# NHGRI IRB

# Human Subjects Research

# Protocol Template

Project title:

Draft/version number (day, month, year)

NHGRI Protocol Number (if assigned)

Principal Investigator:

Title/Section/Branch/Institute:

**Study Staff Roster**

**Medical Advisory Investigator:** (*if applicable*)

**Associate Investigator(s):**

*If the AI is an NIH AI, list the name, degree, and IC/lab of the AI. However, if the AI is not an NIH AI, list the name, degree, institution, and contact information.*

**Collaborating Institutions:** (*if applicable*)

*List the name of the Site and FWA# for each institution; see* [*http://ohrp.cit.nih.gov/search/asearch.asp#ASUR*](http://ohrp.cit.nih.gov/search/asearch.asp#ASUR) *for assurance #s*

**List of Abbreviations** *(as applicable)*

AE Adverse Event/Adverse Experience

CFR Code of Federal Regulations

CLIA Clinical Laboratory Improvement Amendment of 1988

COI Conflict of Interest

CRADA Cooperative Research and Development Agreement

DAC Data Access Committee

dbGaP Database of Genotypes and Phenotypes

DUC Data Use Certificate

DHHS Department of Health and Human Services

DSMB Data Safety and Monitoring Board

FWA Federal Wide Assurance

GCP Good Clinical Practice

GINA Genetic Information Nondiscrimination Act

GWAS Genome-Wide Association Study

HIPAA Health Insurance Portability and Accountability Act

ICF Informed Consent Form

IRB Institutional Review Board

MTA Material Transfer Agreement

N Number (typically refers to number of subjects/sample size)

NHGRI National Human Genome Research Institute, NIH

NGS Next Generation Sequencing

NIH National Institutes of Health

OHRP Office for Human Research Protections

OHSRP Office of Human Subjects Research Program

PHI Protected Health Information

PI Principal Investigator

PK Pharmacokinetics

QA Quality Assurance

QC Quality Control

SAE Serious Adverse Event/Serious Adverse Experience

SOP Standard Operating Procedure

UP Unanticipated Problem

UPnonAE Unanticipated Problem that is not an Adverse Event

Instructions: Insert your responses for each section. Be sure to address each point in all sections that are relevant. (It is not necessary to itemize each point or to specify “not applicable.”)

Please use a readable font, like Times 12-point type, to facilitate legibility. We encourage investigators to limit the overall length of protocols to 20 single-spaced pages or fewer (not including the 3 preceding pages, appendices, and other attachments).

1. **Precis:** *(In 400 words or fewer, describe the study objectives, population, design, and outcome measures*)
2. **Objectives and specific aims.** *(List the objectives concisely; whenever possible, state objectives as hypotheses.)*
3. **Brief Rationale and Background**: *Write a* ***brief*** *[****no more than 5 pages in length****]* *summary of the clinical background, limits of current knowledge, and significance of this protocol. For background on drugs and devices, cite animal studies, prior experience in humans, and discuss potential toxicities. Include* ***up to 20*** *key references.*

1. **Description of study design** *(Brief description of what study design has been selected)*
2. **Description of procedures:** *(what will be done, when will it be done, where will it be done, duration of participant involvement. Specify which procedures are being done for research only, and which are being done both for research + clinical care.* ***Please include a flow-sheet or chart that depicts the subject's participation in the protocol from recruitment and consent to completion of the study procedures).***
   1. Medical information *(what information will be collected, any sensitive information, how long will it be stored, are there future anticipated uses?)*
   2. Diagnostic studies *(include use of radiation or sedation.)*
   3. Biological Specimens *(How much will be collected, what disease categories will be studied, will cell lines be created, how long will sampled be stored, are there future anticipated uses?)*
   4. Approved Drugs Being Used for Research *(Include dosage in study and range approved for clinical use.)*
   5. Unapproved Drugs/Devices *(indicate if approved for other use, include dosages in study, and IND or IDE number, if applicable.)*
   6. Specific results that will be given to participants or their health care providers *(Is laboratory CLIA certified? What are the plans to return DNA sequencing results?)*
   7. Describe questionnaires or other psychological instruments and estimate how long they will take to complete, and whether they address sensitive topics *(Enclose copies.)*
   8. Genetic counseling *(By whom, would counseling happen in person, will understanding be assessed?)*
   9. Description of criteria for withdrawal from study.
3. **Description of Study Population:** 
   1. Estimated number of participants, enrollment ceiling, and anticipated enrollment by year.
   2. Description and justification of clinical inclusion/exclusion criteria. *(affected individuals, family members, controls? Define clinical criteria: Will this determination be made by review of prior records or will a screening evaluation be performed? Justify population choice in regards to age, gender, ethnicity, primary language spoken, prisoners, pregnant women, fetuses, people with impaired decision-making ability, healthy volunteers, lab personnel)*
   3. Location of study *(specify NIH Clinical Center facilities and/or other off-site locations).*
   4. Description of recruitment strategies *(How participants will be identified; note efforts to include under-represented minorities; include copies of recruitment advertisements and letters.)*
   5. For existing sample/data sets, note whether samples were originally collected for research or clinical practice. If obtained for research, include a description of the original purpose of study and prior plans for sample storage. Was consent obtained that would be applicable to this study? (*Include copy of original consent forms.*)
   6. Description of any financial compensation. If participant withdraws early, describe whether compensation will be modified.
4. **Description of study statistical considerations and/or analytic plan:** *Write a* ***brief*** *[****no more than 3 pages in length****]* *description of how data will be used to answer hypotheses, sample size and power calculations, methods of analysis, criteria for significance, as applies to this protocol.)*
5. **Description of potential benefits of study:**
   1. Direct benefits to participants *(Include only those physical or psychosocial benefits that derive directly from an intervention being studied)*
   2. Collateral benefit to participants *(medical or genetic counseling care and other benefits associated with being a research subject at the NIH that are not directly related to the specific study intervention. Do not include financial compensation as a direct or collateral benefit.)*
   3. Benefits to society
6. **Description of likelihood and seriousness of harms and how safety will be maximized:** *(Include potential physical and psychosocial harm from both research-related and medically-indicated procedures, alternative interventions that might be advantageous to participants, and provisions for medical or other professional interventions in the event of adverse events.)*
   1. Therapeutic interventions *(drugs/devices/gene transfer)*
   2. Diagnostic interventions *(blood draws/imaging/biopsies)*
   3. Radiation *(Provide documentation of approval from Radiation Safety Committee.)*
   4. Sedation
   5. Psychological harms *(misunderstanding, anxiety, self esteem, depression)*
   6. Risks to family relationships *(related to determination of genetic/disease status, parentage, adoption)*
   7. Discrimination *(insurance, employment)*
7. **Description of how privacy and confidentiality of medical information/biological specimens will be maximized**

10.1 Will participant identifiers be attached to data, or will samples/data be coded or unlinked*? (Even if names are removed, how likely is potential identification?)*

10.2 Description of any clinical/demographic information that will be included. (*age, ethnicity, sex, diagnosis, stage, treatment*)

10.3 How might this information make specific individuals or families identifiable?

10.4 If research data will be coded, how will access to the “key” for the code be limited? Include description of security measures (e.g., *password-protected database, other*). List names or positions of persons with access to the "key" for the code.

10.5 Will pedigrees be published? Include description of measures to minimize the chance of identifying specific families.

10.7 Will personally identifiable information be released to third parties?

10.8 Under what circumstances will data/samples be shared with other researchers or deposited in various repositories, biobanks, and/or databases voluntarily or as mandated by NIH policies (e.g. dbGaP)?

10.9 Describe any additional features to protect confidentiality.

1. **Assessment of Risk/Benefit Ratio** *(Reasonableness of risks to participants in relation to the anticipated benefits of the study and in relation to the importance of the knowledge that may reasonably be expected to result.)*
2. **Unanticipated Problems: Collection, monitoring, analysis and reporting of adverse events and protocol deviations**
   1. Describe all potential adverse events that can be anticipated and monitored for this protocol. If this is either a natural history or limited encounter protocol, explain this to the IRB and specify the occurrences that will be excluded from adverse event reporting. *(For natural history protocols, describe range of medical events independent of any protocol encounter that are known to occur in subjects who qualify for study enrollment. Natural history protocols will monitor, but not consider as reportable, occurrences that are purely a consequence of an underlying genetic or medical condition under study in a protocol. Furthermore, adverse events need not be ascertained in limited encounter protocols such as linkage studies or tissue array studies, in which NHGRI investigators are not providers of medical services.)*
   2. Describe plan to monitor and report adverse events and protocol deviations, as outlined in SOP 16 (available at <https://federation.nih.gov/ohsr/nih/index.php>).

*All protocols should include the following standard language, at a minimum:*

Adverse events, protocol deviations, unanticipated problems (UP), Unanticipated Adverse Device Effects (UADEs), serious adverse events, sponsor and serious, are defined as described in NIH HRPP SOP 16 ("Reporting Requirements for Unanticipated Problems, Adverse Events and Protocol Deviations"). All adverse events occurring during the study, including those observed by or reported to the research team, will be recorded. Serious unanticipated problems, Unanticipated Adverse Device Effects and serious protocol deviations, will be reported to the IRB and CD (Clinical Director) as soon as possible but not more than 7 days after the PI first learns of the event. Not serious unanticipated problems will be reported to the IRB and CD as soon as possible but not more than 14 days after the PI first learns of the event. Not serious protocol deviations will be reported to the IRB as soon as possible but not more than 14 days after the PI first learns of the event.

Deaths will be reported to the Clinical Director within 7 days after the PI first learns of the event.

*For FDA-regulated protocols, and/or to request that the IRB waive certain categories reporting requirements, see additional language requirements at* [*http://www.genome.gov/Pages/Research/Intramural/IRB/template\_language\_up\_pd\_reporting\_10-1-2013.pdf*](http://www.genome.gov/Pages/Research/Intramural/IRB/template_language_up_pd_reporting_10-1-2013.pdf)

* 1. Describe whether a Data Safety and Monitoring Board (DSMB) and/or any other additional monitoring measures will be used.

1. **Description of alternatives to participation** *(Other clinical or research interventions, if any, that participants should consider.)*
2. **Description of Consent Process**
   1. Who will obtain consent *(PI, AIs)?*
   2. Setting where consent will be obtained *(location of in-person discussion, phone, mail).*
   3. What information will be provided to participants? *(Include consent and/or assent forms, printed or web-based materials, phone scripts and any other related material.).*
   4. Protections for participants who may be vulnerable to coercion or undue influences *(pregnant women, fetuses, children, people with impaired decision-making ability).*

*For adults who may not be able to consent for themselves, the protocol should be consistent with NIH policy M87-4, available at* [*http://cc-internal.cc.nih.gov/policies/PDF/M87-4.pdf*](http://cc-internal.cc.nih.gov/policies/PDF/M87-4.pdf)*. Specifically, all research protocols should state whether adults who are unable to provide initial informed consent are excluded or are eligible to enroll, and the conditions, if any, under which adults who lose the ability to provide on-going consent subsequent to giving initial consent, may continue to participate. If adults who are unable to consent are eligible for enrollment and/or continued participation, the protocol will describe the justification for their inclusion; how adults’ ability to provide initial and on-going consent will be assessed; that the permission of an appropriate surrogate will be obtained per this policy; the risks of the research and likelihood of benefit (if any) for adults unable to consent; the procedures for obtaining assent, and the procedures for respecting dissent; and any additional safeguards that will be used (e.g., consent monitoring).*

* 1. Are there special circumstances regarding obtaining *consent? (Waived consent, opt-out, verbal consent, consent with speakers of other languages and translation of materials into other languages.)*

(template version 11/26/13)