Model Data Use Certification Agreement

[[Genome-wide Association of Platelet Phenotypes]]

(January 21, 2010, version)

Introduction and Statement of Policy

The National Institutes of Health (NIH) has developed central data repositories to archive and distribute the results of studies provided by Contributing Investigators examining the relationship between genomic data (e.g., genotype, sequence, or epigenetic information) and phenotype. Such studies include genome-wide association studies, medical sequencing, and molecular diagnostic assays. Implicit in the establishment of the NIH data repositories, for example the database of Genotypes and Phenotypes (dbGaP), is the view that scientific progress in this area will be greatly enhanced if the data produced by these studies are readily available to all investigators in the research community.

Dataset access will be provided to research investigators who, along with their institutions, have certified their agreement with the expectations and terms of access detailed below. It is the intent of the NIH and the National Heart, Lung, and Blood Institute (NHLBI) that Approved Users of NIH-provided datasets recognize any restrictions on data use delineated within the original informed consent agreements of contributing studies, as identified by the submitting institutions and stated on database websites.

Definitions of terminology used in this document are found in the Appendix.

The parties to this agreement include: the Principal Investigator (PI) requesting access to the GWAS dataset ("the Approved User"), his/her home institution as represented by the Institutional Signing Official designated through the eRA Commons system ("the Requester"), and the NHLBI, NIH. The effective date of this agreement shall be the Project Approval Date, as specified on the Data Access Committee approval notification.

Study Background

The goal of this study was to identify genetic variants in a genome wide association study (GWAS) that are associated with previously obtained platelet function phenotypes measured in each individual under baseline conditions and following 2 weeks of low dose aspirin. During this study we performed a high density 1 million-SNP genome scan on subjects from GeneSTAR (representing 1000 2-generational families with a family history of premature coronary artery disease, 60% white and 40% African American, N=3250). We identified genomic loci associated with quantitative platelet phenotypes prioritized for their biological interest, determined associations between genomic loci and baseline platelet phenotypes (primary phenotypes are platelet aggregation in platelet rich plasma induced by collagen, adenosine diphosphate (ADP), arachidonic acid (AA), and epinephrine (Epi)), determined associations between genomic loci and post-ASA platelet phenotypes, ie, measures of ASA "resistance" (primary phenotypes are as above, plus urinary levels of the prostaglandin metabolite, 11-dehydro-thromboxane B2), and compared peaks of association between genomic loci and three common baseline platelet phenotypes (collagen-, epinephrine-, and ADP-induced aggregation in platelet rich plasma) with associations found for these same phenotypes in the Framingham Heart Study. We also determined whether any significant genotype-phenotype associations in the 1 million SNP genome scan could be localized to any specific genes or potential genes of interest using publicly available databases and further examined whether candidate genes

previously associated with a specific platelet phenotype are located in a genomic region of interest as determined from the SNP genome scan. We conducted replications of our findings, and are presently involved in larger scale meta-analysis of findings for pre-aspirin and post-aspirin associations. .

The study population is constituted of full siblings SIBS (ages 35-78 years) identified from The Johns Hopkins Sibling Study, now called GeneSTAR, the spouses of the SIBS, and their adult offspring (>21 years of age). They include 3200 individuals from 200 African American and 200 white families. "Spouse" refers to the other parent of any SIB offspring, independent of marital status. Sibship sizes among families range from 1 to 16 (excluding index cases). On average, each SIB has 2 potentially eligible offspring. A *family* for this study is defined by all of the full sibships and the total numbers of offspring that come from all SIBS, rather than just the nuclear family.

Aggregate data from all analyses is hereby available in dbGaP. No individual level data are included. Individual level data are prohibited by the original informed consents, but are available to qualified investigators through application to The Johns Hopkins University GeneSTAR Research Program using approved application procedures [appended].

Terms of Access

1. Research Use

The Requester agrees that if access is approved, the Principal Investigator named in the Data Access Request (DAR) submitted to the NIH, those named in the "Senior/Key Person Profile" portion of the DAR, which should include the Information Technology Director or his/her designee, and any trainee or employee working on the proposed research project under the direct supervision of these individuals, shall become Approved Users of the requested dataset(s). Research use will occur solely in connection with the research project described in the DAR, which includes a 1-2 paragraph description of the research objectives and design. New uses of these data outside those described in the DAR will require submission of a new DAR; modifications to the research project will require submission of an amendment to this application (e.g., the addition of new aims related to the approved project, adding or deleting collaborators from the same institution, and the potential addition of new NIH GWAS datasets to an approved project). The Requester and all Approved Users may use the dataset(s) only in accordance with the parameters described on the NIH database Web site for the appropriate research use, and any limitations on such use, of the dataset(s) and as required by law.

Research access to the requested dataset(s) is granted for a period of one (1) year as defined below.

Contributing Investigators, or their direct collaborators, who provided the data used to generate an NIH genomic dataset and who have appropriate IRB approval, if applicable, for broader use of the data are exempt from the limitation on the scope of the research use as defined in the DAR.

NHLBI Specific Terms

DATA USE LIMITATION FOR [Genome-wide Association of Platelet Phenotypes]:

The original consent forms obtained as part of the PROGENI award (L. Becker, Principal Investigator), under which all phenotype information was garnered and all DNA was obtained, specifically precludes transfer of individual genetic level data. Because it is not possible to reconsent participants, the National Institutes of Health has accepted an alternative whereby

individual level data can be sought from the Johns Hopkins Institutions through a special agreement to qualified investigators. However, we are submitting aggregate results for all GWAS analyses to dbGaP. The original consent forms indicate that when the genetic data are used on these individuals, it may only be for cardiovascular and cardiovascular-related investigations.

2. Institutional and Approved User Responsibilities

The Requester agrees through the submission of the Data Access Request (DAR) that the PI named in the DAR has reviewed and understands the principles for responsible research use and data handling of the genomic datasets as defined in the NIH GWAS Data Sharing Policy and detailed in this Data Use Certification agreement. The Requester and Approved Users further acknowledge that they are responsible for ensuring that all uses of the data are consistent with federal, state, and local laws and regulations and any relevant institutional policies. Through submission of the DAR, the Principal Investigator also agrees to submit annual data use reports to the appropriate NIH Data Access Committee (DAC) describing the research use of the Approved Users as described under *"Research Use Reporting"* below.

Approved Users who may have access to personal identifying information for research participants in the original study at their institution or through their collaborators, may be required to have IRB approval. By approving and submitting the attached Data Access Request, the Institutional Signing Official provides assurance that relevant institutional policies and applicable federal, state, or local laws and regulations (if any) have been followed, including IRB approval if required. The Institutional Signing Official also assures through the approval of the Data Access Request that other organizations within the institution with relevant authorities (e.g., the Office of Human Subjects Research, the Office of Information Technology, the Office of Technology Transfer, etc.) have reviewed the relevant sections of the NIH GWAS Data Sharing Policy and the associated procedures and are in agreement with the principles defined.

It is anticipated that, at least in some cases, these datasets will be updated with additional information. Unless otherwise indicated, all statements herein are presumed to be true and applicable to the access and use of all versions of these datasets.

3. Public Posting of Approved User's Research Use Statement

The Principal Investigator agrees that, if he or she becomes an Approved User, information about the PI and the approved research use may be posted on a public, US government web site that describes approved research projects. The information may include the Approved User's name and institution, project name, Research Use Statement, and a Non-technical Summary of the Research Use Statement. In addition, citations resulting from the use of NIH genomic datasets may be posted on NIH data repository websites.

4. Non-Identification

Approved Users agree not to use the requested datasets, either alone or in concert with any other information, to identify or contact individual participants from whom phenotype data and DNA samples were collected. This provision does not apply to research investigators operating with specific IRB approval, pursuant to 45 C.F.R. 46, to contact individuals within datasets or to obtain and use identifying information under an approved IRB research protocol. All investigators conducting "human subjects research" within the scope of 45 C.F.R. 46 must comply with the requirements contained therein.

5. Non-Transferability

The Requester and Approved Users agree to retain control over the data and further agree not to distribute data obtained through this Data Access Request to any entity or individual not covered in the submitted Data Access Request. If Approved Users are provided access to NIH genomic

datasets for inter-institutional collaborative research described in the Research Use Statement of the Data Access Request, and all members of the collaboration are also Approved Users through their home institution(s), data obtained through this Data Access Request may be securely transmitted within the collaborative group. All data security practices and other terms of use defined in this agreement and the *dbGaP Security Best Practices* for the raw data are expected to be followed for the derived data, including any transmission of the data.

The Requester and Approved Users acknowledge responsibility for ensuring the review and agreement to the terms within this Data Use Certification and the appropriate research use of NIH genomic data by research staff associated with any approved project, subject to applicable laws and regulations. NIH genomic datasets obtained through this Data Access Request, in whole or in part, may not be sold to any individual at any point in time for any purpose.

Approved Users agree that if they change institutions during the access period, they will submit a new Data Access Request and Data Use Certification in which the new institution agrees to the NIH GWAS data use policy before data access resumes. Any versions of data stored at the prior institution for the approved use will be destroyed and documented through a final Data Use Report as described below. However, if advance written notice and approval by the NHLBI Data Access Committee is obtained to transfer responsibility for the approved research project to another Approved User within the same institution the data may not need to be destroyed.

6. Data Security and Data Release Reporting

The Requester and Approved Users, including the institutional Information Technology Director or his/her designee, acknowledge the intent of the NIH that they have reviewed and agree to handle the requested dataset(s) according to the current *dbGaP Security Best Practices*, including its detailed description of requirements for security and encryption. These include, but are not limited to:

- all Approved Users have completed all required computer security training required by their institution, for example, the http://irtsectraining.nih.gov/, or the equivalent;
- the data will always be physically secured (for example, through camera surveillance, locks on doors/computers, security guard);
- servers must not be accessible directly from the internet, (for example, they must be behind a firewall or not connected to a larger network) and unnecessary services should be disabled;
- use of portable media, e.g., on a CD, flash drive or laptop, is discouraged, but if necessary then they should be encrypted consistent with applicable law;
- use of updated anti-virus/anti-spyware software;
- security auditing/intrusion detection software, detection and regular scans of potential data intrusions;
- use of strong password policies for file access.
- all copies of the dataset should be destroyed, as permitted by law, whenever any of the following occurs:
  - the DUC expires and renewal is not sought;
  - access renewal is not granted;
  - the NHLBI requests destruction of the dataset;
  - the continued use of the data would no longer be consistent with the DUC.

In addition, the Requester and Approved Users agree to keep the data secure and confidential at all times and to adhere to information technology practices in all aspects of data management to assure that only authorized individuals can gain access to NIH genomic datasets. This agreement includes the maintenance of appropriate controls over any copies or derivatives of the data obtained through this Data Access Request.

Requesters and Approved Users agree to notify the NHLBI Data Access Committee of any unauthorized data sharing, breaches of data security, or inadvertent data releases that may compromise data confidentiality within 24 hours of when the incident is identified. As permitted by law, notifications should include the known information regarding the incident and a general description of the activities or process in place to fully define and remediate the situation. Within 3 business days of the NHLBI Data Access Committee notification, the Requester, through the Approved User and the Institutional Signing Official, agree to submit to the NHLBI Data Access Committee a more detailed written report including the date and nature of the event, actions taken or to be taken to remediate the issue(s), and plans or processes developed to prevent further problems, including specific information on timelines anticipated for action.

All notifications and written reports of data security incidents should be sent to:
NHLBI Data Access Committee
Email: nhlbigeneticdata@mail.nih.gov

The NHLBI, the NIH, or another entity designated by the NIH may, as permitted by law, also investigate any data security incident. Approved Users and their associates agree to support such investigations and provide information, within the limits of applicable local, state and federal laws and regulations. In addition, Requesters and Approved Users agree to work with the NHLBI and the NIH to assure that plans and procedures developed to address identified problems are mutually acceptable consistent with applicable law.

7. Intellectual Property

By requesting access to genomic dataset(s), the Requester and Approved Users acknowledge the intent of the NIH that anyone authorized for research access through the attached Data Access Request follow the intellectual property principles within the NIH GWAS Policy for Data Sharing as summarized below:

> Achieving maximum public benefit is the ultimate goal of data distribution through the NIH genomic data repositories. The NIH believes that these data should be considered as pre-competitive, and urges Approved Users to avoid making IP claims derived directly from the genomic dataset(s). However, the NIH also recognizes the importance of the subsequent development of IP on downstream discoveries, especially in therapeutics, which will be necessary to support full investment in products to benefit the public.
>
> It is expected that these NIH-provided data, and conclusions derived therefrom, will remain freely available, without requirement for licensing. The NIH encourages broad use of genomic datasets coupled with a responsible approach to management of intellectual property derived from downstream discoveries in a manner consistent with the NIH's Best Practices for the Licensing of Genomic Inventions and the NIH Research Tools Policy.

8. Research Dissemination and Acknowledgement of NIH GWAS Datasets

[Example below assumes standard 12-month publication exclusivity]

It is the intent of the NIH to promote the dissemination of research findings from NIH genomic dataset(s) as widely as possible through scientific publication or other appropriate public dissemination mechanisms. Approved Users are strongly encouraged to publish their results in peer-reviewed journals and to present research findings at scientific meetings, etc.

In accord with the NIH GWAS Policy for Data Sharing, and as expressed through the submission of the DAR, Approved Users acknowledge the NIH's expectation **that they will not *submit* findings using the [Genome wide Association of Platelet Phenotypes] dataset(s), or updated versions thereof, for publication or presentation for a period of exclusivity for**

Contributing Investigators concluding with the Embargo Date identified on the dbGaP or other NIH genomic data repository homepage. Please note that different variables may have different embargo dates.

Approved Users agree to acknowledge the NIH data repository, the Contributing Investigator(s) who contributed the phenotype data and DNA samples from his/her original study, and the primary funding organization that supported the contributing study in all oral and written presentations, disclosures, and publications resulting from any analyses of the data. Approved Users further agree that the acknowledgment shall include the dbGaP accession number to the specific version of the dataset(s) analyzed.

A sample statement for the acknowledgment of the [Genome Wide Association of Platelet Phenotypes] dataset(s) follows:

Genome wide association data on [native platelet function phenotypes; or aspirin response platelet function phenotypes; or both native and aspirin response platelet function phenotypes] were obtained from the Johns Hopkins University GeneSTAR Research Program.

9. Research Use Reporting

To assure that NIH policies and procedures for genomic data use are adhered to, Approved Users agree to provide to the NHLBI Data Access Committee annual feedback on how these data have been used and any results that have been generated as a result of access to the data, including patents and publications. This information will be used by the NHLBI Data Access Committee staff for program evaluation activities, and may be considered by the NIH GWAS Governance committees as part of the NIH effort to provide ongoing oversight and management of all NIH genomic data sharing activities.

Approved Users thus agree to provide a brief Annual Data Use Report on the research specified within the DAR submitted with this DUC. Approved Users who are seeking renewal agree to provide specific information in a renewal DAR. Those not seeking renewal agree to provide specific information to the Data Access Committee via the contact information below. Annual Data Use Reports will provide information regarding potentially significant findings and publications or presentations that resulted from the use of the requested dataset(s), a summary of any plans for future research use, any violations of the terms of access described within this Data Use Certification and the implemented remediation, and information on any downstream intellectual property generated as a result of the data. Approved Users also may include general comments regarding topics such as the effectiveness of the NIH genomic data access process (e.g., ease of access and use), appropriateness of data format, challenges in following the policies, and suggestions for improving data access or the program in general if desired.

Approved Users agree to send the Annual Data Use Report prior to the anniversary of the Approved Access Date assigned by the DAC and specified within the manifest file provided to Approved Users by the NIH Data Repository at the time that data access is provided. It is agreed that the Annual Data Use Report will be shared with the NIH within the context of a renewal Data Access Request, or via a letter signed by the Institutional Signing Official and the Approved User.

Annual Data Use Reports should be submitted to:

NHLBI Data Access Committee Chair
Email: nhlbigeneticdata@mail.nih.gov

Note that any inadvertent or inappropriate data release incidents should be reported to the NHLBI Data Access Committee according to the agreements and instructions under Term 6.

10. Non-Endorsement, Indemnification

The Requester and Approved Users acknowledge that although all reasonable efforts have been taken to ensure the accuracy and reliability of NIH genomic data, the NIH, the NHLBI Data Access Committee, and Contributing Investigators do not and cannot warrant the results that may be obtained by using any data included therein. The NIH, the NHLBI Data Access Committee, and all contributors to these datasets disclaim all warranties as to performance or fitness of the data for any particular purpose.

No indemnification for any loss, claim, damage or liability is intended or provided by any party under this agreement. Each party shall be liable for any loss, claim, damage, or liability that said party incurs as a result of its activities under this agreement, except that the NIH, as an agency of the United States, may be liable only to the extent provided under the Federal Tort Claims Act, 28 U.S.C. 2671 et seq.

11. Termination and Violations

This Data Use Certification will be in effect for a period of one (1) year from the date the dataset(s) are made accessible to the Approved User ("Approved Access Date"). At the end of the access period, Approved Users agree to destroy all copies of the requested dataset(s), except as required by publication practices or law to retain them.

Consideration will be given to a renewal of this agreement upon submission of a new DAR. Copies of NIH genomic dataset(s) may not need to be destroyed if, with advance notice and approval by the NHLBI Data Access Committee, the project has been transferred to another Approved User. In this case, documentation must be provided that other Approved Users are using the dataset(s) under an active DAC approved research project at the same institution.

The Requester and Approved User acknowledge that the NIH or the NHLBI may terminate this agreement and immediately revoke access to all NIH genomic datasets at any time if the Requester is found to be no longer in agreement with the policies, principles and procedures of the NIH and the NHLBI.

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By submission of the attached Data Access Request, the Requester through the Institutional Signing Official attests to the Approved Users' qualifications for access to and use of NIH genomic dataset(s) and certifies their agreement to the NIH principles, policies and procedures for the use of the requested datasets as articulated in this document, including the potential termination of access should a violation of any of these agreement terms be identified.

Requesters and the Principal Investigator further acknowledge that they have shared this document and the NIH GWAS data sharing policies and procedures for access and use of genomic datasets with any Approved Users, appropriate research staff, and all other Key Personnel identified in the DAR.

Institutional Signing Officials acknowledge that they have considered the relevant NIH GWAS policies and procedures, that they have shared this document and the relevant policies and procedures with appropriate institutional organizations, and have assured compliance with local institutional policies related to technology transfer, information technology, privacy, and human subjects research.

Appendix

Definitions of Terminology

Annual Data Use Report: A report submitted to the DAC on the anniversary of access approval summarizing the analysis of NIH genomic datasets obtained through the Data Access Request and any significant findings derived from the work.

Approved User: Post-DAC approval will include the PI, collaborators at the home institution who are named in the "Senior/Key Person Profile" portion of the DAR, the IT Director or designee named in the "Senior/Key Person Profile" portion of the DAR, and trainees or staff to these investigators.

Contributing Investigator: The researcher who submitted the genomic dataset to dbGaP.

Data Access Request: SF 424 (R&R) cover pages and requested attachments, if any.

Data Derivative: any data including individual-level data or aggregate genomic data that stems from the original dataset obtained through dbGaP. Excepted from this term is summary information that is expected to be shared through community publication practices.

Final Data Use Report: A final report submitted to the DAC at the conclusion of the approved access period when no additional access is sought, or when leaving an institution. This report should summarize the analysis of GWAS datasets obtained through the Data Access Request and any significant findings derived from the work.

Information Technology Director: Someone with the authority to vouch for the IT capacities at an institution, or higher-level division of an institution (e.g., the School of Medicine).

Institutional Signing Official: Someone with the authority to sign on behalf of the Requester and credentialed through the eRA system as such.

Requester: The home institution/organization for the Primary Investigator (PI) that will use the requested data.

Senior/Key Persons: Collaborators at the home institution, and the IT Director or designee.

Appendix Data Use Plan Submitted to the National Institutes of Health 3/24/2010, updated February 25, 2011:

Genome-wide Association of Platelet Phenotypes:

The Johns Hopkins GeneSTAR Research Program

Volume

1

JOHNS HOPKINS

THE JOHNS HOPKINS GENESTAR RESEARCH PROGRAM: GENOME-WIDE ASSOCIATION OF PLATELET PHENOTYPES

VERSION 2: MARCH 18, 2010; *UPDATED FEBRUARY 25, 2011*

NIH STAMPEED

DATA SHARING, DATA ACCESS MANUAL FOR INDIVIDUAL GENOMIC DATA, PLATELET PHENOTYPES

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GeneSTAR

National Institutes of Health

All individual level data are fully available from the Study as described in the Manual but not through dbGaP because of the nature of the consent forms for the participants in the original GeneSTAR Study. All genomic data are available either in individual level form via the Limited Access Agreement or as aggregate data from dbGaP congruent with the policies outlined in the Appendix. Summary aggregate data will be available through dbGaP to investigators approved under a DUC, for platelet variables, the primary phenotypes of interest.

Data Use Certification

Certification exists for aggregate data for platelet phenotypes, and risk factors as noted in this manual. Certification for individual level data exists only under Limited Access Agreements as discussed in Section 3.

Institutional Certification

The Institution provides certification only under the terms of the Limited Access Agreement for individual genotypes and non-primary phenotypes as per the conditions outlined in Section 3.

Background: GeneSTAR Design and Population

The attached general study description, in whole or part, may be used in publications using the available GeneSTAR data.

The GeneSTAR Study (Genetic Study of Aspirin Responsiveness) represents an amalgam of studies with identical ascertainment criteria, enrollment procedures, and measurement protocols commencing in 1983, and continuing to the present. GeneSTAR participants were enrolled in the original Johns Hopkins Sibling Study, Johns Hopkins Family Heart Study, or the Genetic Study of Aspirin Responsiveness. We present a summary of the design and the population for various portions of the study. The study represents only families with a member who experienced a documented premature coronary artery disease event. All ascertainment was done on that phenotype. The current study represents data in two generational kindreds, with no genotyping available for the parents of the original proband, the ascertainment portal through which all other participating family members originally entered.

Siblings were accessed from patients, each hospitalized at any of 10 hospitals in Baltimore. All probands had a documented coronary artery disease (CAD) event prior to 60 years of age. The genetic portion of the study represents 2-generational families which are generally 45% African American, with full genotyping on 3282 individuals, ~1000 nuclear families. Genotyping includes 200 candidate genes in known CAD mechanistic pathways with approximately 10-20 SNPs/gene, a 550 STR marker scan, a 32 STR marker HapMap ancestry panel, and a whole genome scan with 1 million SNPs using the Illumina Human1Mv1_C BeadChip, with 50,000 ancestry informative SNPs from the Human Diversity Panel.

Participants are all healthy family members who took part in a 2 week study of 81 mg/day of aspirin, with extensive platelet phenotyping before and after aspirin.

Phenotype and genotyping data are available through Johns Hopkins Limited Licensing Agreements whereby all requests are reviewed by a Data Access team at Johns Hopkins as per the protocols listed herein. Data will be presented via an FTP site to an approved

qualified investigator upon request and presentation of a brief research protocol, accompanied by institutional IRB approval, or a waiver of informed consent at the requesting institution. Johns Hopkins will not indemnify users of GeneSTAR GWAS data and will not permit use for purposes other than health care and medical research related to cardiovascular disease and associated risk factors and entities. All data are available to the public via this mechanism only with approval of all current data protocols by the National Institutes of Health. Aggregate data for study results are available in dbGaP.

Section 2

Primary Platelet Phenotypes : Description

The general description of our primary phenotypes, consisting of ex vivo platelet function, may be used in publications using the available GeneSTAR data.

The GeneSTAR Study obtained most of its genotyping for the purposes of examining native platelet function and platelet responsiveness to low dose aspirin in the kindreds described above. Platelet function was measured as part of the original GeneSTAR aspirin study. All measures were performed both before and after 14 days of 81 mg/day of aspirin. In total, 2146 participants completed both pre and post aspirin studies, and an additional 379 participants completed post-only studies. Change was calculated as post minus pre. Post|pre was calculated from linear regressions predicting post values from pre values. Many platelet measures are not normally distributed and required log transformation.

Optical aggregation was measured in platelet rich plasma (PRP) after stimulating samples with arachidonic acid (0.5, 1, 1.6, 2 mM), collagen (0.25, 0.5, 1, 2, 5, 10, 20 μg/ml), adenosine diphosphate (ADP 2, 10 μM), or epinephrine (2, 10 μM). Whole blood impedance aggregation was measured after stimulating samples with arachidonic acid (0.5 mM), collagen (1, 5 μg/ml), or ADP (10 μM); also, one whole blood sample was incubated with ASA in vitro (20μM for 15 min) prior to stimulation with arachidonic acid. Peak aggregation within 5 minutes of agonist stimulation was recorded as percent aggregation for PRP and ohms for whole blood. Time from addition of collagen to start of aggregation was recorded as lag time. Platelet release of thromboxane (TxB2) and β-thromboglobulin (BTG) ex vivo were quantified by commercially available ELISA and results normalized to platelet count.

Shear related platelet function was assessed by platelet function analyzer-100 (PFA) cartridges containing a combination of collagen and epinephrine and closure time was recorded (maximum of 300 sec). Thromboxane production in vivo was assessed by urinary 11-dehydro thromboxane B2 (Tx-M), which was quantified by commercially

available ELISA and normalized to urinary creatinine. A complete list of phenotypes, coding, and the phenotype data for the platelet function studies is available upon request.

Section 3

Obtaining the Genotypic Data and Platelet Phenotypic Data

These steps govern individual level data.

The steps for obtaining data are listed below and may be followed to obtain de-identified individual level genotypic data, and platelet phenotypes (a full list and coding manual is available upon request). Other phenotypes, primarily cardiovascular, exist and a full list is available upon request. Only aggregate data will be available on dbGaP. Individual level data will be available as noted, using the Limited Access Agreement methods described. All individual level data are thereby available using this mechanism, approved by the Legal Counsel of the Institutional Review Board of the Johns Hopkins University.

Steps to Obtain Permission to Access Data

1. Access the GeneSTAR Website and read rules and procedures for obtaining and using the data. Access information can be obtained from lryanek@jhmi.edu.

2. Download preliminary application form.

3. Complete and submit preliminary application (electronic, mail, or fax)

    a. Précis of planned data use, which must include a formulated research question and brief analysis plan.

    b. Principal Investigator curriculum vitae or NIH Biographical Sketch

    c. Brief description of computing facilities and resources to be used for the analyses

    d. Data protection and security information

4. Once the review of the preliminary application is approved by the GeneSTAR Data Access and Steering Committee and the applicant is notified, complete and submit the Limited Access Agreement (Appendix A: Sample of a completed form), also available for download on the GeneSTAR website. Information about how to obtain Help and assistance is available on the GeneSTAR website.

Steps to Access Data Following a Signed Limited Access Agreement

1. Access the GeneSTAR Website and read rules and procedures for obtaining the data once an LAA is approved.

2. Provide a full list of data requested in the formats specified by the GeneSTAR and recipient IT or database managers.

3. Data will be transferred using a **File Transfer Protocol** (**FTP**). Our FTP is of the client-server architecture and utilizes separate control and data connections between the client and server applications.

4. Applicants will be given a temporary password authentication by the GeneSTAR Cluster Manager, and the site will be open for download at a pre-defined time for a limited period, whatever is necessary to make the compete transfer.

5. The GeneSTAR Manager will provide information about how the transfer is to be performed.

6. Alternative measures for transfer will be considered.

7. We will not mail hard drives with data to applicants for security reasons.

8. Any hard drive transfer of data must be completed by a bona fide and designated secure courier (not through the mail).

9. The recipient will complete a signed form within 1 week of data transfer acknowledging that the data was received, the date, and will note any possible transfer errors for remediation.

10. Complete and submit preliminary application (electronic, mail, or fax)

    a. Précis of planned data use, which must include a formulated research question and brief analysis plan.

    b. Principal Investigator curriculum vitae or NIH Biographical Sketch

    c. Brief description of computing facilities and resources to be used for the analyses

d. Data protection and security information

11. Once the review of the preliminary application is approved by the GeneSTAR Data Access and Steering Committee and the applicant is notified, complete and submit the Limited Access Agreement (Appendix A), also available on the GeneSTAR website.

Section 4

Application Review Criteria for Individual Level Data and Committee Membership

The review criteria and general responsibilities of the principal investigator and any related Institutional Review Board are noted, and Committee membership is listed.

The review of Preliminary Application and the Limited License Agreement are two separate stages. Adequacy according to review criteria must be met for each separately before data will be transferred. Principal investigators for each data-seeking protocol must be fully qualified to perform the research procedures. Requests for sequential, new, or different proposals using the same database require a full LAA for each. The LAA is considered active only for the proposal submitted. For research involving Johns Hopkins GeneSTAR data, the following information must be provided on the LAA application form:

- Name of sites where data will be stored and analyzed
- Security procedures for data management
- Assurances that persons managing the data have completed compliance training
- Name(s) of data management/analysts at the sites
- Contact information (address, phone, and email)
- IRB approval or a waiver

If a site does not have an IRB, the appropriate Johns Hopkins IRB will serve as the IRB of record and the form of the submission may be considered on an individual basis.

Each principal investigator must comply with federal regulations, state and local laws, and LAA policies. Principal investigators are responsible for training staff and for conducting the research at the designated site and may not transfer responsibility for the research to another principal investigator without notifying the GeneSTAR Steering Committee. The principal investigator, by signing the LAA, agrees that they are responsible for the safety of the security and appropriate management of the data.

Review criteria for the Preliminary Application and Limited Licensing Agreement

Preliminary applications and Limited Licensing Agreements (LAA) will be reviewed for the criteria listed below:

1. No significant overlap with the specific aims of current GeneSTAR research.
2. Acceptable and achievable workload for the GeneSTAR data team based on available bioinformatics resources
3. Compatible with the consent forms signed by GeneSTAR participants (*data are available only for platelet function and cardiovascular disease and any associated co-morbidity and risk factors based on the participant consent forms*).
4. Compatible with the population characteristics of the GeneSTAR participants.
5. Achievable aims and scientific merit as adjudicated by the Steering Committee
6. Experienced Principal Investigator
7. Experienced data analysis team
8. Institutional IRB approval or an IRB waiver
9. Acceptable and secure data storage and data processing facilities
10. Agreement not to attempt to identify individuals
11. Agreement not to use the data for anything beyond what has been proposed in the Preliminary and Limited Licensing Agreement
12. Agreement not to share data with another party or 2nd source
13. No risk to the GeneSTAR Study, its participants, or to Johns Hopkins
14. Agreement to allow the GeneSTAR Steering Committee to view results and to verify any findings for which there are accuracy and precision concerns by allowing Johns Hopkins to reanalyze the data. *(Johns Hopkins waives intellectual property rights and reserves the step solely for assuring the integrity of data representing participants in the GeneSTAR study)*

15. Investigators agreement to destroy on-site databases containing GeneSTAR data once the proposed study is completed.

16. Investigator's agreement to update the LAA annually while the study is in progress, and to formally terminate the agreement when the study is completed.

Review Committee Co-chairs

- Dr. Lewis C. Becker, Robert L. Levy Professor, Cardiology
- Dr. Diane M. Becker, Professor, Medicine

Membership

- Rasika Mathias, ScD, Assistant Professor, Medicine and Epidemiology,
- Jay Vaidya, MBBS, PhD, MPH, Assistant Professor, Medicine,
- Taryn F. Moy, MS, Research Associate, Director, GeneSTAR Projects
- Lisa R. Yanek, Research Associate, Director GeneSTAR Analysis Unit

Governance

All data used for qualifying research are fully available to the public with no claim of intellectual property rights by the Johns Hopkins University unless the proposal is designed to be collaborative in nature, which will be so designated a priori under the LAA. The process shall be governed by the Office of the Vice Dean for Clinical Investigation at The Johns Hopkins University School of Medicine. The LAA has been designed by the IRB counsel. All concerns should be addressed to Dr. Lewis C. Becker, or Dr. Diane Becker of the Steering Committee, and should there be any legal concerns, they will be relayed to the appropriate individual in the Office of Research Administration Legal Department and the counsel for the IRB at Johns Hopkins. Such information will be provided upon request to lbecker@jhmi.edu, or 410-955-5998, Halsted 500 The Johns Hopkins Medical Institutions, 600 N. Broadway, Baltimore, Maryland 21287.

Process and Timeline

The following figure represents approximate times and steps from the receipt of a query and preliminary application to transfer of data to the investigator, and annual renewal of the Limited Access Agreement, or termination thereof.

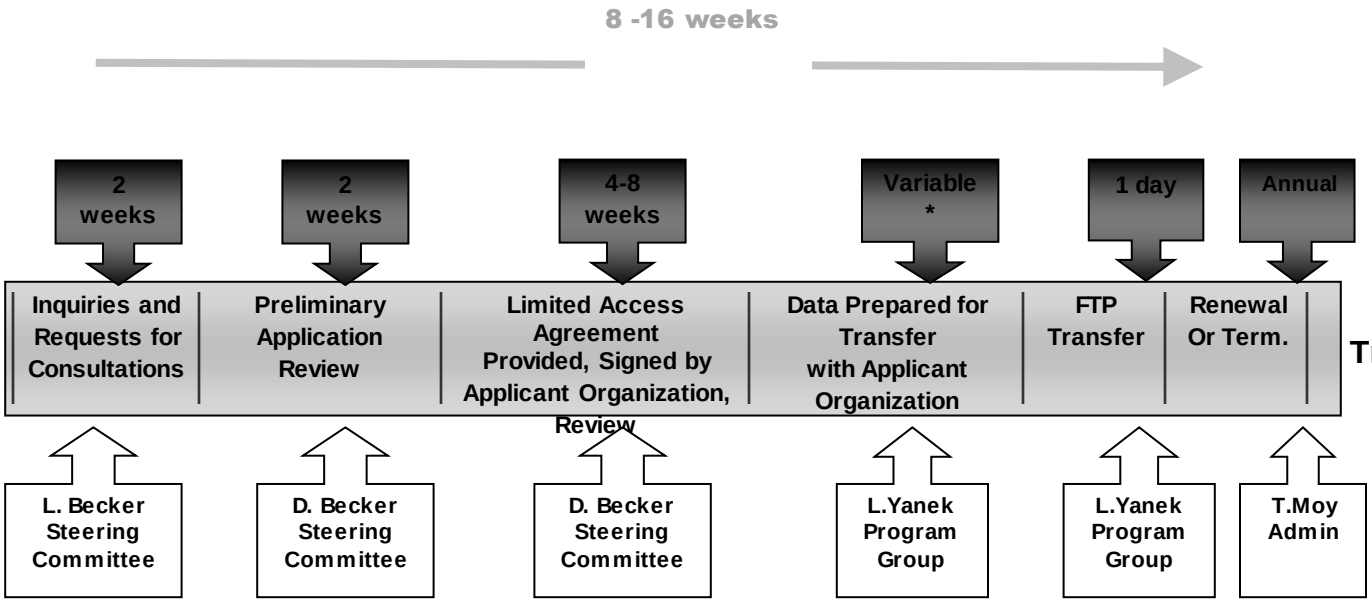

FIGURE 2. Steps and approximate times for access to data. Times will vary based on the amount of preparation involved in creating the requested data. See Section 5.1 to 5.2 for contact information.

Section 5

Data Tracking and Security for Limited Access Agreements

The following are requirements for tracking specific data, security, and for maintaining a database using GeneSTAR data.

The GeneSTAR Study presents tracking requirements in its Limited Licensing Agreement. All information is required to be updated annually in the GeneSTAR central core, and an annual updated LAA will be signed until the investigator completes analysis of the GeneSTAR data at which time a termination agreement is signed. All LAA information will be maintained on site in the GeneSTAR core. All operations where the data reside will be known to the GeneSTAR Steering Committee. No study data or information about the study supplied by an individual applicant will be revealed or shared by the GeneSTAR team. The files maintained are for the purposes of assuring secure management of the data in whatever sites they are being maintained.

Submission, Tracking, and Renewal of Applications

Initial inquiries and applications may be submitted to:

Diane M. Becker, MPH, ScD
Professor, Medicine
The Johns Hopkins GeneSTAR Research Program
Division of General Internal Medicine
1830 East Monument Street, Suite 8028
Baltimore, Maryland, 21287
410-955-7781
dbecker@jhmi.edu

Scientific consultations are directed to:

Lewis C. Becker, MD
Robert L. Levy Professor, Cardiology
Halsted 500
The Johns Hopkins Hospital
600 N. Wolfe Street
Baltimore, Maryland 21287
410-955-5997
lbecker@jhmi.edu

Data management and transfer are directed by:

Lisa R. Yanek, MPH
Director, GeneSTAR Analysis Unit
The Johns Hopkins GeneSTAR Research Program
Division of General Internal Medicine
1830 East Monument Street, Suite 8028
Baltimore, Maryland, 21287
410-955-7671
lryanek@jhmi.edu

LAA tracking, changes, annual renewal, record-keeping, and correspondence are to be directed to:

Taryn F. Moy, MS
Director, GeneSTAR Projects
The Johns Hopkins GeneSTAR Research Program
Division of General Internal Medicine
1830 East Monument Street, Suite 8028
Baltimore, Maryland, 21287
410-614-2440
tmoy1@jhmi.edu

Tracking

The Johns Hopkins GeneSTAR Research Program will maintain a confidential hard copy and electronic copy of all Limited Access Agreements, with a spreadsheet of all locations where data are held, the date of the initiation, and the renewal date. Renewal letters will be sent with a new LAA annually until the project is terminated. A Termination Agreement must be submitted when the project is completed and the data are not being used.

Annual Renewal of the LAA is required for Tracking and Monitoring Purposes

The Project Director will maintain all current and former preliminary and Limited Access Agreements, and all such information will be held strictly confidential. All projects that are not currently using the GeneSTAR data must sign the Termination Agreement and indicate with a signature that they have destroyed the raw database. All analytical output and results are the property of the user.

Section 6

Forms and Applications

The following are full copies of the forms required. Downloadable copies are available on the GeneSTAR website.

The GeneSTAR Study requires four forms for access to, monitoring, and termination of the raw data available for public use. These forms are presented in their entirety in the Supplements attached to this document.

Preliminary Application

The preliminary application is a one page document allowing the Study Steering Committee to determine if the request for raw data meets the general criteria for use of the data. The application will be reviewed within two weeks and the Principal Investigator will either receive a series of queries to clarify any concerns or will receive the Limited Access Agreement to process. If the intent is to obtain raw individual level data, even though de-identified, the applicant must have an IRB approval or waiver. Some IRB's have determined that the use of de-identified data does not constitute human subjects research, while others have not. Each applicant organization must determine this with their own IRB and be prepared to provide evidence of a ruling. In the absence of an IRB, Johns Hopkins may agree in unusual circumstances to review the proposal. In general, because the consent forms that were used to obtain the data contain specific language that limits the use of the data, we particularly wish to determine if the request is congruent with the original consents signed by participants.

Limited Access Agreement

The purpose of the LAA is to assure good stewardship and security of the data provided by GeneSTAR participants and fidelity to the consents they provided, even though the data are now fully de-identified. Study ID numbers will be necessary to use the family-based data appropriately so that the identity of an individual is potentially discoverable, although highly unlikely. A master list of ID numbers and names and contact information for participants is maintained in the GeneSTAR Research Program as the cohort study is ongoing. Thus, given this potential, we require that each LAA assure that they will make no attempt to identify subjects or families using the ID numbers provided.

Security of the data is tantamount to the covenant made with participants when they enrolled in the study. We thereby reserve the right to know the resources used to house the data and to analyze them. In addition, we reserve the right to re-analyze data solely for the purposes of assuring accuracy if the results are discordant with our knowledge of the dataset. Johns Hopkins claims no intellectual property rights, nor will it unnecessarily delay any publications or use of the data by more than 60 days should this situation arise. Johns Hopkins also offers a validation service to persons using the data if there are questions about the data after they have been used or analyzed by a requesting investigator. The timeliness of any re-analysis will be dependent on resources available in the study at the time of a request. Johns Hopkins does not however, reserve the right to withhold permission to publish results or to use them for the intended purposes proposed by the investigator.

Annual Renewal

An annual LAA will be sent to the investigator one year after the initial LAA is signed. It must be returned within 30 days or the use of the database will be disallowed. The purpose of this is to maintain high quality tracking of the sites and resources being used for the database. The Johns Hopkins GeneSTAR Steering Committee, requests a written amendment to reflect any change in the sites or any of the resources being used to analyze the data during the year of the LAA. No new proposal may be pursued using the same database without a new LAA. This is again to assure that we maintain fidelity to the consent forms signed by the GeneSTAR participants.

Termination

When the project is terminated, and the data have been published or used in the intended fashion, a termination of the LAA for the use of RAW data will be requested. Results and any analyses performed are the property of the investigators and institution using the data, but the data may not persist in another site for any other use. A new LAA may be submitted for new proposals and the data may be maintained until that new proposal is reviewed and approved.

Section 7

Supplementary Materials

Preliminary Application

Investigators: Please complete this Preliminary Data Use Application. The Study Steering Committee will notify you in writing when your Preliminary Data Use Application is approved and you may then complete a Limited Access Agreement (next section). Scientific and data consultations are available to assist in this process.

Title of Proposed Study

Principal Investigator:
Position *(please attach a biographical sketch)*

Study précis: Please include a brief background, research question and/or aims

Investigators signature_____
Date:_____

Johns Hopkins University

GENESTAR Limited Access Agreement

Agreement for Limited Use of De-identified Phenotype and Genotype Data

Provided and Approved by the Legal Counsel for Office of the Johns Hopkins Vice Dean for Research 2009

Pursuant to the terms and conditions of this Limited Use Agreement ("Agreement"), The Johns Hopkins University ("JH") will disclose certain de-identified genotype and phenotype data maintained by The Johns Hopkins Sibling and Family Heart Study under the GENESTAR and related protocols ("Covered Data") to _____ ("Institution"). The Covered Data may be used by Institution solely as specified in the Data Use Application at Attachment A, and may not be used or re-disclosed except as permitted by this Agreement.

This Agreement must be executed by an official of Institution who has the authority to bind the Institution to the promises and obligations herein. Upon execution by Institution, Qualified Investigators may be designated by Institution and approved by JH as specified in Section 3 below.

1. **General.** GENESTAR genotype and phenotype data are maintained by JH under agreements with the National Institutes of Health and by other sponsors, each of whom have established criteria for maintaining the security, quality, and confidentiality of these data. JH will provide Investigators access to and the right to use these data only under terms and conditions that meet sponsors' criteria. Specifically, GENESTAR data will be provided only in de-identified form for use during a specified period of time by those qualified Investigators who have signed this Agreement.
2. **Study Steering Committee.** The Study Steering Committee consists of Dr. Diane M. Becker, Co-Chair Professor, Medicine; Dr. Lewis C. Becker, Robert L. Levy Professor, Cardiology Co-Chair; Rasika Mathias, ScD, Genetic Epidemiologist, Assistant Professor, Medicine and Epidemiology, Jay Vaidya, MBBS, PhD, MPH, statistician, Assistant Professor, Medicine, Taryn F. Moy, MS, Research Associate, Co-ordinator of Sibling Study and GeneSTAR Projects; and Lisa R. Yanek, Research Associate, Director GeneSTAR Analysis Unit; all of The Johns Hopkins University School of Medicine, 1830 East Baltimore, Suite 8028, Baltimore, Maryland 21287
3. **Qualified Investigators.** Institutions holding a Federal-Wide Assurance approved by the federal Office of Human Research Protections may designate employees to apply for Qualified Investigator status.
    - **a.** Any such investigator must complete the Data Use Application at Attachment A, describing in detail the data elements requested and any proposed analyses, and must submit the Data Use Application and documentation of Institutional Review Board approval (or determination of exemption, if applicable) to the Study Steering Committee.
    - **b.** In Attachment A, the applicant must list every member of the study team who will have access to the data under the applicant's supervision. The applicant and each such study team member must acknowledge their confidentiality obligations by signing Attachment A.

c. The Study Steering Committee will review the completed Attachment A and grant written approval for the Institution to designate an applicant as a Qualified Investigator.

4. **Responsibility** Although this Agreement must be signed by an official of Institution, the Qualified Investigator agrees to review and abide by all of the terms and conditions herein, and to ensure that all data users under Qualified Investigator's supervision understand and abide by the same.

5. **Communications.** All updates to a Qualified Investigator's Data Use Application must be submitted to the Steering Committee in writing.

6. **Duration of Permission**. A Qualified Investigator may use the Covered Data for a period of one (1) year from the date upon which the Study Steering Committee grants written approval of the Qualified Investigator's Data Use Application ("Term of Use"). Extensions of time must be granted by the Study Steering Committee in writing, provided that the Term of Use for a given Qualified Investigator shall expire automatically at the end of three (3) months from the completion of final data analyses for the projects described in the Data Use Application. Absent a written extension, a Qualified Investigator's permission to use the Covered Data will expire at the end of the Term of Use.

7. **Expiration of Permission**. Upon expiration of the Term of Use for a given Qualified Investigator, or termination of this Agreement for any reason, a Qualified Investigator will delete or destroy all copies of the Covered Data that exist in any medium, including but not limited to all paper and electronic copies, or return all such copies to the Study Steering Committee. Under no circumstances may a Qualified Investigator or the Institution retain a copy of the Covered Data beyond the end of any Term of Use applicable to those Covered Data.

8. **Scope of Permitted Uses and Disclosures**. One copy of the Covered Data may be created by the Qualified Investigator. During the Term of Use, the original Covered Data supplied by JH (if applicable) and this one copy may be stored as specified in the approved Data Use Application. Neither the Qualified Investigator nor the Institution may make or store any other copies of the Covered Data.

    a. The Covered Data may be used solely for scientific and academic purposes. No use of the Covered Data or any subset or derivative of the Covered Data may be made for commercial purposes. The Covered Data (including any subset of the Covered Data) may not be sold, reproduced, distributed, or stored in any limited access or public access retrieval system.

    b. The Institution and the Qualified Investigator agree to take all reasonable precautions to ensure that no one with access to the Covered Data will undertake or permit any attempt, by any direct or indirect means (including unauthorized access to electronic systems) to use the Covered Data for an unauthorized purpose, to re-identify subjects of the Covered Data, or to obtain a listing of subjects' identities.

    c. JH, at its discretion, may terminate this Agreement immediately upon learning of any unauthorized disclosure of Covered Data or attempt to re-identify the subjects of the Covered Data.

d. Neither the Covered Data nor the results of any analyses of the Covered Data may be published, presented, referenced, or included in any grant application without the prior written permission of the Study Steering Committee.

e. Pursuant to restrictions contained in the consent forms signed by subjects of the Covered Data, all analyses of Covered Data must pertain to cardiovascular disease or related factors.

9. **Authorized Users, Confidentiality**. Only those persons who have signed an approved version of the Data Use Agreement may access or use the Covered Data, except as provided herein.

    a. Institution may grant access to Covered Data, to the extent reasonably necessary, to those Institution personnel who must review the Covered Data to fulfill research oversight responsibilities or to maintain Institution's electronic systems. If Institution engages contractors or other third parties to perform these functions, the Institution will bind those contractors or third parties to the restrictions upon use and disclosure of Covered Data that apply to Institution under this Agreement.

    b. If Institution believes that it is required by law to disclose the Covered Data to any third party not specified herein, Institution shall provide JH reasonable prior notice of the disclosure and an opportunity to resist the disclosure or seek legal protection for subjects' identities.

10. **Location of Data**. The Data must be stored and secured in the manner described in the approved Data Use Application. The Qualified Investigator must provide the Study Steering Committee written notice of any change in the location or storage of the Covered Data or change in security or privacy protections for the Covered Data within three (3) business days. At its discretion, the Study Steering Committee may terminate this Agreement upon learning of any changes that decrease the privacy or security of Covered Data.

11. **Property Rights.** Neither Institution nor any Qualified Investigator or study staff member shall have any right, title, or ownership interest in the Covered Data. All rights, title, and interests in the Covered Data shall belong to JH. Institution and each Qualified Investigator and study staff member agree that none of them shall claim or attempt to exercise any right, title, or interest in the Covered Data, except for the limited right to use the Covered Data strictly as permitted in the approved Data Use Application.

12. **Results.** Institution and Qualified Investigators agree to share the results of any analyses of the Covered Data with the Study Steering Committee within three (3) months of completion of final analyses and prior to the drafting of any manuscript or presentation containing such analyses.

    a. At its discretion, the Study Steering Committee may require the Qualified Investigator to permit the Johns Hopkins Sibling and Family Heart Study biostatisticians to replicate the results of any analyses prior to granting permission to the Investigator to publish, present, or disclose any results.

    b. Institution and Qualified Investigator agree to notify the Study Steering Committee immediately and in writing of any result that may be relevant to the

health or health care of current or future participants. At the discretion of the Study Steering Committee, such information may be communicated to the reviewing IRB, study participants, or sponsors.

13. **Termination.** JH may terminate this Agreement immediately upon learning of a breach of any of its terms and conditions. Institution may terminate this Agreement at any time by notifying the Study Steering Committee in writing, and by destroying, deleting, or returning all Covered Data to JH. The parties agree that JH may pursue an injunction or any other available legal remedy to enforce the terms of this Agreement against Institution, any Qualified Investigator, any study team member, or any other user of Covered Data.
14. **Assignment.** This Agreement may not be assigned without the prior written permission of JH.
15. **Waiver.** No delay in acting or failure to act shall constitute a waiver of any right or obligation under this Agreement. Any waiver of such right or obligation must be in writing and signed by the Institution and a representative of the Study Steering Committee.
16. **Governing Law.** This Agreement shall be governed by the laws of the State of Maryland. Any dispute shall be brought in the state or federal courts of Maryland.
17. **Indemnification.** Institution shall indemnify and hold harmless JH, The Johns Hopkins Hospital, and their respective employees, agents, faculty, staff, students, trustees, and board members, as well as any of their successors or assigns ("JH Indemnitees"), for any costs or losses arising out of the use or non-use of Covered Data by Institution, including by any Qualified Investigator or study team member or any third party who obtains Covered Data from Institution.
18. **Liability.** IN CONSIDERATION OF JH'S AGREEMENT TO RELEASE COVERED DATA, INSTITUTION, ON BEHALF OF ITSELF AND ITS EMPLOYEES, AGENTS, FACULTY, STAFF, STUDENTS, TRUSTEES, AND BOARD MEMBERS, AND ANY OF THEIR SUCCESSORS OR ASSIGNS, HEREBY VOLUNTARILY WAIVES ALL CLAIMS AND RELEASES AND DISCHARGES JH, THE JOHNS HOPKINS HOSPITAL, AND THEIR RESPECTIVE FACULTY, STAFF, EMPLOYEES, AGENTS, HEIRS, SUCCESSORS, AND ASSIGNS, FROM ANY AND ALL LIABILITY FOR ANY CLAIM, DAMAGE, OR LOSS ARISING OUT OF THE USE OR NON-USE OF THE COVERED DATA FOR ANY PURPOSE WHATSOEVER.

As a duly authorized official of Institution, I hereby agree that Institution shall be bound to the terms and conditions of this Agreement.

_____

Signature

_____

Printed Name and Title

_____

Date

LAA: Attachment A

Data Use Application-*may also be used to update renewals*

Investigators: Please complete this Data Use Application and obtain the signature of every study team member who will have access to the Covered Data. Return the signed Data Use Application to the Study Steering Committee.

The GeneSTAR Study Steering Committee will notify you in writing when your Data Use Application is approved and you have permission to use the Covered Data.

1. Title of Proposed Study and Protocol Number:
   _____
   _____

2. List any co- Investigators who will be managing or analyzing, or interpreting data (note, if not an employee of Institution, the co-investigator's home institution must execute the Limited Use Agreement).
   _____
   _____
   _____
   _____

3. Please list all other persons who will have direct access to the data, and indicate their roles in the study (e.g., data management, data analysis, technical support, other)

_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____

4. IRB Approval: Yes □ No□ NIH IRB Assurance Number _____

Date ___/___/___

Attached Yes □ No □

If there is no IRB approval from the Institution, please explain its absence (if the IRB has determined project is exempt, please attach letter of documentation):

Data Storage and Data Management: All applicants retaining the data (JHPD and/or JHGD)

Describe how Covered Data will be PROCESSED AND MAINTAINED

Please complete the following for each physical site where Covered Data will be processed, maintained, or analyzed:

Name of Site	Address/ Room Number	Locked (Yes, No) Form of Lock	Persons with Access

Will these data and/or analytic output be stored on any additional CPUs maintained by individuals?

Yes No If Yes, please list with address

Name of Individual	Address/ Room Number	Locked (Yes, No)	Persons with Access

Please list the following information about any processing units (laptops, desktops and or servers) used in the analysis, storage, or management of the Covered Data

Name of Unit	Manufacturer Serial Number	Operating System (s)	Security	Room Number	Back-up	Maintenance and who supplies

5. Attach 1 page aims or research questions or grant abstract.

6. List data elements required and specific aims of the proposed research:

_____
_____
_____

7. Acknowledgment of Obligations: Each of the undersigned has read the Limited Use Agreement and agrees to abide by the terms and conditions thereunder:
   - Principal Investigator: _____

     [DATE] _____
   - Co-Investigators:

     _____
     _____
     _____ [DATE] _____
   - Other study staff listed in this Data Use Application:

     _____
     _____
     _____
     _____
     _____

     [DATE]_____

APPROVAL:

Upon review of this Data Use Application, the undersigned approve the applicant as a Qualified Investigator and agree to permit applicant and all listed personnel to use and disclose data for the limited purposes described in this Application, subject to the terms and conditions of the Limited Use Agreement.

Please note that the permitted Term of Use expires one (1) year from the date indicated below. The Qualified Investigator must request any extension in writing. All changes or updates to this Data Use Application must be submitted in writing for the prior approval of the Study Steering Committee.

REVIEWED AND APPROVED:

Date ____/____/_____ (mm/dd/yy)

_____

Steering Committee Chair, Lewis C. Becker, MD

_____

Steering Committee, Co-Chair, Diane M. Becker, MPH, ScD

_____

Steering Committee, Lisa R. Yanek, MPH

_____

Steering Committee, Rasika Mathias, ScD

_____

Steering Committee, Jay Vaidya, MBBS, PhD, MPH

_____

Steering Committee, Taryn F. Moy, MS

Annual Renewal Form

Title of Study and Protocol Number:

_____

_____ Date:_____

Principal Investigator:

In the past year, has there been-

Any change in the IRB for the use of the database since the last approval. _____ No _____ Yes

If yes, please provide a copy of the most recent IRB changes.

Any change in the proposed use of the data beyond their original intent. _____ No _____ Yes*

If yes, please complete Attachment A of the main LAA again for adjudication.

Any change in the sites or computer resources used for the database. _____ No _____ Yes*

If yes, please complete the relevant sections of Attachment A of the original LAA.

Have any data been used in a publication, presented at a national meeting, or served as the substrate for a grant application. _____ No _____ Yes*

If yes, please list below:

_____

_____

_____

APPROVAL:

Upon review of this Data Use Application Renewals, we agree to permit the investigator to use and disclose data for the limited purposes described in the original Application, and any subsequent approved changes subject to the terms and conditions of the Limited Use Agreement.

Please note that the permitted Term of Use expires one (1) year from the date indicated below. The Qualified Investigator must request any extension in writing. All changes or updates to this Data Use Application must be submitted in writing for the prior approval of the Study Steering Committee.

RENEWAL REVIEWED AND APPROVED:

Date ____/____/_____ (mm/dd/yy)

_____

Steering Committee Chair, Lewis C. Becker, MD

_____

Steering Committee, Co-Chair, Diane M. Becker, MPH, ScD

Termination

Termination of Data Use

Title of Study and Protocol Number:

_____

Principal Investigator:_____

Date:_____

Any change in the IRB for the use of the database since the last approval. _____ No _____ Yes*

If yes, please provide a copy of the most recent IRB changes.

Any change in the proposed use of the data beyond their original intent. _____ No _____ Yes*

If yes, please describe:

Have any data been used in a publication, presented at a national meeting, or served as the substrate for a grant application. _____ No _____ Yes*

If yes, please list below:

_____

_____

_____

I hereby certify that all RAW data associated with this application/study have been eliminated from all sites at the research organization and no longer exist on any computer or storage device(s), nor do any of the analysts or IT team have access to any GeneSTAR raw data any longer. Only results and aggregate analyses remain in our possession.

Signature of the Principal Investigator_____

Date:_____

TERMINATION REVIEWED AND APPROVED:

Date ____/____/_____ (mm/dd/yy)

_____

Steering Committee Chair, Lewis C. Becker, MD

_____

Steering Committee, Co-Chair, Diane M. Becker, MPH, ScD

Logged in:

_____ Date:_____

Taryn F Moy, MS, GeneSTAR Project Director
Annual Renewal Approval

Addendum to the Data Use Certification Agreement
Modification of Data Security Terms and Best Practices

Effective for all dbGaP Data Access Requests submitted on or after March 23, 2015,
Section 6 of the Data Use Certification Agreement is replaced in its entirety by the following:

6. Data Security and Data Release Reporting

The Requester and Approved Users, including the institutional IT Director, acknowledge NIH's expectation that they have reviewed and agree to manage the requested dataset(s) according to the current NIH Security Best Practices for Controlled-Access Data Subject to the GDS Policy and the institutional IT security requirements and policies, and that the institution's IT security requirements and policies are sufficient to protect the confidentiality and integrity of the NIH controlled-access data entrusted to the Requester.

If approved by NIH to use cloud computing for the proposed research project, as outlined in the Research and Cloud Computing Use Statements of the Data Access Request, the Requester acknowledges that the IT Director has reviewed and understands the cloud computing guidelines in the NIH Security Best Practices for Controlled-Access Data Subject to the GDS Policy.

Requesters and PIs agree to notify the NHLBI DAC of any unauthorized data sharing, breaches of data security, or inadvertent data releases that may compromise data confidentiality within 24 hours of when the incident is identified. As permitted by law, notifications should include any known information regarding the incident and a general description of the activities or process in place to define and remediate the situation fully. Within 3 business days of the NHLBI DAC notification, the Requester, through the PI and the Institutional Signing Official, agree to submit to the NHLBI Data Access Committee a detailed written report including the date and nature of the event, actions taken or to be taken to remediate the issue(s), and plans or processes developed to prevent further problems, including specific information on timelines anticipated for action.

All notifications and written reports of data security incidents should be sent to:
NHLBI Data Access Committee URGENT: nhlbigeneticdata@nhlbi.nih.gov
GDS mailbox: gds@mail.nih.gov

NIH, or another entity designated by NIH may, as permitted by law, also investigate any data security incident. Approved Users and their associates agree to support such investigations and provide information, within the limits of applicable local, state, and federal laws and regulations. In addition, Requesters and Approved Users agree to work with the NHLBI and NIH to assure that plans and procedures that are developed to address identified problems are mutually acceptable and consistent with applicable law.

Addendum to the Data Use Certification

Effective for all dbGaP study datasets registered prior to July 31, 2013

- Annual Data Use Reports will no longer be submitted by email to the relevant Data Access Committee(s) (DACs), as stated in the Data Use Certification(s) associated with the datasets you are requesting.

- Principal Investigators are now expected to submit online research progress updates through the dbGaP system, as part of the annual renewal process or close-out process.