigerated, and then at the end of each day packed in a styrofoam box with ice packs and sent via Federal Express for next day early morning delivery to the Molecular Epidemiologic Laboratory at Vanderbilt-Ingram Cancer Center for processing. At the laboratory, the buccal cell samples (in mouthwash) are typically processed on the same day of arrival.

3.02 Biospecimens – processing details

Blood samples were processed and aliquoted into cryovials for long-term storage. Blood samples were spun at 2,500g for 20 minutes, using a refrigerated centrifuge (at 4°C). The plasma was then removed and pipetted into four sterile 2ml cryovials. White blood cells were aliquoted into two 2ml vials and red blood cells into two 2ml vials. The serum tubes were spun in a similar manner. For each sample, serum was pipetted into six 2ml vials and blood clot into a 4ml vial.

The buccal cells were centrifuged and suspended using TE buffer, then aliquoted into a 2ml vial.

Genomic DNA will be extracted from white blood cells (buffy coat), blood clot, or buccal cells for future proposed studies.

3.03 Biospecimens – storage details

All samples are stored in appropriate freezer boxes and kept at -70°C.

3.04 Details of laboratory methods and selection of laboratories

The following issues should be addressed in the Biospecimen Request Form (part III of the synopsis).

Applicants should bear in mind that each SCCS participant has a finite amount of biospecimen stored for the study, thus they are encouraged to identify the laboratory method that uses the smallest amount of biospecimen for the biomarker under investigation. Applicants should provide information regarding the validity and reliability of the proposed assay and compare the pros and cons of alternative laboratory methods, if more than one laboratory method is available for the biomarker under investigation.

Typically, one study/analysis may not use up an entire tube of sample, and thawing and re-freezing samples could degrade some biomarkers. It would therefore be helpful for the Applicant to provide some data regarding the effect of thawing and re-freezing on the biomarker under investigation. In order to minimize the number of thawing/re-freezing cycles for SCCS biospecimens, the staff at the SCCS repository will coordinate the assays of several studies, and sometimes several assays will need to be conducted in the same laboratory at about the same time. Thus, the laboratory selected by the Applicant may not be the one where the assays will be eventually performed.

Only a very small amount of DNA is needed for each genotyping assay, and the aliquoting of a small amount of DNA into multiple tubes causes some attrition (and thus waste). Also, it is likely that DNA produced using the whole genome amplification method may be used in many future genotyping assays, so native DNA would be saved for other assays where native DNA is absolutely needed. Some quality control procedures will need to be implemented when amplified DNA samples are used in genotyping assays. Therefore, in general, DNA samples will not be shipped to the Applicant. However, the Applicant will need to describe the proposed genotyping method and the amount of DNA needed in their application. The Applicant could suggest a laboratory for their proposed genotyping assays. The staff at the SCCC biorepository will work with the Applicant to identify a suitable laboratory. In order to efficiently use DNA, some coordination may be required so that genotyping assays from several studies could be conducted at the same time in the same laboratory.

4.00 Requesting use of SCCS data and/or biospecimens for analyses leading to the preparation of a grant application.

Analyses intended to be included within the body of a grant application are typically simple tabulations or simple preliminary analyses. Unless the Applicant has a compelling reason to request the raw data (and gains permission from the Co-Chairs of the Committee), these types of analyses will be performed by an SCCS data manager, with the results supplied to the Applicant. The Applicant should follow the instructions shown in Section 6.00.

In general, existing SCCS biospecimens will not be used to generate preliminary data in support of a grant application.

5.00 Submitting a grant application for an ancillary study that proposes to use existing SCCS data/biospecimens and/or access the SCCS population.

Applicants must submit an ADBU, along with an Ancillary Study Proposal. The Applicant should be the Principal Investigator of the ancillary study.

The Applicant must also submit:

- an exact copy of the proposed data collection instrument (e.g., questionnaire, medical record abstraction form, etc.), if new data are being collected.
- a Data Request Form, so that it is clear what variables from the existing SCCS dataset are being sought for the ancillary study.
- a Biospecimen Request Form, so that it is clear what existing biospecimens are being sought for the ancillary study (if applicable)

If the ADBU is approved, the Applicant must also submit to the Committee for its files:

- a copy of the final grant proposal submitted to the funding agency. The final submitted grant proposal should match the original ADBU in its scope and content; if it does not, then an amendment to the ADBU must be submitted.
- the IRB application(s).
- the final IRB approval letter(s).
- the final IRB-approved consent forms.

Ancillary studies that involve the collection of new data or biospecimens from SCCS participants will need IRB review at both Vanderbilt University and Meharry Medical College (facilitated by SCCS Investigators), in addition to the IRB review at the institutions of the ancillary study investigators. Final approval from all relevant IRBs will be necessary before work begins on the ancillary study.

The grant application process can be lengthy, and there is no guarantee that the grant proposal will be funded. For non-SCCS Investigator Applicants, even if the ADBU is approved (i.e., the Committee has agreed that the applicant may use the SCCS data, biospecimens and/or population for the specified purpose), the data and biospecimens can not be reserved. Other Applicants may still apply to use to the same data or biospecimens for the same hypothesis. Thus, the data and biospecimens will ultimately be made available to the approved Applicant who receives funding first.

For SCCS Investigator Applicants, once the ADBU is approved, the data and biospecimens will be reserved until the time when either the grant is approved (and work on the ancillary study begins) or denied (and the ADBU becomes null).

Applicants should promptly update the Committee with the review results (e.g., merit score and percentile) of the submitted grant proposal and send to the committee a copy of the summary statement of grant review.

5.01 Inclusion of SCCS Investigators in ancillary studies

An SCCS Investigator must be included as a co-investigator (or Principal Investigator) in every ancillary study proposal. In addition, every ancillary study proposal must provide funds for SCCS data

managers, SCCS laboratory personnel and/or other relevant staff, whose time will be needed to coordinate between the main and ancillary study, prepare data or biospecimens, review and confirm final analyses, etc. The Applicant should coordinate closely with SCCS Investigators prior to submitting an ADBU, so that appropriate coverage of SCCS personnel effort (and other associated costs) is incorporated into the proposal.

5.02 Providing progress reports for ancillary studies

If an ancillary study grant proposal is awarded funding, the Principal Investigator of the ancillary study must notify the Co-Chairs of the Committee in writing, and the Committee will consider this ancillary study to be active.

For active ancillary studies, the Principal Investigator of the ancillary study must submit a one-page progress report to the Committee every six months. This report should include the status of study funding, any changes to the timeline, the general status of study work (i.e., the number of ancillary study participants enrolled and the progress of field work, data collection, etc.), and any unanticipated problems.

5.03 Consent forms used in ancillary studies

Consent forms used for ancillary studies should clearly identify the ancillary study as one being performed in addition to the main study, and inform subjects that their participation in the ancillary study is not necessary for them to continue in the SCCS. A copy of the consent form signed by every SCCS participant in the ancillary study must be given to the SCCS, for filing and storage.

5.04 Data collected from ancillary studies

If an ancillary study involves the collection of any new data from SCCS participants or the generating of new data from laboratory assays, these data must be shared with the SCCS data managers, in their entirety and in a format jointly agreed upon with the data managers. In addition to the raw data, the ancillary study investigators must provide the SCCS data managers with an appropriate codebook for the data. Also, while the ancillary study investigators will retain the newly collected analytic data for their analyses, they will delete (and confirm in writing that they have deleted) any identifying information used for the collection of these data (including but not limited to name, address, social security number) from all of their datasets and/or databases (including back-ups). They must retain, however, the study ID numbers (that are linked to SCCSID numbers) on their datasets, so that coordination with SCCS data managers is possible.

When the ancillary study analyses are completed, the data from the ancillary study (now attached to the SCCS database) will be made available for other Applicants to apply to use.

5.05 Biospecimens collected from ancillary studies

Often there is a finite amount of sample (e.g. tumor tissue) available from each ancillary study subject, and it may not be feasible to include the same subject in multiple ancillary studies for sample collection. Thus, the collection of certain biological samples in an ancillary study would prevent future

studies from collecting additional samples. For this reason, the Applicant must agree to share biospecimens collected from their ancillary study with the SCCS. It is recommended that approximately one third of the biospecimen amount collected in an ancillary study should be sent to the SCCS central biorepository for long-term storage for future studies. The investigators who collected the biospecimens would need to apply for the use of these biospecimens should they need additional material. Furthermore, one year after completing the ancillary study, the Applicant should submit to the committee a report listing the remaining amount of biospecimen in their possession and a plan to use these samples in the next two years. Any unused biospecimen that will not be used in the next two years should be sent to the SCCS central biorepository for long-term storage for future studies.

5.06 Criteria used to assess priority of ancillary studies

Highest priority will be given to studies which:

- do not interfere with or duplicate SCCS research objectives
- have the highest scientific merit
- produce the least burden on SCCS participants
- have objectives in accord with those of the SCCS
- require the unique characteristics of the SCCS cohort
- have minimal negative impact on future studies/analyses using the SCCS cohort

5.07 When to submit an application

Applications dealing with ancillary study grant proposals should be submitted well in advance of the deadline to submit the grant application. We suggest at least three months in advance. Applications submitted with less time are not guaranteed to be processed by the time of grant submission.

Applicants should not submit a proposal for research funding before they receive approval from the Committee regarding the use of SCCS resources.

6.00 Requesting analyses to be done and results supplied to support a grant application

In addition to the ADBU, the Applicant must submit an Analysis Request Form. If the grant application falls into the category of an ancillary study that proposes to use SCCS data, or gain access to SCCS study participants, applicants should also be following the guidelines in Sections 5.00-5.07.

Analyses should be requested well in advance of the deadline to submit the grant application. We suggest at least three months in advance. Requests submitted with less time are not guaranteed to be processed in time for grant submission.

In general, analyses of existing SCCS biospecimens will not be used to generate preliminary results in support of a grant application.

7.00 Gaining approval of manuscripts prior to submitting them to journals for publication

The development of potential manuscripts generated from any SCCS data (interview data and/or biospecimen data, including data collected in ancillary studies) must adhere to the following guidelines:

The lead author of the manuscript (the Applicant) will submit a Manuscript and Abstract Review Form (MARF) to:

William J. Blot, Ph.D., Co-Chair of Data Use and Publications Committee
International Epidemiology Institute
1455 Research Blvd., Suite 550
Rockville, MD 20850

This initial MARF must be accompanied by a Manuscript Proposal, which will include a tentative title for the manuscript, one or two sentences describing the objective(s) of the manuscript, a general outline of the analyses to be presented in the manuscript, the overall conclusions of the paper (if known), and a tentative list of authors. The lead author will agree to accept as additional co-authors SCCS Investigators who have expertise in the subject matter of the manuscript, have offered to participate in the writing and/or editing process, and whose participation is deemed to be merited by the Co-Chairs of the Committee.

If the Manuscript Proposal is approved, the manuscript can be started. When the manuscript has been finalized, is in ready-for-publication form, and has been approved by all co-authors, it should be submitted to the Committee (along with another MARF) for review. The cover letter accompanying the MARF should reference the MARF number assigned to the manuscript from the initial submission of the Manuscript Proposal.

The Committee will give written comments on the manuscript to the Applicant (lead author) within 4 weeks of receiving the manuscript. The Committee will indicate whether:

I. they have approved the manuscript as is.
II. they have approved the manuscript contingent upon certain minor revisions being made to the manuscript.
III. they do not approve the manuscript, and require a revision and re-submission

In the case of a contingent approval (scenario II), prior to submitting the manuscript to a journal, the Applicant must resubmit the final version of the manuscript, with the appropriate changes made, to the Committee for its files, but does not have to wait for a second response/review from the Committee.

In the case of a manuscript rejection (scenario III), the lead author must resubmit a new version to the Committee for another review. The authors may not submit a manuscript to a journal before they receive approval from the Committee. It may take several reviews before a manuscript is approved by the Committee.

In addition to the manuscript itself, the analyses that are presented in the manuscript must be verified prior to submission to a journal. For this reason, we request the programming code used to produce the

results. SCCS analytic staff will review the code. Their analytic review will be included with the overall review of the Committee, and could be the basis for rejection of the manuscript.

Once the manuscript is submitted for publication, the lead author is responsible for reporting to the Committee on the manuscript's progress. This includes notification when a manuscript receives final approval from a journal, is rejected from a journal, or when it has been sent to another journal. When the manuscript is published, the lead author must provide a reprint to the Committee.

8.00 Gaining approval of abstracts

Abstracts generated from any SCCS data (interview data and/or biospecimen data, including data collected in ancillary studies) must be submitted to the Committee for review, using the MARF.

If the abstract is reporting on the same data from a manuscript that has already been reviewed by the Committee, the abstract should be submitted to the Committee at least two weeks prior to the deadline for the abstract's submission. However, if the abstract is the first reporting of the data to the Committee, it must be submitted at least four weeks prior to the deadline for the abstract's submission. All authors on the abstract should have approved of the final version before it is submitted to the Committee.

9.00 Requesting amendments to a previously approved ADBU or MARF

Amendments to a previously approved ADBU or MARF can be submitted at any time. It is not necessary to resubmit the entire application (i.e., the ADBU/MARF along with all attached forms, proposals and other supporting documents). The original Applicant must submit a cover letter clearly describing the proposed amendment, and provide the relevant revised documents with all changes highlighted. For example, if there has been a change made only to the Data Analysis Proposal, it is only necessary to resubmit that document with changes highlighted, along with a cover letter (no revised ADBU required).

The changes proposed in the amendment may not be initiated until the Committee has approved them in writing.

10.00 Properly referencing your application when corresponding with the Committee

Each ADBU and MARF will be assigned a permanent reference number. When corresponding with the Committee for any reason (e.g., when submitting a revised manuscript, an amended ADBU, a progress report, etc., or for any type of general correspondence), please reference this number.