

Genome-Wide Association Studies

A Genome-Wide Association Study (GWAS) is defined as “any study of genetic variation across the entire human genome that is designed to identify genetic associations with observable traits (such as blood pressure or weight), or the presence or absence of a disease or condition”. Whole genome information, when combined with clinical and other phenotype data, offers the potential for increased understanding of basic biological processes affecting human health, improvement in the prediction of disease and patient care, and ultimately the realization of the promise of personalized medicine.

When funded by NIH, the data obtained in Genome-Wide Association Studies must be deposited in the NIH GWAS repository.

The NIH GWAS policy provides detailed requirements for GWAS data submission and GWAS data access. The process for data submission and data access differ substantially and requirements for each are summarized below.

GWAS DATA SUBMISSION AND ACCESS

Overview of Differences in Submission and Access

Data Submission

Requires IRB approval and IO signature

Data Access (*general process applicable to majority of requests*)

Data access requires signature of USC SO and application to (and approval from) NIH Data Access Committee

Data Access (*for selected datasets requiring IRB approval*)

Data access for selected datasets requires IRB approval, USC SO signature and application to (and approval from) NIH Data Access Committee

Data Submission

All investigators who receive NIH funds to conduct genome-wide analysis of genetic variation in a study population must include in their protocol a description of the PI's plan to submit study data to the GWAS repository and to maintain data confidentiality.

Investigator Responsibilities

Investigators submitting GWAS data are expected to:

- Provide descriptive information about their studies
- Describe which data will be shared and when
- Submit coded genotypic and phenotypic data to the GWAS data repository
- Submit certification by the USC Institutional Official (IO) indicating approval of data submission to the NIH GWAS repository

- To obtain IO certification, investigators must provide complete information in the IRB application (iStar sections 9.6 and 9.6.1) which will trigger a request for IO certification

IRB Responsibilities

The USC IRB must review GWAS as applicable, and verify that:

- the submission of data to the NIH GWAS data repository and subsequent sharing for research purposes are consistent with the informed consent of study participants from whom the data were obtained
- the investigator's plan for de-identifying datasets is consistent with the standards outlined in the [NIH policy](#)
- it has considered the risks to individuals, their families, and groups or populations associated with data submitted to the NIH GWAS data repository
- the genotype and phenotype data to be submitted were collected in a manner consistent with 45 C.F.R. Part 46

Note: the NIH will not accept data into their GWAS repository without proof of IRB review and approval.

Institutional Official Responsibilities

All submissions to the repository should be accompanied by a certification by the Institutional Official (IO) stating the IO approves submission to the NIH GWAS data repository.

The certification should verify that:

- The data submission is consistent with all applicable laws and regulations, as well as institutional policies
- The appropriate research uses of the data and the uses that are specifically excluded by the informed consent documents are delineated
- The identities of research participants will not be disclosed to the NIH GWAS data repository

Institutional Official Approval Memo

Once a GWAS study is approved by the IRB and the informed consent declarations are made, the IRB Chair forwards the information request to the Office for the Protection of Research Subjects (OPRS) Director. The OPRS Director assures the approval memo is complete and that the informed consent information has been included and forwards it to the Institutional Official for review, signature, and distribution. Electronic copies of the approval will be sent to the investigator, HSIRB Director, and OPRS office. HSIRB staff will upload the electronic copy to the study in the iStar system.

Data Access

Investigators and institutions seeking data from the NIH GWAS data repository will be required to meet data security measures (such as physical security, information

technology security, and user training) and will be asked to submit a data access request, including a Data Use Certification agreement, that is co-signed by the investigator and the designated Signing Official through the Data Access Request application (see below).

If you would like to access data in the GWAS repository in connection with research you are conducting or intending to conduct, please contact the [Office of Compliance](#) as soon as feasible by clicking on the attached link or by calling (213) 740-2500.

Generally, access to GWAS data does not require IRB approval. However, some data sets specifically require IRB approval (e.g., Framingham SHARe study). Investigators can determine when IRB approval is required for a study by checking the study description in the GWAS database, [dbGaP](#). If access to data requires IRB approval, investigators can submit a coded specimens application through iStar. Furthermore, if a full board or expedited IRB review is required, investigators should contact the IRB.

Data Access Request

To submit a Data Access Request (DAR), investigators must complete the NIH SF 424 (R&R) form. To complete the form, investigators must have an NIH eRA Commons account which is the same account used to apply for NIH grants (refer to the end of this section for links to the NIH SF 424 form and eRA Commons).

Completion of the DAR application involves designating a Signing Official (SO). To do this, investigators must select USC's SO, Contracts and Grant Executive Director Jerry Muniz, from the propagated list in DAR section 19.

Data access requests should include a brief description of the proposed research use of the requested GWAS dataset(s). The Data Use Certification requires that investigators agree to:

- Use the data only for the approved research
- Protect data confidentiality
- Follow appropriate data security protections
- Follow all applicable laws, regulations and local institutional policies and procedures for handling GWAS data
- Not attempt to identify individual participants from whom data within a dataset were obtained
- Not sell any of the data elements from datasets obtained from the NIH GWAS data repository
- Not share with individuals other than those listed in the request any of the data elements from datasets obtained from the NIH GWAS data repository
- Agree to the listing of a summary of approved research uses within the NIH GWAS data repository along with his or her name and organizational affiliation
- Agree to report, in real time, violations of the GWAS policy to the appropriate DAC
- Acknowledge the GWAS policy with regard to publication and intellectual property

- Provide annual progress reports on research using the GWAS dataset

Data Access Committees will review requests for access to determine whether the proposed use of the dataset is scientifically and ethically appropriate and does not conflict with constraints or informed consent limitations identified by the institutions that submitted the dataset to the NIH GWAS data repository. In the event that requests raise concerns related to privacy and confidentiality, risks to populations or groups, or other concerns, the DAC will consult with other experts as appropriate.

Note: IRBs are not involved in the transaction between PI and SO or PI and DAC.

Investigator Responsibilities

At USC, investigators requesting and receiving GWAS data are expected to:

- Complete a data access request, including a Data Use Certification
- Protect data confidentiality
- Ensure that data security measures are in place
- Notify the appropriate Data Access Committee of policy violations
- Submit annual progress reports detailing significant research findings to the GWAS DAC

Generally, access to GWAS data does not require IRB approval. However, some data sets specifically require IRB approval (e.g., Framingham study). Investigators can verify if IRB approval is required for a study by checking the study description in the GWAS database, [dbGaP](#). If access to data requires IRB approval, investigators can submit a coded specimens application through iStar. Furthermore, if a full board or expedited IRB review is required, investigators should contact the IRB.

IRB Responsibilities

Generally, IRB review is not required for research utilizing data from the GWAS repository.

However, on rare occasions, GWAS datasets stipulate IRB approval. When this occurs, PIs can submit an application for coded specimens through iStar. If use of a dataset specifically stipulates full board or expedited IRB review, investigators will contact the IRB to discuss the best course of action.

Signing Official Responsibilities

After the PI completes the data access request, the Signing Official (SO) will be notified by email. The SO will review the request and will have the option to edit the application, return the form to the PI for revision or sign off and validate the submitted application.

The data access request is then reviewed by the appropriate Data Access Committee at NIH, and both the PI and SO will be notified by email of approval or disapproval.

GWAS PUBLICATION RIGHTS

The NIH expects that investigators who contribute data to the NIH GWAS data repository will retain the exclusive right to publish analyses of the dataset for a defined period of time following the release of a given genotype-phenotype dataset through the NIH GWAS data repository (including the pre-computed analyses of the data). During this period of exclusivity, the NIH will grant access through the DACs to other investigators, who may analyze the data, but are expected not to submit their analyses or conclusions for publication during the exclusivity period. The maximum period of exclusivity is twelve months from the date that the GWAS dataset is made available for access through the NIH GWAS data repository, although a shorter period of exclusivity may be determined by the NIH funding IC.

The NIH expects all investigators who access GWAS datasets to acknowledge the Contributing Investigator(s) who conducted the original study, the funding organization(s) that supported the work, and the NIH GWAS data repository in all resulting oral or written presentations, disclosures, or publications of the analyses.

Additional GWAS guidance can be accessed in the following links:

NIH Office of Extramural Research website

<http://grants.nih.gov/grants/gwas/index.htm>

Policy for Sharing of Data in NIH Supported or Conducted GWAS

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-088.html>

Database of Genotypes and Phenotypes (dbGaP)

<http://www.ncbi.nlm.nih.gov/gap>

Form SF 424 (R&R) – necessary to request access to GWAS repository data
424R&R link

Form SF 424 (R&) Application Guide

http://grants.nih.gov/grants/funding/424/SF424_RR_Guide_General_Adobe_VerB.pdf

dbGaP FAQ Archive

<http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=helpdbgap>