

University of Hawai`i Human Studies Program

Investigator's Handbook

Guide to Protecting Human Participants in Research

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University of Hawai`i

Human Studies Program (IRB)

Investigator's Handbook

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Chapter 1: Purpose of the Handbook

The Investigator's Handbook will help to guide you through policies and procedures related to the ethical conduct of Human Subjects Research that are specific to the University of Hawaii (UH).

General information regarding Human Research Protection and relevant federal regulations and guidance can also be found in UH's required human protections training. See "[What training does my staff and I need prior to conducting human subjects research?](#)" below for additional information.

Chapter 2: What is Human Subjects Research?

UH's Human Studies Program defines the activities that this institution considers to be "Human Subjects Research"^{1,2}. The **WORKSHEET 301: Is my project human subjects research?** located in the IRB Policies & Guidance section of the Human Studies Program website, can help you determine whether your study qualifies as Human Subjects Research per DHHS or FDA definition. You may also follow the **WORKSHEET 302: Requirements for Exempt Approval** found on the Program website to assist you with making initial determination. Please keep in mind, however, that the Human Studies Program staff, by extension of its Institutional Review Boards (IRBs), makes the ultimate determination as to whether a study constitutes Human Subjects Research that will require IRB oversight.

Human Subjects Research must not be conducted without prior IRB review and approval (or an IRB determination that the study is Exempt). If you have questions about whether an activity is Human Subjects Research, contact the Human Studies Program office for a determination. If you wish to have a written determination without having to complete a full protocol submission, provide a written request to the Human Studies Program (HSP) office via email.

Chapter 3: What is the UH Human Studies Program?

The Human Studies Program (the Program) is the administrative unit at UH responsible for compliance with federal and state regulations, and UH policies, applicable to the protection of human research subjects. Human Subjects Research performed by UH faculty, staff or students or that uses UH facilities or resources must have prospective approval by the Human Studies Program or one of its authorized IRBs unless the Human Studies Program has ceded review authority to another federally-approved IRB under an IRB authorization agreement or other agreement executed for this purpose. The Human Studies Program is established under the University of Hawai'i's Federalwide Assurance (FWA 00003526) from which its authority is derived. The Human Studies Program is administratively placed within the Office of Research Compliance, which reports to the Office of the Vice President for Research and Innovation (UH System).

¹ DHHS regulations 45 CFR § 46.102(d) and 45 CFR §46.102(f)

² FDA regulations 21 CFR §56.102(c), 21 CFR §56.102(e), and 21 CFR §812.3(p)

The primary responsibility of the UH Human Studies Program is to ensure that the rights, safety and welfare of human subjects are protected, and that human subject research is conducted ethically, and in compliance with applicable Federal regulations, the requirements of State law, and UH policies. The Human Studies Program accomplishes this by way of prospective and continuing review of all human subjects research. This includes the review of research applications, informed consent documents and processes, study tools, and other pertinent documents.

The Human Studies Program, through its several IRBs, has statutory authority to take any action necessary to protect the rights and welfare of human subjects in all UH-related human subjects research projects. Specifically, the IRBs have authority to:

1. Approve, request to modify or disapprove studies based upon consideration of human subject protection aspects;
2. Require progress reports from investigators and oversee the conduct of the study;
3. Suspend or terminate approval of a study; and
4. Place restrictions on a study.

The Human Studies Program has the authority to draft, approve and issue policies and procedures that assure the protection of human research subjects and compliance with applicable government regulations and UH policies.

Chapter 4: Principal Investigator Standards and Expectations

4.1 Who can be listed as a Principal Investigator?

Per UH Board of Regents policy, Chapter 12, only university board appointees may serve as Principal Investigators (source:

<http://www.hawaii.edu/policy/?action=viewPolicy&policySection=rp&policyChapter=12&policyNumber=202&menuView=closed>). Therefore, in undergraduate research, the faculty member/ instructor should be listed as the Principal Investigator (PI) and the student(s) as co-investigator(s). Include the faculty member's/ instructor's name and contact information in the consent form as well as the names of students who will obtain consent from participants.

Graduate (Doctoral and Masters) students may be listed as a student investigator, or a co-Investigator, and should indicate the faculty supervisor's name in the application form as the primary PI. Medical residents cannot be listed as the PI. They must provide a faculty supervisor's name as the PI contact name in the application form.

The Principal Investigator is the person ultimately responsible for the research and the protection of human participants involved in the research.

4.2 What interests, financial or otherwise, do my staff and I need to disclose before

conducting Human Subjects Research?

Individuals involved in the design, conduct, or reporting of research, research consultation, teaching, professional practice, institutional committee memberships, and service on panels such as Institutional Review Boards or Data and Safety Monitoring Boards are considered to have an institutional responsibility.

PIs and research staff are expected to follow UH policies addressing the disclosure of conflicts of interest as described in **Section 203.5** of the **General Policy Manual**, **SOP 107 Investigators' Conflict of Interest**, and the policies referenced therein. For all individuals involved in the design, conduct, or reporting of research are required to disclose the financial interest listed in the "General Significant Financial Interest Disclosure Assessment" found in the Office of Research Services Financial Conflicts of Interest page. Additionally, each member of a particular research project must also report any Significant Financial Interest (SFI) and other Conflicts of Interests (COI) in the "**Potential Conflict of Interest**" section (**section 15**) of the **eProtocol online application form**.

Specific policies, procedures and forms regarding financial interest can also be found under the UH Office of Research Services Financial Conflict of Interest page (<http://www.ors.hawaii.edu/index.php/fcoi>).

In addition, investigators may need to provide disclosure of financial or other significant conflict of interest to participants in the consent document. See the Human Studies Program website for suggested consent form language for disclosing conflict-of-interest found under the "[Policies & Guidance](#)" Quicklink.

4.3 Importance of Sound Study Design

The significance of the research depends upon the validity of the results. It is unethical to put participants at risk or to inconvenience them through participation in a research project that may produce little or no reliable information. Regardless of the source of funding, it is the responsibility of the PI to judge the research design to be sound enough to meet its objectives before submitting the research protocol or proposal for IRB review. The Protocol Application includes questions addressing the various considerations for sound study design.

When designing research, the PI should consult the **SOP 104: Ensure Sound Design and Minimize Risk** and include all pertinent information in the Protocol Application. The Protocol Application should include a description of the provisions for monitoring the data and reporting to the IRB and other entities (see Section 206.3 of the GPM).

In developing, or in evaluating the adequacy of, a research design involving investigational drugs or biological products, the PI should refer to the FDA [Guidance Documents](#) representing the agency's current stance on good clinical practice (GCP) and the conduct of clinical trials.

4.4 Detecting Harm, Minimizing Risks and Mitigating Potential Injuries through Study Design and During Research Conduct

Risks may affect physical, psychological, social, legal or economic well-being, including loss of privacy or breach of confidentiality. The PI must minimize risks at all times by using procedures that are consistent with sound research design and that do not expose participants to unnecessary risks, and whenever appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes.

When submitting a Protocol Application to the IRB, the PI must:

- Describe the potential risks.
- Include, when possible, a scientific estimate of their frequency, severity, and reversibility. If statistical incidence of complication and the mortality rate of proposed procedures are known, this data should be included
- Explain how risks will be minimized.
- Justify the level of risk.
- Describe adequate provisions for monitoring the data during the conduct of the research to minimize risk to participants (see GPM Section 206.3).

For proposed changes to the research, including any change to mitigate potential harm to participants, the PI must submit a protocol Modification Request to the IRB describing any resulting changes in the level of risk to participants, and explaining the risk level and potential benefits.

At Continuing Review, the PI must indicate whether there has been an increase, no change, or a decrease in the level of risk to participants in the study. If the risk level has changed the PI must update the information in the **Risks** section of the protocol.

Studies considered more than low risk must include a data and safety monitoring plan which describes how the PI will oversee the participants' safety and welfare and how unanticipated problems involving risks to participants or others, and adverse events will be characterized and reported.

See also:

- SOP 104: Ensure Sound Design and Minimize Risk
- GUIDE 617: Other Federal Agencies – Additional Requirements
- SOP 116: Reporting and Reviewing Unanticipated Problems
- GPM Section 206.3 (Data and Safety Monitoring)
- [Chapter 4.3](#) above (Importance of Sound Study Design)

4.5 Adequate Resources to Protect Human Research Participants

PIs are required to indicate in the Protocol Application whether they will have access to adequate resources to carry out their research. Resources, including space, personnel, services and equipment required for conducting the proposed research properly and safely, must remain available as needed throughout the research project. The PI must provide information about the qualifications and number of study staff, personnel training, available facilities, and the time available to conduct and complete the research, and must demonstrate sufficient access to a population allowing recruitment of the required number of participants.

PIs should continually monitor the resources allocated for their research and notify the IRB if any change in the availability of resources may adversely impact the rights and welfare of participants in the study.

In addition to IRB approval of the protocol, human participant research (including recruitment and enrollment) which is sponsored cannot begin until a contract has been finalized, or a grant award active.

4.6 Consent Process

See **Section 209** of the General Policy Manual (GPM) on **Informed Consent and Assent**.

4.6.1. Informed Consent is a Continuous Process

Informed consent is a continuous process whereby the investigator and research participant have an ongoing dialogue about aspects of a research study that might inform a participant's decision to volunteer in a study, and their decision to continue their involvement as a participant. Although consent is given, it may be withdrawn at any point. The informed consent process should be regarded as continuing throughout the duration of the research. The purpose of the consent process is to assure knowledgeable decision-making and voluntary participation.

This process generally includes:

- Bring the research study to the notice of potential participants.
- Presentation and explanation by the investigator or delegate of the study and study activities to participant or their legally authorized representative (LAR).
- Documentation of informed consent via a signed and dated written consent document (see below).
- Ongoing discussions between the investigator and the participant regarding continued participation in the study.

The PI is expected to be familiar with:

- The informed consent policies in Section 209 of the GPM, including the criteria for a legally effective informed consent process, and any additional federal, state (Hawaii), and institutional requirements.
- Additional requirements might apply depending on the source of support/ funding; see **GUIDE 617: Other Federal Agencies – Additional Requirements**.
- The consent process information and consent form templates provided on the Human Studies Program website quicklinks [Templates](#) and [Policies & Guidance](#). The **GUIDE 608: Informed Consent Requirement Checklist**, is also available, and might provide additional insight to investigators on particular items that should be included.

The basic and possible additional consent requirements, and those specific to certain types of research activity, are addressed in **Sections 209.1** and **209.3** of the General Policy Manual.

Consent requirements for research involving vulnerable and other special populations – including consent from a legally authorized representative (LAR) – are described in **GPM Section 209.6**. This section addresses adults with diminished decision-making capacity, children, prisoners, children, pregnant women, fetuses and neonates, and UH employees and students.

4.6.2. The Consent Document

The Human Studies Program Website provides consent form templates, which address the required elements of informed consent, as well as providing language for other situations in which certain additional information may need to be disclosed to participants. For research involving children, assent templates are also provided.

To assist PIs in preparing consent documents comprehensible to lay person (i.e., at approximately 8th grade level) a glossary of lay terms is also available on the [website](#).

The IRB encourages and recommends the use of a full consent form, translated into the participant's language whenever possible. In certain situations, the use of a "short form consent process" may be permitted by the IRB, incorporating the use of a short form consent document translated into the participant's language.

In the event that the PI proposes to use a consent document based on one already developed by the sponsor or a cooperative multi-site research group, the PI is responsible for reviewing the existing document to determine if it fairly and describes the research aims, procedures, risks, and benefits. The explanation of risks in the consent document should be based upon information presented in such documents as the protocol, the investigator's brochure, any previous research reports, and, where applicable, the labeling for the drug or device.

If the research involves extensive screening procedures, the PI may wish to develop a separate consent document that explains the screening procedures in detail and provides a brief summary of the underlying research. In such circumstances, screening could begin after the individual signed the screening consent form but before the signing of the main consent document, which would be signed only if the individual satisfied the screening criteria and was actually enrolled in the study.

See **GPM Section 209.5** for detailed information on consent documents, the long form, and the use of the short form consent process.

4.6.3. Providing Consent Process Information to the IRB

In the Protocol Application, the PI must:

- Describe the consent process in enough detail to allow for appropriate review by the IRB,
- Include the proposed written informed consent document(s) that address(es) each of the required elements of informed consent in the context of the research (unless the IRB waives the documentation requirement – see below). And
- Include any written material to be given to prospective participants to explain the nature of the research.

The PI is responsible for making all revisions to the proposed consent document as requested by the IRB. Any other change to the consent document must be submitted to the IRB for prior review and approval.

4.6.4. Requesting Waivers or Alteration of Consent Requirements

Under specific circumstances, the PI may request that the IRB grant a:

- Waiver or alteration of the consent process (i.e., the requirements for obtaining informed consent), or
- Waiver of documentation (i.e., the requirement to obtain a signature on a written consent document).

The requirements for these two options differ. Refer to **GPM Section 209.5** for explanation.

4.6.6. Obtaining Informed Consent

The PI is responsible for obtaining and documenting the informed consent of individuals who participate in research, unless the requirement to obtain and document informed consent is altered or waived by the IRB.

No research procedures, including screening procedures to determine if an individual is eligible to enroll in the research, may begin until after the participant has signed the consent form, unless the IRB has approved a waiver or alteration of consent. Retroactive consent – i.e., consent obtained or documented after the participant has undergone one or more research procedures – is not acceptable.

The PI may delegate all or a portion of the informed consent process to others on the research team, such as co-investigators or research coordinators. However, it is ultimately the responsibility of the PI to ensure that those individuals carry out their tasks properly and in accordance with regulatory and IRB requirements.

The PI must use the consent document currently approved by the IRB. The IRB approval date must appear on (at least) the signature page of the consent document.

No participants should be involved in research prior to the IRB approval date, and no participants should be involved in research using a consent document whose approval period has expired.

The PI or their delegate should plan to discuss research with potential participants at a time when they are not under duress, and to allow sufficient time and opportunity to ask questions and to consider whether or not to participate in the research before agreeing to participate.

In discussing research with potential participants, the PI or their delegate:

- May not describe items or procedures under investigation as if they were known to be safe and effective as a treatment for the potential participant's disease or condition, or as if they present a known benefit, and
- May not understate the risks of the research, as there may be not countervailing benefits to participants.

The PI or their delegate is responsible for giving the participant a copy of the signed informed consent document, and for maintaining the original form.

4.6.7. Obtaining Informed Consent in the Clinical Research Context - Special Considerations

The distinction between treatment and research is especially important if the PI is also the potential participant's attending physician, a situation that increases the risk of confusion. Thus, it must be clearly stated to the participant that they will be involved in research and that if randomization is involved, that this is also described.

The purpose of medical or behavioral treatment is to provide interventions designed solely to enhance the well-being of the patient or client. By contrast, research is designed primarily to develop generalized knowledge rather than to benefit each participant in the research. Research involves activities to test a hypothesis and draw conclusions, and any therapeutic benefit to the participants is secondary to the objectives of the research.

Research involving randomization of participants, whether to proven or experimental procedures, raises further issues. In these circumstances, the PI should ensure that each participant understands that the assignment will not be based upon the attending physician's clinical judgment as to which treatment may prove more beneficial to that participant, and may involve additional testing that would not be performed as clinical care.

4.6.8. Consent Situations Requiring Prompt Reporting to the IRB

Situations where informed consent is not properly obtained or not documented, and no corresponding waiver or alteration of the consent process has been granted by the IRB, may constitute noncompliance. Such circumstances may require reporting to the IRB. These include, but are not limited to:

- Involving an individual in research without first obtaining their informed consent and a signed informed consent document (unless the IRB has explicitly waived these requirements).
- Involving an individual in research using a consent form other than the current IRB-approved form.
- Situations where the PI believes informed consent documents have been lost, misplaced, or destroyed.

See also:

- [Chapter 6](#) on Responsibilities of the PI after Approval for information on reporting to the IRB
- [Events and Information that Require Prompt Reporting to the IRB](#) [GUIDE 614].

4.7 Responding to Participants' Request for Information and Complaints

4.7.1. Requests for Information

The PI and research staff are required to respond promptly and adequately to all requests for information received from participants, prospective participants and their family members or designated representatives. In addition to providing information and answering questions that arise as part of the informed consent process, the PI must inform the participant that he/she is available to answer any questions that arise about the research in the future. The consent form must include the full name and contact information for the PI, and other research study staff as appropriate. The consent form must also inform participants how to reach the IRB if they have any questions about their rights as research subjects (see *UH consent form templates* for contact information language).

4.7.2. Responding to Complaints

Participants may contact the Human Studies Program to report a complaint about a PI and/or research staff. It is expected that if an investigation by the Human Studies Program and UH IRB is warranted, the PI and research staff fully cooperate with the investigating party in providing pertinent information that is requested. The Principal Investigator and research staff may be required to meet with the investigative party (i.e., on-site visit) or provide study documentation.

Chapter 5: Pre-approval Procedures

5.1 What training do my staff and I need to complete prior to conducting human subjects research?

Investigators and study staff must complete the online Collaborative Institutional Training Initiative (CITI) human subjects online training program. Please note that PIs and study staff must complete the CITI training (or NIH training, if appropriate) prior to review of any submitted documents to the Human Studies Program. The UH-specific CITI site can be accessed at <http://www.citiprogram.org/>. The CITI curriculum you will need to take depends on the study subject matter, the type of IRB review, and your study role. Details and instructions on what you must take and how to register and select your courses can be found in “[Training](#)” section of the Human Studies Program website.

5.2 How do I submit new Human Subjects Research to the IRB?

To submit new Human Subjects Research, you will need to complete the Human Subject Research Protocol application form, using the eProtocol online application form (Unified IRB form). You may access the eProtocol application form on the Human Studies Program website at <https://www.hawaii.edu/researchcompliance/irb-eprotocol>. The Human Studies Program eProtocol system is an online application form, that will allow users to log in using their UH username and password. It is the PI's responsibility to submit a written protocol or proposal to the IRB for review. Although the online application system will allow selected personnel such as co-investigators or study personnel to create, edit and submit an application, the PI listed on the application is ultimately responsible for the submission of the application, and the conduct of the protocol. At submission, the obligations of the PI with respect to oversight of their research protocols and research staff during recruitment, selection of study participants, and conduct of the study according to the protocol or proposal as approved by the IRB are stated in the [application form](#), and must be agreed to by the PI for the submission to be accepted. The PI is responsible for ongoing adherence to the determinations and requirements of the IRB for the duration of the research.

5.2.1. Is my project “Not Human Subjects Research” (NHSR)?

Unless formal documentation from the Human Studies Program is needed, you do not need to submit a UH IRB application to the Program if the project is considered “not human subjects research.” For guidance assessing your proposal, you may consult Worksheet 301 (on the HSP website at: <https://www.hawaii.edu/researchcompliance/policies-guidance>). However, if an official determination of whether the project is NHSR is required, you will need to complete and submit the “New Research Protocol” application form to be reviewed by the Human Studies Program. Once Program staff verifies that the project is deemed NHSR, an email notice will be generated by the eProtocol system, and a letter with the Program's determination will be available in eProtocol.

5.2.2. How do I apply for exempt status?

Certain types of human subject research activities will qualify for a special “exempt” status. This means that this research does not require normal IRB approval and monitoring. To qualify as exempt research, the research

activities must all fall under one or more specific categories defined in regulations (45 CFR 46.104). Guidance on these categories may be viewed in [Worksheet 302](#), Requirements for Exempt Approval.

To apply for exempt status, you will need to submit a completed new protocol application form using [eProtocol](#) as described above. All appropriate supporting documents should be appended to the application form (e.g., informed consent documents, study instruments, recruitment materials, etc.)

There are no submission deadlines for exempt research applications.

When a research proposal has been determined to meet the requisite exempt criteria, a notice will be forwarded to the PI. Exempt research is not subject to the normal requirements for continuing review by the IRB. However, if there are subsequent modifications in the study design, methods or IRB-approved documents after initial approval of the research, a request for review and approval of a modification to an exempt study should be submitted. A modification application may be filed using the Human Studies Program online application [system](#). The Human Studies Program staff will review the proposed modification(s) and communicate its response via the comments feature in the online application system.

Sometimes, a modification to an exempt study changes the status of the study to non-exempt. If it does, you will be notified of the need to revise your application for IRB review.

5.2.3. How do I apply for approval of non-exempt research (Expedited or Full-board IRB)?

Non-exempt research may qualify for expedited review. This means the research would not require review by the full convened IRB, but may instead be reviewed by a single (or multiple) IRB members outside the normal convened meeting. To be approved under expedited review, the research must pose minimal risk to participants, and meet one or more expedited review criteria. Guidance on the expedited criteria may be viewed on [Worksheet 313](#). If the research does not meet expedited review criteria, the application will require review by the full IRB at a convened meeting.

The application process for all non-exempt research is the same with one exception: IRB applications for research requiring full IRB review need to be submitted with consideration for the IRB meeting calendar. To have an application reviewed at a given IRB monthly meeting, the application must be submitted to the Human Studies Program on, or prior to the meeting deadline for that month. Applications for review of research that qualifies for expedited review do not need to meet this deadline, and will be reviewed typically in the order they are received. For information on IRB submission deadlines, see the current IRB calendar found in the IRB section [HERE](#).”

5.2.4. How do I apply for approval of changes to IRB-approved research?

If changes to an IRB-approved study or documents are proposed, federal and UH regulations require that these changes have documented IRB approval prior to implementing the change(s). For information on how to apply for approval to modify a research project, see [guidance on the HSP website HERE](#).

5.3 What do I need to include in an IRB submission?

In addition to a completed application, the following materials must be submitted when applicable:

- Research proposal or protocol
 - Completed grant proposal or protocol (without CVs or budget), or a complete sponsor protocol including DHHS-approved protocol, if applicable
- Data collection instruments (spreadsheets, logs, etc.)
- All written material to be provided to, or meant to be seen or heard by, participants, including:
 - Evaluation instruments and surveys
 - Interview questions
 - Recruitment materials and scripts (printed, audio, and video)
 - Pictures, audio, or video used while conducting Human Subject Research
- Consent documents
 - Written adult consent document
 - If consent will not be documented in writing, a script of information to be provided orally to participants is required
 - Assent forms for research involving children as participants, with accompanying written parental consent forms; assent forms should be age appropriate. See **GPM Section 209: Informed Consent and Assent** and **GUIDE 606: Consent Form Guidance**.
- DHHS- approved sample consent document
 - If a research is sponsored by any of the existing federal agencies and departments (e.g., FDA, NIH, NSF, etc.) that have adopted the Common Rule, consent documents that have been approved by such an agency or department need to be included in the application packet.
- For industry-sponsored trials (or clinical trials):
 - Current investigator brochure (IB) for each investigational drug, if applicable
 - Current package insert for each marketed drug, if applicable
 - Current product information for each investigational device, if applicable
- Foreign language version of any written material to be provided to, or meant to be seen or heard by, participants
- Required UH human subjects research training (See <https://www.hawaii.edu/researchcompliance/get-training-0>)

The application and its supporting research documents should be submitted electronically through the [HSP online application](#) system for review.

5.3.1. How do I write a Human Subjects Research Protocol/ Proposal?

The Human Studies Program provides guidelines for quantitative, traditionally for biomedical research, and for qualitative, for mainly social behavioral research. You can find the guidelines on the Human Studies Program website under the Policies & Guidance section [HERE](#) (**GUIDEs 603, 604, and 605**) to assist in creating a protocol or proposal.

When compiling your protocol/ proposal, remember these helpful tips:

- Keep an electronic copy of the protocol/ proposal that includes the version date somewhere in the document. This copy should be used to show proposed changes to the protocol when submitting a modification request.
- When making changes, provide both a “track changes” version that shows what changes are being added to the approved protocol, and a final, clean version that includes the proposed changes.
- If you believe your project may not be Human Subjects Research, contact the Human Studies Program prior to developing your protocol.
- Provide an appendix with the protocol that includes study materials that will be used to conduct the research. For any items described in the protocol, reference the appendix number next to the description.

5.3.2. How do I create a consent form?

PIs are responsible for assuring the quality of the informed consent process and for making sure that consent is obtained and documented before subject participation, unless waivers are granted by the IRB. For a detailed discussion of the informed consent process requirements, see GPP 211 Informed Consent: Process and Documentation.

- A written consent form needs to have the following elements:
 - Title of the Project (this should be identical to the Project Title provided in the IRB application)
 - Name of the Principal Investigator
 - Purpose of the research
 - Summary of the research activities involving human participants
 - Risks and Benefits
 - Voluntary Participation
 - Contact information
 - Principal Investigator (and faculty advisor, if student-run research) for information about the research project
 - The Human Studies Program for information about rights of the participant
 - Separate consent section for, when applicable:
 - Future Use of Biological Specimen
 - Contact for Future Studies
 - Audio/ Video Recording
 - Use of participants’ real names in final report
 - Signature line
 - Participant (signature, printed name, and date of signature)
 - Legally Authorized Representative (signature, printed name, and date of signature), if applicable
 - For clinical trials, Person Obtaining Consent (signature and date) and Principal Investigator (signature and date)

Use the appropriate model consent form from the Program website as a template for creating your consent form. Model consent forms are available on the Human Studies Program website under the “[Templates](#)” section. Further guidance on creating informed consent documents can be found [HERE](#).

5.3.3. How do I create an assent form?

Assent forms should be provided for research involving minors (<18 years of age) and participants with diminished mental capacity

When the participants in the research are minors (<18 years of age), an assent form is generally required (an exception would be if the research was on classroom curriculum in a normal educational setting [exemption category 1]). In line with Hawaii Department of Education (HIDOE) policy, the UH IRB requires that even research involving normal educational curriculum an assent form or script to be provided to student minors who may become involved in the research in the school setting. Assent forms provide the child an opportunity to learn about the research before being involved and to make an informed decision about whether or not to participate. A child cannot participate in the research unless both the parental consent and assent forms are signed/ initialed.

Assent forms may also be provided if the research involves participants with diminished mental capacity, such as those with dementia or a learning disorder.

An assent form is unique to the consent form mainly for its readability. The assent form is written in very simple language and is limited in length appropriate for the age range and/or mental capacity of the participants.

In general, there are three levels of child assents:

1. Oral assent for minors who cannot read
2. Written signed assent
 - a. 7-13 years of age
 - b. 14 to 17 years of age

5.3.4. Recruitment Materials

The Principal Investigator (PI) is responsible for ensuring recruitment activities, whether undertaken by research staff or the PI, are via methods set forth in the IRB-approved protocol or proposal application.

Recruitment materials include any advertisements used to aid in the recruitment of potential participants. This can include physical flyers, email announcements, scripts, and online advertisements. For more information on how to create a recruitment flyer, go to [GUIDELINES FOR DESIGNING A RECRUITMENT FLYER FOR A RESEARCH STUDY](#).

If the research project will be advertised on a website, a screenshot of the advertisement needs to be included in the IRB application, if available.

If recruitment is done orally (either through phone or done in-person), a recruitment script must be submitted to the Human Studies Program for review and approval.

5.3.5. Survey Instruments

All survey instruments and interview questions must be submitted with your IRB application and be approved before its use. Any changes to the sentence structure of the interview or survey questions must also seek approval before its use, even if it seems that the content of the question is unchanged.

5.4 *What other organizational or intra-departmental approvals may be needed in addition to IRB approval?*

Depending on the nature of the research, certain additional reviews and approvals may be required. These additional approvals may include, but are not limited to:

- UH Biosafety Committee
- Conflict of Interest Committee (ORS)
- Health Insurance Privacy and Accountability Act (HIPAA) Privacy Officer
- Family Educational Rights and Privacy Act (FERPA) and/or Protection of Pupil Rights Amendment (PPRA) Review
- UH Information Technology Services
- Office of the Dean for Students
- UH Counseling Services
- UH Data Governance
- Hawaii Department of Education (HIDOE) Data Governance

5.5 *What are the different regulatory classifications that research activities may fall under?*

- Not “Human Subjects Research”: Activities must meet the DHHS or FDA definition of “research” involving “human subjects” for the activity to fall under IRB oversight. Activities that do not meet either definition of “Research” involving “Human Subjects” are not subject to IRB oversight or review. Review the HSP’s [WKSH 301: IS MY PROJECT HUMAN SUBJECTS RESEARCH](#) for reference. Please contact the Human Studies Program Office if you are still unclear about whether or not an activity meets the regulatory definition of Human Subjects Research.
- Exempt: Certain categories of Human Subjects Research may be exempt from some federal regulations. It is the responsibility of the IRB, not the investigator, to make the final determination of whether the Human Subjects Research is exempt. Review the the categories of Human Subjects Research that may be exempt in GPM ().
- Expedited Review: Certain categories of non-exempt Human Subjects Research may qualify for review using expedited procedures (i.e., review by a designated IRB reviewer). Review the HSP’s [WORKSHEET 313: ELIGIBILITY CRITERIA FOR EXPEDITED REVIEW](#) for reference regarding the categories of Human Subjects Research that may be reviewed using the expedited review method.

- Full-Board IRB Review: Non-exempt Human Subjects Research that does not qualify for review using the expedited method must be reviewed by the convened IRB.

5.6 What are the decisions the full-board IRB (aka “convened IRB”) can make when reviewing a protocol?

The IRB may take the following actions with respect to a research study submitted for review:

- Approval: Approval of the study as submitted. The study may begin once the investigator receives the approval letter from the Human Studies Program.
- Approval with Stipulations: Approval with stipulations is acceptance of the protocol with requests for clarification and/or modifications as a condition of final approval. The project cannot begin until the stipulations have been verified as satisfactory by the IRB Chair or other IRB member, usually the IRB primary reviewer, or staff as designated by the IRB. No study may begin before receiving final written approval from the UH Human Studies Program.
- Recommendations: The IRB, in approving a study, may make recommendations for changes to protocols and/or informed consent documents. These recommendations are most often made to enhance protocol and/ or informed consent document clarity, but unlike stipulations, recommendations are *not* required changes.
- Deferral: Deferral of the application requires a written response from the investigator to substantive questions raised by the IRB during its review. The response to a deferred protocol will be reviewed by the convened IRB.
- Disapproval: Disapproval of a research application means that the proposal does not meet requisite standards and the study, as presented, cannot be performed at UH or by a UH faculty member, an employee, or a student.
- Tabled: Made when the IRB cannot approve the research at a meeting for reasons unrelated to the protocol, such as loss of quorum. When taking this action, the IRB automatically schedules the protocol for the next meeting.

5.7 How does the IRB decide whether or not to approve Human Subjects Research?

The criteria for IRB approval for non-exempt Human Subjects Research can be found in **General Policy Manual Section 204.4** under “*Criteria for Approval by an IRB.*”

5.8 What will happen after IRB review?

The Program staff will draft and transmit a letter to the investigator, communicating the IRB’s decision and any follow-up actions required of the investigator. All such communications to investigators will be in writing.

Research must not commence until the Principal Investigator receives written approval from the Human Studies Program.

- If the IRB has approved the protocol: The Human Subjects Research may commence once all other organizational approvals have been met. The investigator will be notified of the duration of the approval, which will not be longer than one year from the date of approval.
- If the IRB has approved the protocol with stipulations: The investigator will receive an email notice from the eProtocol system, that the IRB has comments or stipulations that the PI will need to address. The comments may be accessed by the PI (and co-investigators or other authorized study personnel) by logging into the eProtocol system and accessing the comments section for the application. The investigator must respond to these stipulations within 3 months of receiving the notice. If the IRB does not receive a response within 3 months, the investigator will need to resubmit a new application to have the Human Subjects Research be reconsidered for approval.
- If the IRB has deferred the protocol: The investigator will be notified by email from the eProtocol system of the IRB's action. The PI will be able to access comments and requests by the IRB, by logging into the eProtocol system and accessing the comments section for the application. If the IRB does not receive a response within 3 months, the investigator will need to resubmit a new application to have the Human Subjects Research be reconsidered for approval.
- If the IRB has disapproved the protocol: The investigator will be notified by email from the eProtocol system of the IRB's action. Comments detailing the reason(s) for the IRB action may be accessed in eProtocol. A separate letter may also be forwarded to the PI by HSP staff, by email with a description of reason(s) for the disapproval.

The date of the approval letter reflects the date in which all conditions are determined by the IRB committee or designated reviewer to be met.

Chapter 6: Post- Approval Procedures

6.1 The responsibilities of the Principal Investigator after IRB approval

The PI is responsible for conducting the study in a manner that is scientifically and ethically sound and for ensuring the use of appropriate methods and correct procedures, according to the approved protocol. Any new information, modification, or unanticipated problem involving risks to participants or others must be promptly reported to the IRB, **GUIDE 614 Events and Information that Require Prompt Reporting to the IRB**, and research participants must be informed of any change that may affect their willingness to participate.

PIs may delegate research responsibility. However, PIs maintain oversight and retain ultimate responsibility for the conduct of those to whom they delegate responsibility. The conduct of a study usually requires the

involvement and contribution of other individuals under the direction of the PI, based on their qualifications and capabilities. In delegating study-specific tasks and responsibilities to other members of the research team, the PI must ensure that those assuming a duty are well trained and competent.

Do not start Human Subjects Research activities until you have received the IRB approval letter, and all other required institutional approvals, including approvals of departments or divisions that require approval prior to commencing research that involves their resources. See the section: [What other organizational approvals may be needed in addition to IRB approval?](#)

- Research Staff and Support:
 - Ensure that there are sufficient resources to carry out the research safely. This includes, but is not limited to, sufficient investigator time, appropriately qualified research team members, equipment and space.
 - Ensure that Research Staff are qualified (e.g., including but not limited to appropriate training, education, expertise, credentials, protocol requirements and, when relevant, privileges) to perform procedures and duties assigned to them during the study. *Suggestion: Use [REGULATORY DOCUMENT: DELEGATION LOG](#) to document each research staff member's roles and responsibilities in the Human Studies Research.*
- After approval of the initial application, submit to the Human Studies Program:
 - Proposed modifications as described in “[How do I apply for approval of changes to IRB-approved research?](#)”
 - Update the IRB office with any changes to the list of study personnel using the form MODIFICATION APPLICATION [\(HERE\)](#). If adding new study personnel, you must include their CITI Training Certificate of Completion to the Modification application.
 - A continuing review application at least one month prior to the expiration date described in the preceding approval letter. See “How do I submit a continuing review?” It is highly recommended that you submit your continuing review application two months prior to the expiration date if the application needs to be reviewed by the convened IRB committee.
 - A closure or final report form to close out Human Subjects Research at the time you close a research study. See HSP website [\(HERE\)](#)”
- Conduct their research according to the IRB approved protocol, complying with all IRB determinations.
- Ensure that each prospective subject understands the nature of the research and of the subject's participation, taking the steps necessary to gain that comprehension.
- Provide a copy of the IRB-approved informed consent document to each subject at the time of consent, unless the IRB has waived this requirement.
- Promptly report proposed changes in previously approved human subjects research activities to the IRB. The proposed changes may not be initiated without prior IRB approval except where necessary to eliminate apparent immediate hazards to subjects or others (see SOP 115, *Submitting Modification Requests to the IRB*).
- Report progress of approved research to the IRB as often as and in the manner prescribed by the IRB.
- Promptly report protocol violations according to Human Studies Program policies and procedures as documented in SOP 108, *Determining and Reporting Non-Compliance and Protocol Violations*.
- Promptly report to the IRB any unanticipated problems involving risks to subjects or others as documented in SOP 116, *Reporting and Reviewing Unanticipated Problems*.
- Do not start Human Subjects Research activities until you have received the IRB approval letter.

- Do not start Human Subjects Research activities until you have obtained all other required institutional approvals.

6.2 What are the documentation requirements for standard “long form” consent?

Consent templates approved by the UH IRB includes a standard signature section at the end of the written informed consent.

The following are the documentation requirements for the “long form” consent document for non-exempt research:

- The participant or representative (e.g., legally authorized representative, or “LAR”) signs and dates the consent form.
- The individual obtaining consent signs and dates the consent document.
- If required by the IRB, the participant’s or a representative’s signature is to be witnessed by an individual who signs and dates the consent document.
- For participants who cannot read and if required by the IRB or the sponsor, a witness to the oral presentation signs and dates the consent document.
- A copy of the signed and dated consent document is to be provided to the participant.

The following are the documentation requirements for the “short form” consent document (i.e., written consent documents stating that the required elements of informed consent have been presented orally to the participant’s LAR in the presence of a witness to the oral presentation):

- The participant or representative signs and dates the consent form.
- The individual obtaining consent signs and dates the consent document and the summary.
- The witness to the oral presentation signs and dates the consent document and the summary.
- A copy of the signed and dated consent document is to be provided to the participant.

For minimal risk studies that qualify for a waiver of written documentation of consent, participant names and signatures do not need to be obtained on the consent form.

6.3 Making changes to my IRB-approved protocol, consent, and/or study materials

If you need to make protocol or study document changes on your IRB-approved project, you need to first obtain IRB approval prior to implementation of the change.

Obtain IRB approval before implementing changes

For research reviewed as *exempt* or *non-exempt*, the PI will need to complete the **MODIFICATION APPLICATION** and submit the completed application and applicable study documents (i.e., consent forms, new study instruments) via eProtocol.

Please note that modifications to an exempt research may move the protocol to a non-exempt status, if the UH IRB deems that the modification increases the potential risk to participants from less than minimal risk to no

more than minimal risk or higher. In such a case, the PI will be notified by Human Studies Program staff to complete a **MODIFICATION FORM** and a new **NON-EXEMPT APPLICATION FORM**.

6.4 Reporting Unanticipated Problems

Principal Investigators (PIs) are responsible for reporting unanticipated problems involving risks to participants or others (UPs) and other reportable information to the IRB. For industry sponsored projects, PIs are responsible for maintaining contact with the sponsor, and receiving reports from the sponsor, and if applicable, the monitoring entity (e.g., DSMB, DMC) and reporting suspected UPs and other reportable information to the IRB. For sponsor-investigator projects, the PI is solely responsible for reporting UPs and other reportable information to the IRB.

Any occurrence that qualifies as an Unanticipated Problem should be reported to the IRB within 24 hours of the PI becoming aware of the occurrence by calling the Human Studies Program office at 808-956-5007 or sending an email to uhirb@hawaii.edu. The PI, sub-investigators or the study staff must also submit a report to the Human Studies Program about the occurrence within 10 business days following the discovery of the problem using the [Serious Adverse Event Form in eProtocol](#). The report form may be found by accessing the protocol in the approved protocol section on the investigator dashboard.

Report unanticipated problems to the Program within 10 business days
from the date of discovery.

Certain unanticipated problems can be considered as an *adverse event* if an untoward or unfavorable medical (physical, emotional, psychological) outcome in a study participant is temporarily associated with the subject's participation in the research study. *Serious adverse events*, however, are construed as those events that result in any of the following outcomes to a research participant: death, life-threatening event, new or prolonged in-patient hospitalization, persistent or significant disability, or congenital anomaly or birth defect. Determination regarding whether an unanticipated problem is an adverse event or serious adverse event should be the responsibility of the principal investigator, or a data safety monitoring board (DSMB), if one is assigned.

The Unanticipated Problem (UP) Report should provide a full description of the UP, including an assessment by the UH Principal Investigator of the causal relationship between the UP and the protocol/ proposal, and a proposed corrective action plan (CAP) to address or remedy the issue, as appropriate. To know more about the policies and procedures for PI Reporting Unanticipated Problems and Adverse Events see [SOP 116.: Reporting and Reviewing Unanticipated Problems](#).

6.5 How do I report Protocol Violations?

Any deviation or departure from the IRB-approved protocol that does not have prior approval is considered a protocol violation. The exception to this rule is if the change is necessary to remove an apparent immediate hazard to one or more study participants.

There are two types of protocol violations: minor and major.

A minor protocol violation *does not* impact the safety or welfare of study participants, compromise the integrity of study data, or affect participants' willingness to participate in the study. Such violations only need to be reported at the time of continuing review.

Major protocol violations *do* impact the safety or welfare of study participants, compromise the integrity of study data, or affect participants' willingness to participate in the study. Major protocol violations should be reported to the IRB within 24 hours of the PI becoming aware of the occurrence by calling the Human Studies Program office at 808-956-5007 or sending an email to uhirb@hawaii.edu. The PI, sub-investigators or the study staff must also submit a report to the Human Studies Program about the occurrence within 10 business days following the discovery of the problem using the [Protocol Violation Report Form in eProtocol](#). The report form may be found by accessing the protocol in the approved protocol section on the investigator dashboard.

Report major protocol violations to the Program within 24 hours of the
occurrence

If the PI is not sure the protocol violation is minor or major, it is always better to report the protocol violation as a major to the UH IRB.

If a protocol change has been initiated to remove an apparent immediate hazard to one or more study participants, the PI needs to report this change by submitting a modification application to the IRB.

To know more about the policies and procedures for PI Reporting Unanticipated Problems and Adverse Events see [SOP 108: Determining and Reporting Non-Compliance and Protocol Violations](#).

6.6 How do I submit a study closure request?

At the conclusion of the study, PIs involved in research approved under regular review should submit a final report to the IRB within 30 days of study closure.

Human Subjects Research are considered active and must undergo continuing review until all four criteria are met:

1. The research is permanently closed to enrollment.
2. All participants have completed all research-related interventions/ procedures.
3. Collection of private identifiable information is completed.
4. Analysis of private identifiable information is completed.

To close a protocol (both exempt and non-exempt), the investigator should complete and submit the "Final Report" form on eProtocol. The report form may be found by accessing the protocol in the approved protocol section on the investigator dashboard..

For non-exempt protocols that pre-date the eProtocol system, the investigator should complete the form, **APP 08: Study_Closure Form**. The form may be found on the HSP website at:

<https://www.hawaii.edu/researchcompliance/closing-protocol>

The non-eProtocol form may be submitted by email to: uhirb@hawaii.edu.

6.7 How long do I keep records?

Maintain your Human Subjects Research records, including signed and dated consent documents, for at least *three years* after closing out the Human Subjects Research, per DHHS and UH data retention policies under the [UH Human Studies Program Record Keeping Policy \(dated 11-20-2012\)](#). Please check with your affiliated medical institution on the duration of retaining records of HIPAA authorizations and other records related to HIPAA compliance.

If your Human Subjects Research is sponsored, contact the sponsor before disposing of Human Research records. Otherwise, see <https://www.hawaii.edu/svpa/apm/recmgmt/a8450.pdf> for more information about UH's policy on record retention.

Chapter 7: Collaborative Research

7.1 Research to be reviewed by the UH Cooperative IRB

The Cooperative IRB's purpose is to serve as a single (or central) IRB – the members of which include representatives of those local institutions that have entered into a joint review arrangement with the UH to rely upon the findings of the Cooperative IRB – in order to avoid duplication of effort. For research to be reviewed by the UH Cooperative IRB, the following criteria must be met:

- Non-exempt research
- Federally-funded
- Investigator(s) is UH-affiliated and research involves one or more of the following institutions:
- The Queens Medical Center
- Hawaii Pacific Health (e.g., Kapiolani Women and Children, Straub, Pali Momi, Wilcox)
- Castle Medical Center

New research to be reviewed by the Cooperative IRB requires completion and submission of the “UH Cooperative IRB New Research Project Application,” which can be downloaded [HERE](#).

Be aware, the Queens Medical Center IRB will review these studies independent of UH Cooperative IRB's review, but investigators will not need to complete a separate application. All other listed institutions will accept the UH Cooperative IRB's review and decision.

7.2 Multiple IRBs: What if I plan to conduct research at or with another site outside

of UH?

Contact the Human Studies Program Director to discuss the situation.

If the other research site has its own IRB, there are situations in which both the UH IRB and the external IRB may need review the study. In such situations, the investigator will need to receive approval for the protocol from all IRBs involved. If an IRB requests changes to be made, all other involved IRBs must be notified of this change and provide their approval before research begins or requested changes can be implemented.

It is also possible that one institution can rely upon the other institution's IRB and cedes its authority to the other IRB. For one institution's IRB to rely on another, an IRB Authorization Agreement must be completed and signed by the institutional official of both institutions before ceding can take place.

If the UH IRB relies upon another IRB for your research, you will not need to go through a review process here at UH. Unless otherwise stated as part of the agreement, the investigator should submit a copy of the IRB application to Human Studies Program concurrently with their submission to the designated IRB. Once approved by the designated IRB, it is the investigator's responsibility to submit a copy of the approval documentation to the Human Studies Program for their IRB records.

Likewise, other institutions may rely on UH IRB. For more information about Ceded Research, see [SOP 120: Collaborative Research](#) and the section below.

7.3 Institutional Ceded Agreements

Ceding IRB authority not only applies to individual research studies, but also institutional research sites. The purpose of ceded agreements is to help investigators avoid unnecessary redundancy in paperwork. The UH IRB maintains IRB Authorization Agreements with select institutions that regularly support and conduct human subjects research with UH. Based on the language of each agreement, certain studies can apply to have their research be reviewed by one IRB, instead of two or more.

For a list of research institutions in which UH IRB either relies or is relied upon for IRB authority, please visit the Human Studies Program website under "[Institutional Review Board \(IRB\)](#)." Please note, that the list of active agreements can change intermittently.

Chapter 8: Special Circumstances

8.1 118 Designation

Certain types of applications for grants, cooperative agreements, or contracts may be submitted to agencies with the knowledge that human subjects may be involved within the period of support, but definite plans would not normally be included in the applications. Such projects need not be reviewed by an institutional review board (IRB), per 45 CFR 46.118.

These types of projects fall into three general categories:

1. Institutional type grants: selection of specific subgrants is the institution's responsibility;
2. Training grants: research activities involving human subjects remain to be selected; or
3. Indefinite projects: human subjects' involvement will depend on
 - a. Completion of instruments;
 - b. Prior animal studies; or
 - c. Purification of compounds

Examples in which 118 Designation may be granted include projects requiring some type of conditional approval for Just-in-Time, or infrastructure projects that support sub-studies involving human subjects for a particular research goal.

Such designation does not waive a project from IRB review and approval. Once the plan on human subjects becomes definite, it is the investigator's responsibility to seek IRB review and approval before executing any research activities involving human subjects.

To learn more about the policies and procedures for PI seeking 118 Designation see [SOP 123: Section 118 Designation](#).

8.2 Transferring a Protocol to Another Investigator

When faculty members leave UH, they should terminate their active protocol(s) or submit a request to transfer the protocol to another qualified investigator who will take over responsibility for the research. This request should be co-signed by the new investigator. Appropriate changes to consent forms, advertisements, etc. must be submitted to the IRB for approval when there is a change in investigator.

A change in investigator is considered to be a study modification. The PI must submit a completed modification request form to the IRB, following policies and procedures outlined in the Human Studies Program. See guidance on submitting a modification on the HSP website at: <https://www.hawaii.edu/researchcompliance/modify-protocol>

8.3 Emergency Use: What should I do if I need to use an unapproved drug or medical device in a life-threatening situation prior to IRB approval?

Contact the Human Studies Program immediately by phone at 808-956-5007. If there is not time to make this contact, see the Policies and Procedures for "Emergency Use" (**SOP 121: Emergency Use of a Test Article** and **SOP 122: Planned Emergency Research**) to see if your situation meets the regulatory criteria and the procedures.

Although prior approval to use an investigational drug or device in an emergency is often difficult to obtain from the IRB, the IRB Chair can provide an acknowledgement letter in advance of administration of the test article. Investigators must submit a letter that includes the following information:

- The drug or device name;
- Provider/ sponsor of the drug or device;
- IND/ IDE number;
- Participant's initials;
- Details about the participant's disease or condition; and
- Justification or rationale for the emergency use.

Along with the letter, the investigator must also include a copy of the consent form. The investigator must notify the IRB no later than 5 working days after the emergency use.

Chapter 9: Recruitment

9.1 Considerations for Recruiting UH Employees and Students as Research Participants

While employees and students are not considered vulnerable populations by federal regulations, they may perceive that they are under some pressure from their superiors to agree to participate. PIs must provide a rationale for involving their employees or students as their research participants. When students are involved, the PI must explain:

- How they will be protected from coercion and undue influence, and
- What alternatives to participation exist. For example, if course credit is offered, what alternative means of obtaining that credit would be available.

9.2 Considerations for Recruiting Children as Research Participants

Children should be included in research, along with adults, unless there is a compelling rationale for their exclusion. Research that limits enrollment to children is generally not appropriate unless:

- The situation, condition, or disease is limited to children, OR
- The research seeks to obtain information on a test article or procedure that previously had been studied only in adults.

9.3 Appropriate Compensation

Compensation to research participants may not be of such an amount as to result in coercion or undue influence of the participant's decision to participate.

In general, the term "payment" to research participants should be avoided and replaced with "compensation." Research participants consent to participate on a voluntary basis, and therefore the use of "payment" is not suitable.

9.4 May I use raffles, lotteries, or drawings as compensation for my research

participants?

Generally, due to Hawaii's strict state laws regarding gambling, the IRB does not allow lotteries of any form as compensation for research participation. The use of chance winnings gives the appearance of unequal share to participants, and the Human Studies Program has discouraged investigators who want to use lottery for compensation as it also elicits a coercive environment in research studies.

Compensation value should be equal and given to all participants who complete equal amount of research activities.

For more information about Hawaii's law on gambling, see http://www.capitol.hawaii.gov/hrscurrent/Vol14_Ch0701-0853/HRS0712/HRS_0712-1220.htm.

Chapter 10: How do I get additional information and answers to questions?

This handbook and other information about the Human Studies Program are available on the Human Studies Program website, under the Office of Research Compliance at www.hawaii.edu/researchcompliance.

If you have any questions or concerns about the Human Studies Program, or its IRBs, contact the office at:

Human Studies Program
1960 East-West Road, Biomed Bldg. B-104
Honolulu, HI 96822
Ph. 808-956-5007
Fax 808-956-8683
E-mail: uhirb@hawaii.edu

Chapter 11: Appendices

*A-1: Additional Requirements for DHHS-Regulated Research*³

1. When a participant decides to withdraw from a clinical trial, the investigator conducting the trial should ask the participant to clarify whether the participant wishes to withdraw from all components of the trial or only the primary experimental component of the trial. If the latter, research activities involving other components of the clinical trial, such as follow-up data collection activities, for which the participant previously gave consent may continue. The investigator should explain to the participant who wishes to withdraw the importance of obtaining follow-up safety data about the participant.
2. Investigators are allowed to retain and analyze already obtained data relating to any participant who chooses to withdraw from a research study or whose participation is terminated by an investigator without regard to the subject's consent, provided that such analysis falls within the scope of the analysis described in the IRB-approved protocol. This also applies to data that includes identifiable private information about the participant.
3. For research not subject to regulation and review by FDA, investigators, in consultation with the funding agency, can choose to honor a research participant's request that the investigator destroy the data already collected from the participant or that the investigator exclude the participant's data from any analysis.
4. When seeking the informed consent of participants, investigators should explain whether already collected data about the participants will be retained and analyzed even if the participants choose to withdraw from the research.

³ <http://www.hhs.gov/ohrp/policy/subjectwithdrawal.html>

A-2: Additional Requirements for FDA-Regulated Research

1. When a subject withdraws from a study:⁴
 - a. The data collected on the participant up to the time of withdrawal remains part of the study database and may not be removed.
 - b. An investigator may ask a participant who is withdrawing whether the participant wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the participant would distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the participant's information.
 - c. If a participant withdraws from the interventional portion of the study, but agrees to continued follow-up of associated clinical outcome information as described in the previous bullet, the investigator must obtain the participant's informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). IRB approval of informed consent documents is required.
 - d. If a participant withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the investigator must not access for purposes related to the study the participant's medical record or other confidential records requiring the participant's consent.
 - e. An investigator may review study data related to the participant collected prior to the participant's withdrawal from the study, and may consult public records, such as those established survival status.
2. For FDA-regulated research involving investigational drugs:
 - a. Investigators must abide by FDA restrictions on promotion of investigational drugs:⁵
 - i. An investigator, or any person acting on behalf of an investigator, must not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug.
 - ii. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of

⁴ <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126489.pdf>

⁵ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=312.7>

- the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution.
- iii. An investigator must not commercially distribute or test market an investigational new drug.
- b. Follow FDA requirements for general responsibilities of investigators:⁶
 - i. An investigator is responsible for ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; for protecting the rights, safety, and welfare of participants under the investigator's care; and for the control of drugs under investigation.
 - ii. An investigator must, in accordance with the provisions of 21 CFR § 50, obtain the informed consent of each participant to whom the drug is administered, except as provided in 21 CFR § 50.23 or §50.24 of this chapter.
 - iii. Additional specific responsibilities of clinical investigators are set forth in this part and in 21 CFR §50 and 21 CFR §56.
 - c. Follow FDA requirements for control of the investigational drug:⁷
 - i. An investigator must administer the drug only to participants under the investigator's personal supervision or under the supervision of a sub-investigator responsible to the investigator.
 - ii. The investigator must not supply the investigational drug to any person not authorized under this part to receive it.
 - d. Follow FDA requirements for investigator recordkeeping and record retention:⁸
 - i. Disposition of drug:
 1. An investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by participants.
 2. If the investigation is terminated, suspended, discontinued, or completed, the investigator must return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under 21 CFR §312.59.
 - ii. Case histories:
 1. An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered with the investigational drug or employed as a control in the investigation.
 2. Case histories include the case report forms (CRFs) and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. The case history for each individual must document that informed consent was obtained prior to participation in the study.
 - iii. Record retention: An investigator must retain required records for a period of 2 years following the date a marketing application is approved for the drug for the indication for

⁶ <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.60>

⁷ <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.61>

⁸ <http://www.accessdata.fda.gov/SCRIPTS/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.62>

which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.

- e. Follow FDA requirements for investigator reports:⁹
 - i. Progress reports: The investigator must furnish all reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained.
 - ii. Safety reports: An investigator must promptly report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug. If the adverse effect is alarming, the investigator must report the adverse effect immediately.
 - iii. Final report: An investigator must provide the sponsor with an adequate report shortly after completion of the investigator's participation in the investigation.
 - iv. Financial disclosure reports:
 - 1. The clinical investigator must provide the sponsor with sufficient accurate financial information to allow an applicant to submit to submit complete and accurate certification or disclosure statements as required under 21 CFR §54.
 - 2. The clinical investigator must promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following the completion of the study.
- f. Follow FDA requirements for assurance of IRB review:¹⁰
 - i. An investigator must assure that an IRB that complies with the requirements set forth in 21 CFR §56 will be responsible for the initial and continuing review and approval of the proposed clinical study.
 - ii. The investigator must also assure that he/she will promptly report to the IRB all changes in the research activity and all unanticipated problems involving risk to human participants or others, and that he/she will not make any changes in the research without IRB approval, except where necessary to remove apparent immediate hazards to human participants.
- g. Follow FDA requirements for inspection of investigator's records and reports:¹¹
 - i. An investigator must upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee to have access to, and copy and verify any records or reports made by the investigator pursuant to 312.62.
 - ii. The investigator is not required to divulge participant names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained.
- h. Follow FDA requirements for handling of controlled substances:¹²
 - i. If the investigational drug is subject to the Controlled Substances Act (21 U.S.C. Chapter 13 §801), the investigator must take adequate precautions, including storage of the investigational drug in a securely locked, substantially constructed cabinet, or other

⁹ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.64>

¹⁰ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.66>

¹¹ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.68>

¹² <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.69>

securely locked, substantially constructed enclosure, access to which is limited, to prevent theft or diversion of the substance into illegal channels of distribution.

3. For FDA-regulated research involving investigational devices:
 - a. General responsibilities of investigators:¹³
 - i. An investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations, for protecting the rights, safety, and welfare of participants under the investigator's care, and for the control of devices under investigation. An investigator also is responsible for ensuring that informed consent is obtained in accordance with 21 CFR §50.
 - b. Specific responsibilities of investigators:¹⁴
 - i. Awaiting approval: An investigator may determine whether potential participants would be interested in participating in an investigation, but must not request the written informed consent of any participant to participate, and must not allow any participant to participate before obtaining IRB and FDA approval.
 - ii. Compliance: An investigator must conduct an investigation in accordance with the signed agreement with the sponsor, the investigational plan, and other applicable FDA regulations, and any conditions of approval imposed by an IRB or FDA.
 - iii. Supervising device use: An investigator must permit an investigational device to be used only with participants under the investigator's supervision. An investigator must not supply an investigational device to any person not authorized to receive it.
 - iv. Financial disclosure:
 1. A clinical investigator must disclose to the sponsor sufficient accurate financial information to allow the applicant to submit complete and accurate certification or disclosure statements required under 21 CFR §54.
 2. The investigator must promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study.
 - v. Disposing of device: Upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator must return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.
 - c. Maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:¹⁵
 - i. All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports.
 - ii. Records of receipt, use or disposition of a device that relate to:
 1. The type and quantity of the device, the dates of its receipt, and the batch number or code mark.
 2. The names of all persons who received, used, or disposed of each device.

¹³ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=812.100>

¹⁴ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=812.110>

¹⁵ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=812.140>

3. Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.
- iii. Records of each participant's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. Such records must include:
 1. Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent.
 2. Documentation that informed consent was obtained prior to participation in the study.
 3. All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each participant upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.
 4. A record of the exposure of each participant to the investigational device, including the date and time of each use, and any other therapy.
 - iv. The protocol, with documents showing the dates of and reasons for each deviation from the protocol.
 - v. Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.
- d. Inspections:¹⁶
 - i. Entry and inspection: A sponsor or an investigator who has authority to grant access must permit authorized FDA employees, at reasonable times and in a reasonable manner, to enter and inspect any establishment where devices are held (including any establishment where devices are manufactured, processed, packed, installed, used, or implanted or where records of results from use of devices are kept).
 - ii. Records inspection: A sponsor, IRB, or investigator, or any other person acting on behalf of such a person with respect to an investigation, must permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation.
 - iii. Records identifying participants: An investigator must permit authorized FDA employees to inspect and copy records that identify participants, upon notice that FDA has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the investigator to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.
 - e. Prepare and submit the following complete, accurate, and timely reports:¹⁷

¹⁶ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=812.145>

¹⁷ <http://www.accessdata.fda.gov/SCRIPTs/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=812.150>

- i. Unanticipated adverse device effects. An investigator must submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.
- ii. Withdrawal of IRB approval. An investigator must report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.
- iii. Progress: An investigator must submit progress reports on the investigation to the sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly.
- iv. Deviations from the investigational plan:
 1. An investigator must notify the sponsor and the reviewing IRB of any deviation from the investigational plan to protect the life or physical well-being of a participant in an emergency.
 2. Such notice must be given as soon as possible, but in no event later than 5 working days after the emergency occurred.
 3. Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human participants, FDA and IRB also is required.
- v. Informed consent: If an investigator uses a device without obtaining informed consent, the investigator must report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.
- vi. Final report: An investigator must, within 3 months after termination or completion of the investigation or the investigator's part of the investigation, submit a final report to the sponsor and the reviewing IRB.
- vii. Other: An investigator must, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

A-3: Additional Requirements for Department of Education (DOE) Research

1. Each school at which the research is conducted must provide an assurance that they comply with the Family Educational Rights and Privacy Act (FERPA) and the Protection of Pupil Rights Amendment (PPRA).
2. Provide a copy of all surveys and instructional material used in the research including teachers' manuals, films, tapes, or other supplementary instructional material. Upon request, parents of children¹⁸ involved in the research¹⁹ must be able to inspect these materials.
3. The school in which the research is being conducted must have policies regarding the administration of physical examinations or screenings that the school may administer to students.

¹⁸ Children are persons enrolled in research not above the elementary or secondary education level, who have not reached the age of majority as determined under state law.

¹⁹ Research or experimentation program or project means any program or project in any research that is designed to explore or develop new or unproven teaching methods or techniques.

A-4: Frequently-Made Mistakes

The IRB finds the following issues as frequently made mistakes that may increase turnaround time in processing and making determinations on submitted applications. Please take note of the following frequently-made mistakes listed below to assist you in completing your application prior to submission. Mahalo!

Informed Consent Documentation

- Project Title at the top of the consent form should be consistent with the project title provided in the application form, unless the research involves deception
- Use the term “confidentiality” vs. “anonymity” correctly.
 - Confidentiality refers to: Maintaining personal information in a secure fashion. The PI will not divulge identifiable research records about the subject.
 - Anonymity refers to: The PI will not access, collect or maintain any personal or identifiable information as part of research records. An in person interview, for instance, may not be considered anonymous, even if the PI is not collecting the participants’ name.
- Use the term “compensation” instead of “payment”
- Monetary payment or class credit is not considered a “benefit”
- Before signature line, state that “I consent to participate” instead of “I read and understand”
- Add Counseling Services in the informed consent for studies that are at risk for psychological or emotional harm to participants.
 - For studies done in SONA or online anonymous surveys, this information should be provided to all at any point in time, especially important for participants who quit in the middle of survey.
- If requesting a waiver of consent where it’s involving oral consent
- Debriefing form should indicate that participant is consenting to allow the use of the data collected
- Do not use personal email or phone number as contact information for participants. If student-led research, you may use UH email but also include faculty advisor’s UH phone number.
- Provide two consent form documents for each participant, have participant and person obtaining consent sign both, and give participant a copy of the signed consent form; do not tear off signature page.

Application Form

- Make sure to answer every question. If not applicable, state as such.

Questionnaires/ Surveys/ Interview Guides

- Provide the exact material that will be seen or used by the research participants

- If using validated instruments, reference the source of these instruments.

Recruitment Materials

- Indicate somewhere that the project is research
- Do not specify amount if monetary compensation is offered
- Do not use language that promises a benefit to the individual or society/ group in general