

Chapter 15

Biomedical Research

This chapter discusses special types of biomedical research and additional requirements for investigators conducting these types of research.

15.1 Chart Reviews / Case Studies

Chart Reviews

Reviewing medical charts or records for research purposes requires IRB review and approval. This is true even if all the medical records are from patients of the investigator. The IRB will review chart review research under the exempt or expedited review categories. The level of IRB review depends on the nature of the data collected, if any identifying information is recorded, and whether study data already exist (retrospective) or will be created in the future (prospective). In the iStar application, investigators are asked to provide the range of dates for the data and a list of the specific data fields that will be extracted from medical records.

The IRB may authorize a waiver of informed consent for chart review research when the following criteria are met:

- The study involves no more than minimal risk to participants
- The waiver will not adversely affect the rights and welfare of participants
- The research could not practicably be carried out without the waiver
- When applicable, participants are provided with additional pertinent information after participation.

The IRB may also waive the requirement for a Health Insurance Portability and Accountability Act (HIPAA) authorization for chart review research if the [following criteria are met](#):

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1. The use or disclosure of protected health information involves no more than minimal risk to the privacy of individuals, based on, at least, the presence of the following:
 - a. An adequate plan to protect the identifiers from improper use and disclosure
 - b. An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or retention is required by law
 - c. Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of protected health information is permitted
2. The research could not practicably be conducted without the alteration or waiver or alteration
3. The research could not practicably be conducted without access to and use of the protected health information.

HIV test results cannot be recorded for chart review research conducted under a waiver of HIPAA authorization. For more information, refer to [Section 11.5 – Health Insurance Portability and Accountability Act \(HIPAA\)](#).

Case Studies

In socio-behavioral research, case studies are reports about experiences or observations associated with up to three individuals. Medical case studies involve reports of up to three patients identified in the course of clinical care. Reports from individuals receiving investigational drugs or devices or other situations that require FDA oversight cannot be included in case studies.

Case studies normally do not require IRB review because they do not meet the definition of research (they are not generalizable). However, if a series of subject observations are collected to allow possible extrapolation of the results to a larger population, the case

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studies may be generalizable. At USC, the collection of data from **more than three** individuals is considered to be human subjects research and must be submitted to the IRB.

HIPAA regulations apply to collection of protected health information for the purpose of a case study, even though the case study does not require IRB review. A HIPAA authorization form specifically for case studies is available at http://oprs.usc.edu/files/2013/01/USC_HIPAA_Case_Report.pdf. Additional information on HIPAA is available in [Section 11.5 – Health Insurance Portability and Accountability Act \(HIPAA\)](#).

15.2 Specimens (Human Biological Materials)

Human biological materials include blood, urine, saliva, hair, nails, cells, tissue samples (fresh, frozen, or paraffin blocks), other body fluids or tissues, and molecules derived from these materials. Common sources of specimens used in research include:

- Specimens to be collected specifically for a research project
- Specimens collected during previous research projects
- Stored (archived) tissue from diagnostic testing or surgery
- Tissue that is discarded during routine medical care
- Specimens obtained from repositories at USC or outside Institutions
- Specimens purchased from commercial tissue banks

The use of human biological materials in research requires review by the IRB. The level of review depends on the potential risks to participants, how the specimens were collected or will be collected, and what information is associated with the specimens. Some specimen research may require Full Board review, other research may qualify for expedited review, and some research may be granted exempt status. Refer to [Chapter 7 – Types of IRB Submissions](#) for the expedited and exempt review categories that specifically refer to specimens. The IRB makes the determination about the appropriate review type, not the investigator.

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Specimen research involves the potential risk of loss of confidentiality. The level of risk is determined by the type of information obtained with the specimen. Specimens are generally labeled in one of three ways:

- **Identified:** The specimen is directly labeled with personal identifying information (such as a name, patient number, or medical record number)
- **Coded:** The specimen is labeled with a code that researchers can link to personal identifying information
- **Anonymous:** The specimens are not labeled with direct identifiers or a code; researchers cannot retrieve any personal identifying information

Specimens that are truly anonymous carry no risk of loss of confidentiality. Specimens that have direct identifiers carry the greatest risk of loss of confidentiality. Whenever possible, investigators should obtain anonymous or coded specimens to minimize potential risks.

Investigators who obtain coded specimens but do not hold the link to identifiers and cannot obtain identifiable information about the participants are not conducting human subjects research. At USC, investigators are still required to submit this type of research to the IRB using the “Coded Specimens/Data” review category in the iStar application. More information on research involving coded specimens is available in the [OHRP Guidance on Research Involving Coded Private Information or Biological Specimens](#).

Research that uses only cadaver specimens is not considered human subjects research under federal regulations. Research that uses only anonymous specimens is also not considered human subjects research. Investigators conducting research on these types of specimens do not need to submit the research to the IRB.

Newborn Dried Bloodspots

The Newborn Screening Saves Lives Reauthorization Act of 2014 explicitly states that the use of newborn dried bloodspots for research is considered to involve human subjects if the research is federally supported and the bloodspots are collected on or after March 18, 2015. The identifiability (or not) of the bloodspots is irrelevant. In other words, if a researcher is receiving de-identified or anonymous bloodspots for research, the research is considered to involve human subjects. A detailed summary of recommendations is provided by the U.S. Department of Health and Human Services, Secretary’s Advisory Committee on Human Research Protection (SACHRP). The goal of this recommendation

is to provide thoughtful consideration of this act and allow for important research to take place. Refer to: <https://oprs.usc.edu/files/2016/05/SACHRP-Newborn-Dried-Bloodspots.docx>

Retaining Specimens for Future Research

If specimens obtained in a study will be retained for future use in other studies, the informed consent form must disclose this to participants. The consent form should describe who might have access to specimens and information in the future, the potential purposes of the future specimen research, how participants can request destruction or removal of their specimens from future research use, and whether there are plans to compensate participants if a commercial product is developed from use of their specimens. Participants should be given the opportunity to opt out of storing samples for future research.

Material Transfer Agreements (MTAs)

Transfer of materials among collaborators requires the use of **Material Transfer Agreements (MTAs)**. MTAs ensure USC's rights are protected when specimens or reagents are shared with colleagues or private entities.

An MTA is a research contract between a provider and recipient of research materials which governs the terms and conditions under which the material may be used. An MTA protects the intellectual and other property rights of the provider and generally addresses:

- Limits on the use of the research materials, inventions, and results
- Prohibitions on the redistribution of the material
- Conditions of use, including prohibitions of use in animals or humans
- Conditions for publication, usually with provisions that the manuscript must be seen by the donor before submission for publication
- A hold-harmless cause, meaning that the donor has no liability resulting from the use of the material
- The return of unused materials

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There are two main types of MTAs: incoming and outgoing. MTAs at academic Institutions fall into these categories:

- Transfers between academic or non-profit research Institutions
- Transfers from industry to academia
- Transfers from academia to industry

USC is a member of the Uniform Biological Material Transfer Agreement which was developed by the NIH to encourage the signatory Institutions to share research materials.

MTAs need to be reviewed to ensure compliance with USC policies, principles and guidelines, and all MTAs must be signed by an authorized representative of USC.

Review and approval of MTAs is conducted by the Senior MTA Administrator of the USC Stevens Institute (<https://stevens.usc.edu/researchers/mta-cda/>).

Additionally, IRB review and HIPAA consideration may apply when human specimens that contain identifiable subject information are transferred among Institutions.

15.3 Repositories: Banking of Specimens / Data

The banking of specimens/data refers to the creation of tissue banks and/or databases (repositories) to collect, store, and distribute human specimens and data for future research purposes. Repository activities involve three components:

- **Collection** of specimens/data
- **Storage and management** of the specimens/data
- **Distribution** of specimens/data to “recipient” investigators for use in future research projects

Research Repositories

If specimens or data were collected for research purposes, it is a research repository. Collection of specimens/data, repository storage or data management, and use of

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specimens or data are all considered research activities and require IRB review and approval.

Non-Research Repositories

If specimens or data were originally collected for non-research purposes AND were added to the repository/database without any identifiers or links to identifiable private information, it is a “non-research” repository/database. Studies using specimens/data from non-research repositories or databases are considered Not Human Subjects Research (NHSR) (Refer to [Section 7.1 - What Is Not Human Subjects Research](#)).

Specimen/data repositories may include two kinds of specimens/data: (1) those collected with the expressed purpose of distribution to other investigators, and (2) those collected by individual investigators with no original intent to share with others, but which are later shared as part of a repository. Any collection which contains specimens/data that are potentially identifiable, either directly or indirectly with a code, and are distributed to someone other than the named investigator(s) making the collection, regardless of the original intent, is considered to be a repository requiring IRB oversight.

Collecting Specimens / Data for a Repository

Investigators who collect directly or indirectly identifiable specimens/data require IRB review at the site of collection (even if different from the site of the repository). Under most circumstances, written informed consent from the subject is required and HIPAA authorization may be required. The informed consent form should include information about the repository and the conditions under which the specimens/data will be shared with others. Some consent forms give participants choices about what types of specimens/data can or cannot be shared.

Establishing a Repository at USC

Investigators who wish to establish and operate a repository at USC must create Standard Operating Procedures (SOPs) for operating and managing the repository. The USC IRB must review and approve the SOPs. The following documents must be included in the iStar application:

- Standard Operating Procedures for the repository. The operating procedures and policies should include, but are not limited to, the following elements:

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- Purpose of the repository
- Specimen and data collection procedures
- Specimen and data storage/retention
- Specimen derivation and processing
- Specimen and data distribution
- Obtaining informed consent and HIPAA authorization
- Procedures for protecting privacy and confidentiality (for example, anonymizing specimens/data, coding of specimens/data, encryption of data, limiting access/secure storage)
- Employee confidentiality measures and confidentiality agreement
- Procedures for return of research results (if and under what conditions)
- Repository oversight
- Sample informed consents for subjects contributing to the repository
- Sample agreements for investigators collecting tissues for the repository and for investigators receiving tissues from the repository. These agreements should address use of specimens/data, human subject protections, sharing of specimens with third parties, commercial use of specimens, biohazards, and indemnification.
- A Certificate of Confidentiality, if needed. Certificates of Confidentiality are issued by the National Institutes of Health and other federal agencies to protect identifiable research information from forced disclosure. Certificates of Confidentiality may be granted for studies collecting information that, if disclosed, could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation. Additional information is available at the NIH [Certificate of Confidentiality Kiosk](#) web site.

Confidentiality Considerations

Whenever possible, all identifiers should be stripped from the stored samples or data, such that they can never be traced to the individual. If the experimental design requires that the specimens/data be traced back to an individual subject, this creates a lasting confidentiality risk that must be both controlled and disclosed. If the need to link data to the individual is time limited, the data should be stripped of identifiers (rendering the samples truly anonymous) as soon as the time window has closed. Storage with easily traceable identifiers such as patient names, initials, social security numbers, or medical record numbers is almost never appropriate. An additional safeguard for maintaining confidentiality while retaining a link is to use a code in place of identifiers.

Risks of research participation extend beyond the duration of the subject's direct participation in research when records or samples are stored with identifiers. Loss of confidentiality leads to potential risks such as denial of insurance or employment, or disclosure that some members of a family are not genetic relatives. In addition, the ability to re-test samples containing extractable DNA has made it possible that retained samples will later provide sensitive or medically relevant information that was not anticipated at the time of initial collection.

Distribution of Specimens/ Data from a USC Biorepository

Investigators must follow the operating procedures and distribution conditions described in the approved IRB application. These conditions must consider the privacy of the individuals from whom the specimens/data came, the sharing options dictated by participants in the informed consent, and the intent of the person to whom the specimens/data are sent. The recipient of the specimens/data must abide by the conditions specified.

A biorepository committee, established under the IRB guidelines and pursuant to the IRB approval for the repository, should evaluate each request for samples to see if the request is consistent with the IRB's conditions for sharing samples and with the informed consent forms signed by participants. See USC Biorepository Policy

<http://policy.usc.edu/biorepositories/>

Storing Specimens / Data Outside of USC

If a USC investigator wishes to send specimens/data to a repository located at an external Institution or organization, the investigator must include a copy of the external site's IRB approval letter for operation of the repository in the USC IRB submission.

The IRB at the external site where the repository is located must approve and maintain oversight of a protocol that: (a) specifies the conditions under which data and specimens may be accepted and shared with other researchers and (b) ensures adequate privacy protections for subjects contributing to the repository.

Helpful Links

- USC Biorepository Policy:
<http://policy.usc.edu/biorepositories/>
- USC Biobanks Initiative:
<http://oprs.usc.edu/initiatives/biobanks/>
- OHRP “Issues to Consider in the Research Use of Stored Data or Tissues”
<http://www.hhs.gov/ohrp/policy/reposit.html>

15.4 NIH Genomic Data Sharing Policy (GDS) (Formerly GWAS)

The purpose of the National Institutes of Health (NIH) Genomic Data Sharing (GDS) Policy is to ensure the broad and responsible sharing of genomic research data. NIH has longstanding policies to make data publicly available in a timely manner from the research activities that it funds.

The GDS Policy applies to all NIH-funded research that generates large-scale human or non-human genomic data as well as the use of these data for subsequent research. Large-scale data include genome-wide association studies (GWAS), single nucleotide polymorphisms (SNP) arrays, and genome sequence, transcriptomic, metagenomic, epigenomic, and gene expression data, irrespective of funding level and funding mechanism (e.g., grant, contract, cooperative agreement, or intramural support).

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NIH expects all funded investigators to adhere to the GDS Policy, and compliance with this Policy will become a special term and condition in the Notice of Award or the Contract Award.

This Policy applies to:

- Competing grant applications that are submitted to NIH for the January 25, 2015, receipt date or subsequent receipt dates;
- Proposals for contracts that are submitted to NIH on or after January 25, 2015; and
- NIH intramural research projects generating genomic data on or after January 25, 2015.

The NIH GDS policy http://gds.nih.gov/pdf/supplemental_info_GDS_Policy.pdf provides detailed requirements for GDS data submission and GDS data access. The process for data submission and data access differ substantially and requirements for each are summarized below.

GDS Data Submission and Access

Overview of Differences in Submission and Access to the GDS database

- **Data Submission:** Requires IRB approval and Institutional Official (IO) signature
- **Data Access (*general process applicable to majority of requests*):** Data access requires signature of USC Institutional Official (IO) 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 IO signature and application to (and approval from) NIH Data Access Committee

GDS Data Submission Process of Genomic Data at USC

NIH expects investigators and their institutions to provide basic plans for following the Policy in the “Genomic Data Sharing Plan” located in the Resource Sharing Plan section

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of funding applications and proposals. Any resources that may be needed to support a proposed genomic data sharing plan (e.g., preparation of data for submission) should be included in the project's budget. A more detailed genomic data sharing plan is requested by the funding agency prior to award. The Institutional Certification (for sharing human data), should also be provided to the funding agency prior to award, along with any other Just-in-Time information. NIH expects intramural investigators to address compliance with genomic data sharing plans with their funding agency scientific leadership prior to initiating applicable research and encouraged to contact their funding agency leadership or the Office of Intramural Research for guidance. The funding agency will typically review compliance with genomic data sharing plans at the time of annual progress reports or other appropriate scientific project reviews, or at other times, depending on the reporting requirements specified by the funding agency for specific programs or projects.

Investigator Responsibilities

Data Submission Expectations and Timeline

Investigators should submit large-scale human genomic data as well as relevant associated data (e.g., phenotype and exposure data) to an NIH-designated data repository in a timely manner. Investigators should also submit any information necessary to interpret the submitted genomic data, such as study protocols, data instruments, and survey tools.

Genomic data undergo different levels of data processing, which provides the basis for NIH's expectations for data submission and timelines for the release of the data for access by investigators. These expectations and timelines are provided in the Supplemental Information. In general, NIH will release data submitted to NIH-designated data repositories no later than six months after the initial data submission begins, or at the time of acceptance of the first publication, whichever occurs first, without restrictions on publication or other dissemination.

Investigators should de-identify human genomic data that they submit to NIH-designated data repositories according to the standards set forth in the HHS Regulations for the Protection of Human Subjects to ensure that the identities of research subjects cannot be readily ascertained with the data. Investigators should also strip the data of identifiers according to the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule. The de-identified data should be assigned random, unique codes by the investigator, and the key to other study identifiers held by the submitting institution.

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NIH encourages investigators and institutions submitting large-scale human genomic datasets to NIH-designated data repositories to seek a Certificate of Confidentiality as an additional safeguard to prevent compelled disclosure of any personally identifiable information they may hold.

Data Repositories

Investigators should register all studies with human genomic data that fall within the scope of the GDS Policy in dbGaP by the time that data cleaning and quality control measures begin, regardless of which NIH-designated data repository will receive the data. After registration in dbGaP, investigators should submit the data to the relevant NIH-designated data repository (e.g., dbGaP, GEO, SRA, the Cancer Genomics Hub). NIH-designated data repositories need not be the exclusive source for facilitating the sharing of genomic data, that is, investigators may also elect to submit data to a non-NIH-designated data repository in addition to an NIH-designated data repository. However, investigators should ensure that appropriate data security measures and that confidentiality, privacy, and data use measures are consistent with the GDS Policy

To obtain IO certification, investigators must provide complete information in the IRB application (iStar sections 9.4 and 9.4.1) which will trigger a request for IO certification. If the IO certification is requested after a study has been approved by the IRB (including legacy studies), investigators should submit a study amendment to obtain IO certification.

For multi-center data submission to the GDS repository by a USC investigator: the investigator must provide the IRB GDS certifications from each institution. Each participating institution is responsible for conducting the GDS analysis of their submission based on applicable local standards. In these cases, the USC Institutional Official approval memo will note that GDS certification for study data includes appropriate institutional approvals from collaborating sites. There are 3 options for Institutional Certifications:

- For Studies Using Data Generated from Cell Lines Created or Clinical Specimens Collected AFTER January 25, 2015
- For Studies Using Data Generated from Cell Lines Created or Clinical Specimens Collected BEFORE January 25, 2015
 - That Lack Consent

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- For Studies Using Data Generated From Cell Lines Created or Clinical Specimens Collected BEFORE January 25, 2015
 - That Have Consent

IRB Responsibilities

For research that falls within the scope of the GDS Policy, submitting institutions, through their Institutional Review Boards (IRBs), privacy boards, or equivalent bodies, are to review the informed consent materials to determine whether it is appropriate for data to be shared for secondary research use. NIH provides additional information on issues related to the respect for research participant interests in its *Points to Consider for IRBs and Institutions in their Review of Data Submission Plans for Institutional Certifications*.

For studies initiated after the effective date of the GDS Policy, NIH expects investigators to obtain participants' consent for their genomic and phenotypic data to be used for future research purposes and to be shared broadly. The consent should include an explanation about whether participants' individual-level data will be shared through unrestricted- or controlled-access repositories.

For studies proposing to use genomic data from cell lines or clinical specimens that were created or collected after the effective date of the Policy, NIH expects that informed consent for future research use and broad data sharing will have been obtained even if the cell lines or clinical specimens are de-identified. If there are compelling scientific reasons that necessitate the use of genomic data from cell lines or clinical specimens that were created or collected after the effective date of the GDS Policy and that lack consent for research use and data sharing, investigators should provide a justification in the funding request for their use.

For studies using data from specimens collected before the effective date of the GDS Policy, there may be considerable variation in the extent to which future genomic research and broad sharing were addressed in the informed consent materials for the primary research. In these cases, an assessment by an IRB, privacy board, or equivalent body is needed to ensure that data submission is not inconsistent with the informed consent provided by the research participant. NIH will accept data derived from de-identified cell lines or clinical specimens lacking consent for research use that were created or collected before the effective date of this Policy.

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NIH recognizes that in some circumstances broad sharing may not be consistent with the informed consent of the research participants whose data are included in the dataset. In such circumstances, institutions planning to submit aggregate or individual-level data to NIH for controlled access should note any data use limitations in the data sharing plan submitted as part of the funding request. These data use limitations should be specified in the Institutional Certification submitted to NIH prior to award.

Institutional Official Approval Memo

Once a GDS study is approved by the IRB and the informed consent declarations are made, the IRB forwards the information request to the USC Office for the Protection of Research Subjects (OPRS). The OPRS Executive Director assures the approval memo is complete and that the informed consent information has been included and forwards it to the IO for review, signature, and distribution. The IO approval memo is mailed directly to the NIH Program Officer identified in the iStar application. At minimum, electronic copies of the approval will be sent to the investigator, HSIRB Director, IRB administrator and OPRS office. HSIRB staff will upload the IO approval memo(s) in iStar.

Institutional Official Responsibilities

The responsible Institutional Official of the submitting institution should provide an Institutional Certification to the funding agency prior to award consistent with the genomic data sharing plan submitted with the request for funding. The Institutional Certification should state whether the data will be submitted to an unrestricted- or controlled-access database. For submissions to controlled access and, as appropriate for unrestricted access, the Institutional Certification should assure that:

- The data submission is consistent, as appropriate, with applicable national, tribal, and state laws and regulations as well as relevant institutional policies;
- Any limitations on the research use of the data, as expressed in the informed consent documents, are delineated;
- The identities of research participants will not be disclosed to NIH-designated data repositories; and
- An IRB, privacy board, and/or equivalent body, as applicable, has reviewed the investigator's proposal for data submission and assures that:

- The protocol for the collection of genomic and phenotypic data is consistent with 45 CFR Part 46

USC Data Accessing Process

Investigators and Institutions seeking data from the NIH GDS 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).

To access data in the GDS 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.

Investigator Responsibilities

Access to human data is through a tiered model involving unrestricted- and controlled-data access mechanisms. Requests for controlled-access data are reviewed by NIH Data Access Committees (DACs) [http://gwas.nih.gov/04po2_1DAC.html]. NIH DACs will accept requests for proposed research uses beginning one month prior to the anticipated data release date. The access period for all controlled-access data is one year; at the end of each approved period, data users can request an additional year of access or close out the project. A Certificate of Confidentiality could serve as an additional safeguard to prevent compelled disclosure of any genomic data.

Terms and Conditions for Research Use of Controlled-Access Data

Investigators approved to download controlled-access data from NIH-designated data repositories and their institutions are expected to abide by the NIH Genomic Data User Code of Conduct. The Data Use Certification, co-signed by the investigators requesting the data and their Institutional Signing Official, specifies the conditions for the secondary research use of controlled-access data, including:

- Using the data only for the approved research;
- Protecting data confidentiality;

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- Following, as appropriate, all applicable national, tribal, and state laws and regulations, as well as relevant institutional policies and procedures for handling genomic data;
- Not attempting to identify individual participants from whom the data were obtained;
- Not selling any of the data obtained from NIH-designated data repositories;
- Not sharing any of the data obtained from controlled-access NIH-designated data repositories with individuals other than those listed in the data access request;
- Agreeing to the listing of a summary of approved research uses in dbGaP along with the investigator's name and organizational affiliation;
- Agreeing to report any violation of the GDS Policy to the appropriate DAC(s) as soon as it is discovered;
- Reporting research progress using controlled-access datasets through annual access renewal requests or project close-out reports;
- Acknowledging in all oral or written presentations, disclosures, or publications the contributing investigator(s) who conducted the original study, the funding organization(s) that supported the work, the specific dataset(s) and applicable accession number(s), and the NIH-designated data repositories through which the investigator accessed any data.

NIH expects that investigators who are approved to use controlled-access data will follow guidance on security best practices and expected data security protections.

If investigators violate the terms and conditions for secondary research use, NIH will take appropriate action. Further information is available in the Data Use Certification [https://gds.nih.gov/pdf/Model_DUC.pdf].

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).

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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.

IRB Responsibilities

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

Institutional Official Responsibilities

After the PI completes the data access request, the Institutional Official (IO) will be notified by email. The IO 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 IO will be notified by email of approval or disapproval.

GDS Publication Rights

The NIH expects that investigators who contribute data to the NIH GDS 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 GDS 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 GDS dataset is made available for access through the NIH GDS data repository, although a shorter period of exclusivity may be determined by the NIH funding institute or center.

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

Helpful Links

Additional GDS guidance can be accessed in the following links:

- NIH Genomic Data Sharing (GDS) 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) Website:
<http://www.ncbi.nlm.nih.gov/gap>
- Form SF 424 (R&R) Application and Electronic Submission Information
<http://grants.nih.gov/grants/funding/424/index.htm>
- dbGaP FAQ Archive
<http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=helpdbgap>
- National Human Genome Research Institute Consent Form Examples and Model Consent Language
<http://www.genome.gov/27526660>

15.5 Genetic Research

Genetic information is uniquely personal information. Disclosure of genetic information has the potential to influence employment, insurance, finances, education, family relationships, and possibly self-perception. Therefore, genetic information collected during research must be carefully managed to protect individuals or groups from stigmatization, discrimination, or psychological harm.

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Research involving analysis of genetic material can be broadly categorized as genetic testing or genetic research.

- **Genetic Testing:** The gene has a known association with a human trait or medical condition and the results will be disclosed to the participant and/or their health care providers. Genetic testing must be performed in a Clinical Laboratory Improvement Amendments (CLIA)-certified laboratory. A geneticist or genetic counselor should disclose results to participants or be available to answer participants' questions about the implications of the results.
- **Genetic Research:** The genes being studied have no known associations with human traits or medical conditions. The research does not provide meaningful information about participants' health. Genetic research is not performed in a CLIA-certified laboratory and results are not typically shared with participants or their health care providers.

Investigators who are conducting genetic research must pay special attention to the following topics in the iStar application and informed consent form:

- Type(s) of genetic testing or genetic research to be conducted
- Confidentiality measures to protect genetic information
- Risks related to loss of confidentiality
- Disclosure of results to participants and their doctors
- Availability of a geneticist or genetic counselor to counsel participants who receive results of genetic testing
- Participants' rights to opt out of genetic research, to opt out of future research on their genetic specimens, and to request destruction of genetic specimens

Minors and Family Members

Before involving minors in genetic research, the parent(s) or legal guardian(s) must review and sign the informed consent form and HIPAA authorization form (if applicable). The minor subject's assent should also be solicited when appropriate. Investigators should follow the recommendations of a genetic counselor or professional associations when incorporating genetic testing of minors into research protocols. Most

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recommend that genetic testing for adult-onset diseases be postponed until individuals can decide for themselves and consent as an adult (American Academy of Pediatrics and National Society of Genetic Counselors).

In rare cases, it may be possible for investigators to learn that some members of the family are not biological relatives. Investigators may learn that the father is not the child's biological father or that a child was adopted and the child or other family members are not aware of this information. Investigators conducting genetic research in families must plan ahead for this situation and state whether or not the information will be revealed to participants.

Genetic research may involve gathering information about family members of the participant. Family members who are not enrolled as participants but about whom information is collected are called "secondary subjects". Participants may be asked to describe the age, gender, health information, social history, and relationship of family members. The privacy of these secondary subjects must be protected, even though they are not enrolled as participants. The IRB may require informed consent from secondary subjects or may grant a waiver of informed consent for secondary subjects.

Genetic Information Nondiscrimination Act (GINA)

The Genetic Information Nondiscrimination Act (GINA) of 2008 is a federal law that prohibits discrimination in health coverage and employment based on genetic information. GINA generally prohibits health insurers or health plan administrators from requesting or requiring genetic information of an individual or the individual's family members, or using it for decisions regarding coverage, rates, or preexisting conditions. The law also prohibits most employers from using genetic information for hiring, firing, or promotion decisions, and for any decisions regarding terms of employment.

GINA applies to genetic information, including utilization of genetic testing and counseling services, by an individual or family member participating in research. The informed consent form should describe this protection against genetic discrimination when it applies to the research. Additional information on GINA protections and limitations is available at:

<http://www.genome.gov/pages/policyethics/geneticdiscrimination/ginainfodoc.pdf>.

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The HSIRB Informed Consent Template contains suggested language for genetic research, storing specimens for future use, and GINA protections (see <http://oprs.usc.edu/hsirb/hsirb-forms/>).

Return of Results

Genetic testing is a diagnostic tool prescribed by health care provider and results are provided to patients. Genetic research, however, involves testing of genes that have no known associations with human traits or medical conditions. Test results may not provide meaningful information about participants' health, thus, results are not typically shared with participants or their health care providers. As a best practice, results should be returned to subjects when the test results have analytical validity (accurately and reliably measures the property or characteristic of interest), clinical validity (consistently and accurately detects or predicts the intermediate or final outcome of interest), and utility/action-ability (such as instances when a medical intervention can change the course of a serious condition).

15.6 Human Gene Transfer Research (“Gene Therapy”)

Human gene transfer, often called “gene therapy,” refers to the process of transferring specially engineered genetic material (recombinant DNA or RNA derived from recombinant DNA) into a person. To avoid the misconception that this technology is therapeutic, the term “human gene transfer research” is preferred to “gene therapy.” Gene transfer research has additional reviewing, reporting, and consent form requirements. Research involving human gene transfer must be reviewed by the USC Institutional Biosafety Committee (IBC) as well as the IRB. For additional information on research involving recombinant DNA, see the USC IBC web site [<http://capsnet.usc.edu/departement/environmental-health-safety/uscs-institutional-biosafety-committee-ibc>].

The Food and Drug (FDA) and NIH have oversight of human gene transfer research and oversee mandatory safeguards.

FDA

The FDA's role is to determine whether or not a sponsor may initiate study of a gene transfer product and, ultimately, whether it is safe and effective for human use. This process of review and authorization of gene transfer research is conducted by FDA's Center for Biologics Evaluation and Research (CBER). Sponsors of gene transfer products must test their products extensively and meet FDA requirements for safety, purity, and potency before they can be administered to humans or sold in the United States.

NIH

NIH evaluates scientific, safety, and ethical aspects of human gene transfer research and communicates findings to the scientific community, IRBs, IBCs, and the public. The NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines) is available at: <http://osp.od.nih.gov/office-biotechnology-activities/biosafety/nih-guidelines>.

The NIH Guidelines articulate standards for investigators and Institutions to follow to ensure the safe handling and containment of recombinant DNA and products derived from recombinant DNA. These guidelines outline requirements for institutional oversight. [Appendix M](#) of the NIH Guidelines describes points to consider in the design and submission of human gene transfer trials, including the registration of protocols with NIH, the review procedures of the Recombinant DNA Advisory Committee ([RAC](#)), the conduct of informed consent, and annual and expedited reporting requirements. Institutions that receive NIH funding for basic and clinical recombinant DNA research must assure to NIH that all research conducted at or sponsored by the Institution complies with NIH Guidelines.

Investigators have an ongoing responsibility to monitor human gene transfer trials and to keep the NIH Office of Biotechnology Activities (OBA), as well as the IRB, the IBC, FDA, and any sponsoring NIH institutes or centers, informed of any adverse events that occur in a gene transfer trial. If a serious adverse event occurs that is unexpected and could be possibly associated with the gene transfer product, a sponsor is required by regulation to notify FDA within 15 days of the event, and investigators should notify OBA of the problem within 15 days of their notification to the sponsor. Serious adverse events that are fatal or life threatening must be reported within seven days. If warranted by the nature of these events, the FDA may mandate changes to the human study and

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require more preclinical studies, put the clinical study on hold, or stop the study altogether.

The NIH and FDA have developed a national database for gene transfer clinical research, the Genetic Modification Clinical Research Information System ([GeMCRIS](#)) to enable systematic analysis of data across all human gene transfer trials and to enhance communication and application of knowledge gained from the studies. The system provides a standardized means for reporting, organizing, and analyzing data related to adverse events in a format accepted by both the NIH and FDA.

In some cases, the potential risks associated with gene transfer may weigh against the involvement of human subjects in such trials. The IRB will consider the risks and benefits of a human gene transfer study carefully, and, if a protocol is approved, ensure that participants are thoroughly informed of the risks and benefits involved in the trial.

Because gene transfer is innovative and its long-term risks are not well understood, the NIH Guidelines require investigators to inform prospective participants that they will be asked to participate in long-term follow-up that extends beyond the active phase of the study. Investigators need to explain the rationale for long-term follow-up, the specific follow-up activities planned, how long follow-up will continue, and what, if any, procedures participants will be asked to undergo.

The NIH Guidelines state that investigators should inform subjects that an autopsy will be requested at the time of death, no matter what the cause, to obtain vital information about the safety and efficacy of gene transfer. Subjects should be asked to advise their families of the request and of its scientific and medical importance. During the informed consent process, the investigator should explain that the subject is not being asked at this time to consent to autopsy, nor is it required for study participation. However, subjects should be encouraged to express their wishes about an autopsy to their families so that family members are prepared to consider it at the time of the subject's death.

The NIH Guidelines require that investigators describe in the protocol any potential benefits and hazards of the proposed gene transfer to persons other than the human subjects receiving the experimental intervention. Specifically, investigators must address whether there is a significant possibility that the inserted DNA will spread from the human subject to other persons or to the environment and what measures will be undertaken to mitigate any public health risks. The IBC should be involved in assessment of community health risks.

15.7 Research Involving HIV Testing and AIDS

Confidentiality is the most sensitive aspect of AIDS research from the perspective of the rights and welfare of the subjects. Improper disclosure could have severe consequences for research participants, by threatening family relationships, job security, employability, or ability to obtain credit or insurance. In light of these risks, special precautions should be taken to preserve confidentiality. Limits to confidentiality should be carefully explained to potential subjects so they can make fully informed decision about participating.

Each study must be designed with administrative, management, and technical safeguards to control authorized use and disclosure of information and to protect against unauthorized disclosure. Where identifiers are not required by the design of the study, they are not to be recorded. If identifiers are recorded, they should be separated, if possible, from data and stored securely, with linkage restored only when necessary to conduct the research. No lists should be retained identifying those who elected not to participate.

As a general principle, information is not to be disclosed without the subject's consent. The protocol must clearly state who is entitled to see records with identifiers, both within and outside the project. This statement must take into account the possibility of a review of records by the funding agency and by FDA officials if the research is subject to FDA regulations [21 CFR 50](#). The informed consent form must disclose that positive HIV tests will be reported to public health agencies.

California Law and HIV Research

The California Health and Safety Code ([Section 121075-121125](#)) provides additional protections for research records in studies relating to HIV or AIDS.

“Confidential research records” includes any data in a personally identifying form (such as name, social security number, address, employer or other information that could, directly or indirectly, lead to the identification of the individual research subject) developed or acquired by any person in the course of conducting research relating to AIDS.

Confidential research records developed or acquired by any person in the course of conducting research, or a research study relating to AIDS, shall be confidential and shall

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not be disclosed by any person in possession of the research record, nor shall these records be discoverable, nor shall any person produce any confidential research record except in the following situations:

- Confidential research records may be disclosed in accordance with the prior written consent of the research subject to whom the confidential research records relate, but only to the extent, under the circumstances, to the persons and for the purposes the written consent authorizes. Any disclosure made pursuant to such prior written consent shall contain the following statement:

This information has been disclosed to you from a confidential research record the confidentiality of which is protected by state law and any further disclosure of it without specific prior written consent of the person to whom it pertains is prohibited. Violation of these confidentiality guarantees may subject you to civil or criminal liabilities.

- Confidential research records may be disclosed without prior written consent of the research subject to whom the confidential research records relate in the following circumstances:
 - To medical personnel to the extent it is necessary to meet a bona fide medical emergency of a research subject, and
 - To the California Department of Health Services for the conduct of a special investigation of the sources of morbidity and mortality and the effects of localities, employments, conditions and circumstances on the public health and for other duties as may be required in procuring information for state and federal agencies regarding the effects of those conditions on the public health

The content of any confidential research record shall be disclosed to the research subject, the legal representative of the research subject if the research subject is a minor, or the personal representative of a deceased research subject to whom the record pertains within 30 days after a written request is made for such records by the research subject or the legal representative.

For additional information on California laws, please refer to “A Brief Guide to California's HIV-AIDS Laws” at

http://www.cdph.ca.gov/programs/aids/Documents/RPT2010_01HIVAIDSLaws2009.pdf

Policy on Informing Subjects about HIV Serostatus

It is the policy of the IRB, as required by the Public Health Service (PHS), that when HIV testing is conducted as part of a research project, individuals whose test results are associated with personal identifiers must be informed of their test results and be provided with the opportunity to receive appropriate counseling. Individuals may not be given the option to "not know" the results, either at the time of consenting to be tested or thereafter. This policy does not apply to testing situations in which subjects consent to be tested and where results cannot be linked to individual subjects by anyone other than the subjects themselves.

Counseling

Any person tested for HIV infection should receive the results of their tests and counseling in a timely fashion from an individual qualified to provide test counseling and partner notification services.

Exceptions to Informing Subjects about HIV Serostatus

Individual Subjects

When there are compelling and immediate reasons that justify not informing an individual of their positive HIV test results (for example, indications that an individual would attempt suicide), the individual need not be informed of HIV test results. When this exception is made, the details of the exception shall be documented by the responsible individual(s). The investigator must promptly report the exception to the IRB without identifying the individual.

Protocol Design

Because circumstances may exist in which extremely valuable knowledge might be gained from research involving subjects who would be expected to refuse to learn their HIV antibody results, an exception included in the protocol design may be proposed to the appropriate IRB. The IRB will consider the circumstances of the research study, the characteristics of the subjects, and any other factors; and may approve a testing procedure that would allow subjects to participate without being informed of their results. The investigator must demonstrate that research subjects will be informed of their risk of

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infection and will receive counseling whether they receive their test results or not. The investigator must show there is good reason to believe that requiring test result notification would significantly impair the collection of study data that could not be obtained by other means; and the risk/benefit ratio to individuals, their partners, and society will be periodically re-evaluated by the IRB. The re-evaluation by the IRB will consider whether the study should be revised or terminated if it is no longer justifiable to allow subjects to continue to participate without receiving their HIV test results.

Foreign Sites

Research conducted at foreign sites should be carefully evaluated to account for cultural norms, health resource capabilities, and official health policies of the host country. The reviewing IRB must consider if any modifications to this policy must be significantly justified by the risk/benefit evaluation of the research. The IRB may seek expert advice (such as local public health experts) in evaluation of these projects.

Chapter 16: Student Research

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