Subpopulations and Intermediate Outcome Measures in COPD Study

Data and Materials Distribution Agreement

The undersigned parties hereby enter into this Data and Materials Distribution Agreement (DMDA) as of _____ (Effective Date).

INTRODUCTION

The Subpopulations and Intermediate Outcome Measures in COPD Study (SPIROMICS) is a multi-center epidemiologic study supported by contracts with the National Heart, Lung, and Blood Institute (NHLBI) and the COPD Foundation. The study is designed to inform future development of therapies for COPD.

To protect the confidentiality and privacy of SPIROMICS participants and their families, investigators granted access to Data and Materials must adhere to the requirements of this DMDA. Failure to comply with this DMDA could result in its termination, denial of further access to SPIROMICS and other resources, and may leave violators liable to legal action on the part of SPIROMICS participants, their families, 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) and the Genomics and Informatics Center (GIC) for SPIROMICS, on behalf of SPIROMICS and under the direction of the SPIROMICS 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 Genetic and Biomarker Analysis Data, images (e.g., computed tomography scans), or primary signal data (e.g., spirometry tracings) and associated records either obtained directly from SPIROMICS participants or obtained from third parties as authorized by the participants pursuant to the contracts with the NHLBI, as well as data provided to SPIROMICS by ancillary studies.

"Resultant Data" refers to individual level participant data, summary level data, and secondary analysis of 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, blood, and sputum 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 SPIROMICS by ancillary studies.

"SPIROMICS Investigator" is a research investigator who works with SPIROMICS either as an employee of the NHLBI or through a current and active contract or consulting agreement with the NHLBI or one of its 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 SPIROMICS 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. The SPIROMICS GIC agrees 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. Recipient agrees to return or destroy any unused specimens, or portions thereof, in accordance with the requirements of the SPIROMICS Cohort Study, as may be amended from time to time.

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

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. If a separate DMDA is not established with the new institution or other entity,

the Recipient and Recipient's PI agree that all versions of the data and resultant data will be destroyed and their destruction documented. If a separate DMDA is not established with the new institution or other entity and there are remaining materials, the Recipient and Recipient's PI agree to either return the materials to the GIC or destroy them. If materials are destroyed this destruction must be documented. If advance written notice and approval by the GIC is obtained to transfer responsibility for the approved Research Project to a different PI with a relationship with the Recipient, the data, resultant data, and materials may not need to be destroyed. 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 has either a fee-for-service or subcontract agreement or specific authorization from SPIROMICS 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 SPIROMICS.

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. The SPIROMICS Publications and Presentations Subcommittee requests that the Recipient's PI provide to the authorized representative for SPIROMICS GIC (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 SPIROMICS 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 SPIROMICS.

7.1.a If the manuscript is approved by SPIROMICS, the Recipient and Recipient's PI agree to include the following language in an acknowledgment.

"The Subpopulations and Intermediate Outcomes in COPD Study (SPIROMICS) is funded by contract from the National Heart, Lung, and Blood Institute (NHLBI)

(HHSN268200900013C, HHSN268200900014C, HHSN268200900015C, HHSN268200900016C, HHSN268200900017C, HHSN268200900018C, HHSN2682009000019C, HHSN268200900020C)."

7.1.b If the manuscript is not approved by the SPIROMICS Study 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 Subpopulations and Intermediate Outcomes in COPD Study (SPIROMICS) is funded by contract from the National Heart, Lung, and Blood Institute (NHLBI) (HHSN268200900013C, HHSN268200900014C, HHSN268200900015C, HHSN268200900016C, HHSN268200900017C, HHSN268200900018C, HHSN2682009000019C, HHSN268200900020C).

The opinions and conclusions contained in this publication are solely those of the authors, and are not endorsed by SPIROMICS 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 Subpopulations and Intermediate Outcomes in COPD Study (SPIROMICS) is funded by contract from the National Heart, Lung, and Blood Institute (NHLBI) (HHSN268200900013C, HHSN268200900014C, HHSN268200900015C, HHSN268200900016C, HHSN268200900017C, HHSN268200900018C, HHSN2682009000019C, HHSN268200900020C).

This manuscript was not prepared in collaboration with investigators of the SPIROMICS Study and does not necessarily reflect the opinions or conclusions of SPIROMICS or the NHLBI."

7.3 Ancillary Study Investigator Acknowledgments. If Data include data provided to SPIROMICS by ancillary study investigators, Recipient and Recipient's PI also agree to acknowledge their contribution and relevant grants in any and all oral and written presentations, disclosures, and publications resulting from any and all analyses of such Data. Please visit the SPIROMICS website for relevant acknowledgements (SPIROMICS Publication Policies & Forms).

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 individual or participant level Data, Materials, and Resultant Data, and the progeny, or derivatives thereof, will not be used in any experiments or procedures unless said experiments or procedures, including any analyses, are disclosed and approved as part of the Research Project or in accordance with the Manuscript Proposal Process set

forth in Section 13. Recipient shall have full ownership rights in and to summary level data and secondary analysis, Resultant Data and shall be free to use Resultant Data for any purpose consistent with this agreement without restriction.

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 SPIROMICS 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 SPIROMICS and NHLBI.

A copy of any resultant data will be provided to the SPIROMICS GIC upon completion of data cleaning. Data cleaning shall be completed within 12 months of receipt of Data and/or Materials, whichever is received first.

Recipient will provide SPIROMICS committee with a status report starting 12 months from receipt of the Data and/or Materials ("Report Due Date"). The Recipient will file additional status report at least once every 12 months for the duration of the project. Additional reports may be made from time to time before or after the Report Due Date during the term, and such additional reports shall be in the form of a manuscript proposal in accordance with the following "Manuscript Proposal Process". Recipient may submit and SPIROMICS committee will review any manuscript proposal(s) outlining additional analyses to be conducted by Recipient. Additional analyses related to use of Resultant Data and Data outlined in such a proposal cannot move forward unless approved by the SPIROMICS committee. In the event the proposal contains research planned by a university-affiliated SPIROMICS committee member as evidenced in a prior written document, Recipient will agree to collaborate with said university-affiliated SPIROMICS investigator on the proposal and share Resultant Data prior to initiating the analyses outlined in the proposal. 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 SPIROMICS and NHLBI, in accordance with the NIH Data Sharing Policy, 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 a signed DMDA comparable to this DMDA. Subject to the following restrictions, University affiliated SPIROMICS Investigators may access such Resultant Data at any time and may

publish no sooner than six (6) months after Recipient has deposited Resultant Data. Industry SPIROMICS Investigators, other than Recipient Investigators, and the public may access such Resultant Data no sooner than twelve (12) months after deposit of Resultant Data by Recipient and may publish no sooner than twelve (12) months after release of the data to industry SPIROMICS Investigators, other than Recipient Investigators, and the public. Recipient and Recipient's PI will provide all Resultant Data in the precise electronic format specified by NHLBI or SPIROMICS. If errors in family structure, especially paternity, are identified, Recipient and Recipient's PI agree to contact the GIC Authorized 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 SPIROMICS 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 SPIROMICS 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.

16. 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.

17. 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 hold harmless the United States Government, SPIROMICS, 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.

Except where prohibited law, Recipient agrees to defend and indemnify the United States Government, SPIROMICS, 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.

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

19. 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 SPIROMICS Study IRB(s). Recipient agrees to report promptly to SPIROMICS 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 involves 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.

20. 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 http://www.ncbi.nlm.nih.gov/projects/gap/pdf/dbgap_2b_security_procedures.pdf.

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

22. 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 SPIROMICS of such violation. Upon termination of this DMDA: Recipient agrees to destroy all copies of the data containing only participant or individual level information and any remaining materials that are not transferred back to the GIC. Notwithstanding the foregoing, Recipient shall have no obligation to destroy Resultant Data containing summary level data and secondary analysis. An extension of the DMDA may be permitted by the GIC upon submission by the Recipient and Recipient PI of evidence of IRB approval for the extended period.

23. 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 SPIROMICS 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 and agree 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 SPIROMICS participants, their families, or both. Recipient and its affiliates shall be free to confidentially disclose summary level and secondary analysis Resultant Data, which may not include individual or participant level Data, to any governmental regulatory authority to the extent such disclosure is requested or required by such regulatory authority or which Recipient or its affiliates believes is reasonably necessary in complying with applicable laws or

regulations governing such regulatory authority. Any individual or participant level Data requested by any governmental regulatory authority must be handled by the SPIROMICS GIC.

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

25. 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 SPIROMICS and/or the NHLBI.

26. SPIROMICS Contract Terms and Conditions. Recipient recognizes the SPIROMICS GIC's legal obligation to comply with the terms and conditions of the SPIROMICS contract. In the event of a conflict between any provision of this agreement and the terms and conditions of the SPIROMICS contract, the SPIROMICS contract terms and conditions shall prevail.

RECIPIENT PRINCIPAL INVESTIGATOR:

Signature_____

Name_____

Title_____

Email_____

Address_____

_____

Phone_____

Date_____

RECIPIENT INSTITUTION/CORPORATION NAME

_____

Signature of Authorized Representative

_____

Name_____

Title_____

Email_____

Address_____

_____

Phone_____

Date_____

[Signatures Continue on Next Page]

GENOMICS AND INFORMATICS CENTER FOR THE SUBPOPULATIONS AND INTERMEDIATE OUTCOME MEASURES OF COPD STUDY (SPIROMICS)

UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL

Signature_____

On behalf of Terry Magnuson, Ph.D.

Vice Chancellor for Research

Date_____

SPIROMICS GIC

Signature_____

Name_____

Title_____

Date_____

NATIONAL HEART, LUNG AND BLOOD INSTITUTE (NHLBI)

Signature_____

Name_____

Title_____

Date_____