POLICY AND PROCEDURES FOR DATA SUBMISSION TO THE NIH DATABASE OF GENOTYPES AND PHENOTYPES ("dbGaP")

POLICY STATEMENT

The NIH Genome-Wide Association Studies ("GWAS") Policy requires that any GWAS data obtained with NIH support be submitted to the NIH GWAS data repository. All submissions to the NIH GWAS data repository, database of Genotypes and Phenotypes ("dbGaP"), whether required or voluntary, must include a certification by the responsible Institutional Official(s) of the submitting institution that the submission of data to the dbGaP is appropriate and consistent with the NIH GWAS Policy. At Harvard, the Institutional Official of the relevant IRB\(^1\) provides this certification. This policy statement contains guidance that outlines the responsibilities of the Harvard investigator, the relevant IRB, and the Institutional Officials in submitting, reviewing and providing the required Institutional Certification for a submission to dbGaP.

APPLICABILITY

The NIH GWAS Policy applies to all Harvard investigators who:

- Have obtained National Institutes of Health ("NIH") funds on or after January 25, 2008 to conduct Genome-Wide Association Studies ("GWAS");
- Plan to voluntarily submit any genotype/phenotype data into dbGaP, or
- Plan to access data from dbGaP, regardless of funding source.

The NIH GWAS Policy also applies to the relevant Harvard IRBs and Institutional Officials.

Investigator Responsibilities:

- Under the NIH GWAS Policy, Harvard investigators are responsible for developing a data sharing plan describing:
  - The consistency of informed consent with submission to the NIH GWAS data repository and subsequent sharing with other researchers for other research projects,
  - How informed consent will be obtained for prospectively collected samples and data, and
  - How data will be subsequently de-identified prior to submission to dbGaP;

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\(^1\)The relevant IRB is the Harvard IRB that reviews research proposals from the PI’s School. For Faculty of Arts and Sciences, this is the Committee on the Use of Human Subjects, for Harvard School of Public Health and Harvard Medical School, this is the Longwood IRB.
IRB Responsibilities:

- Harvard IRBs must review the Harvard investigator’s plans for data submission and verify that:
  - The submission of data to dbGaP and subsequent sharing for research purposes is 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 GWAS policy,
  - The risks of further research on the GWAS data to particular individuals, their families, and groups or populations (e.g., stigmatization) has been considered and minimized, and
  - The genotype and phenotype data to be submitted were collected in compliance with 45 CFR 46.

Institutional Official Responsibilities:

- After IRB review and verification that submission of the data to dbGaP and the subsequent sharing for research purposes are consistent with the informed consent of study participants and with NIH GWAS policy, the Institutional Official provides a certification letter, verifying that:
  - The data submission is in compliance 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 consent documents are delineated, and
  - The identities of research participants will not be disclosed to dbGaP.

**Definitions**

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 or the presence or absence of a disease or condition.

**dbGaP** is NIH’s GWAS databank for genotypic and phenotypic data. dbGaP contains only data, not specimens.

The human **genome** is all the DNA contained in an organism or a cell, including both the DNA comprising chromosomes within the nucleus and the DNA in mitochondria.

**Institutional Officials:** At Harvard, the Institutional Officials include the University Chief Research Compliance Officer, for the University Area IRB and the Institutional Officials for the HSPH and HMS IRBs.

**Phenotype data** are data on health conditions, behavioral characteristics, or measurable observable traits (such as blood pressure, alcohol consumption, cholesterol, or eye color) that are obtained during physical
or psychological examinations and maintained in a medical or research record. Phenotype data may also include information about medical treatments, drug tolerance, and family medical history as well as responses to questionnaires.

**NIH GWAS Data Sharing Policy:** (“GWAS Policy”) is the policy that GWAS data obtained with NIH support should be shared through a central repository when such data sharing is compatible with the consent provided by the participant. It can be found at: [http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-088.html](http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-088.html).

**Relevant IRB:** the Harvard IRB that reviews research proposals from the PI’s School.

**Retrospective studies:** Studies that are using pre-existing genetic materials and previously collected data. IRBs are expected to determine whether the initial consent process under which the pre-existing genetic materials and data were obtained is consistent with the submission of data to the NIH GWAS repository and sharing of data, and also is in accord with the GWAS policy.

**Prospective studies:** Studies performed in which GWAS was part of the study design at the time research participants provided their consent for phenotype data and samples to be collected for the study. The consent form and process must comply with the requirements of 45 CFR, Part 46 and any other applicable law. The informed consent process and document should state that participants’ DNA will undergo genome-wide analysis and that genotype and phenotype data will be shared for research purposes through the NIH GWAS data repository.

**PROCEDURES**

- For Institutional Certification of a data submission to dbGaP, a Harvard investigator must first submit to the relevant IRB a research summary that includes:
  - A research protocol, including:
    - A description of all data fields (genotype and phenotype) being submitted to dbGaP
    - A copy of the consent form(s) used to enroll participants and collect their samples and phenotype data.
  - For data submissions where the Harvard investigator is submitting data to dbGaP where Harvard was not the IRB of record on the protocol under which the original samples and phenotype data were collected:
    - The IRB may request dbGaP certification from the IRB of record, in lieu of the original consents, as long as the institution where the IRB of record is located has a Federalwide Assurance (‘FWA’).
    - If the institution where the IRB of record is located does not have an FWA, the IRB will review the consent forms in accordance with the procedures outline below, in the section entitled **IRB Review**
and Verification.

- A description of the method(s) used to code identifiers associated with the data for transmission to dbGaP and how the key linking the identity of each study participant will be maintained.
  - A written statement by the Harvard investigator that the key to identifiers of study participants will never be shared by the Harvard investigator with NIH

- IRB Review and Verification: For any proposed submission of phenotype data and genotype data to dbGaP, the relevant IRB will review the research protocol and consents provided by the PI to determine whether:
  - The Common Rule and HIPAA Privacy Rule standards for de-identification have been met;
  - The de-identified data is assigned a random, unique code and the code key will not be shared with NIH;
  - The risks of further research on the GWAS data to particular individuals, groups, or populations (e.g., stigmatization) has been considered and minimized; and
  - Specimens and data were, or will be, collected in compliance with 45 CFR 46 and any other applicable federal or state law.

  - Data from Retrospective studies in which Harvard is the IRB of record: the appropriate Harvard IRB will determine whether each relevant version of the consent form is consistent with submission of genotype and phenotype information into dbGaP.
    - In reviewing this requirement, the IRB may consider the following questions:
      - Do the consent documents identify future research use of the specimens or data?
      - Do the consent documents address disposal of the specimens or data?
      - Do any of the consent forms contain statements such as “your data/specimens will not be shared” or “will only be seen by the research team?”
      - Were any of the contributors of specimens children?
      - Did the original consent forms limit future use to specific projects, conditions, disease states, or to non-commercial research?
      - Were any of the phenotype data (e.g., medical record information) collected under a waiver of consent?

  - Data from Prospective studies in which Harvard is the IRB of record: In addition to the considerations listed above, for the submission of GWAS data on prospectively collected specimens the appropriate Harvard IRB may consider:
    - Whether the consent documents adequately explain genetic testing, heritable traits, DNA, genes, or genotyping?
Additionally, the consent form(s) for prospective studies must:

- Describe the GWAS repository, broad data sharing, and the risks associated with these research activities, and
- Describe the likelihood of re-identification in the future.

**IRB determination:** After reviewing the research protocol, data sharing plan, and the relevant consents, the IRB may determine the following:

- That the consent form(s) and information reviewed (including all relevant materials) is consistent with the proposal to submit to dbGaP;
- That the consent form(s) and information reviewed (including all relevant materials) is not consistent with the proposal to submit to dbGaP; (note: reasons supporting this would include, but not be limited to, the fact that original consent was obtained with a waiver)
- That the consent form(s) and information reviewed (including all relevant materials) is not consistent with the proposal to submit to dbGaP, but that an attempt to cure the deficiency is appropriate. Therefore, as a condition for submission, the IRB may:
  - Require revision of the consent form(s) to be consistent with a submission of data to dbGaP with re-consent of the research participants;
  - Permit the submission, but subject to certain restrictions or limitations on use, as the relevant Harvard IRB may specify; or
  - Request additional information, as necessary;

**INSTITUTIONAL CERTIFICATION**

Once the IRB review is complete, the relevant IRB will forward the GWAS form letter with the IRB determination for signature by the IRB’s Institutional Official. Signed letters will be sent to the Harvard investigator via email, who must then send it to NIH to satisfy the requirements of the NIH GWAS policy for a submission of data to dbGaP.

**CONTACTS AND SUBJECT MATTER EXPERTS**

The Office of the Vice Provost for Research: [http://www.vpr.harvard.edu](http://www.vpr.harvard.edu)
CUHS IRB: [http://cuhs.harvard.edu/](http://cuhs.harvard.edu/)