



University of Hawai`i **Human Research Protection Program (HRPP)** General Policy Manual

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The Human Research Protection Program

GPM 201
Revised: June 8, 2016

201.1 Entities Covered Under the University of Hawai`i HRPP

The University of Hawai`i (UH or University) System is comprised of the following ten campuses:

- University of Hawai`i at Mānoa
- University of Hawai`i at Hilo
- University of Hawai`i at West O`ahu
- Hawai`i Community College
- Honolulu Community College
- Kapi`olani Community College
- Kaua`i Community College
- Leeward Community College
- University of Hawai`i Maui College
- Windward Community College

Any components under these 10 campuses are listed in the UH Federalwide Assurance (FWA) are considered part of UH for purposes of the Human Research Protection Program (HRPP) and are therefore covered by the Human Studies Program (HSP) General Policy Manual (GPM).

The UH Cancer Center and the John A. Burns School of Medicine are part of UH at Mānoa, and therefore, are covered under the UH FWA. The two components conduct numerous clinical research with local hospitals such as the Queens Medical Center, Hawaii Pacific Health Systems, and Castle Medical Center.

Non-UH organizations who have filed their FWA appointing the UH Institutional Review Boards (IRBs) to review their human participant research, maintain an IRB Authorization Agreement and/or Memorandum of Agreement with the University of Hawai`i specifying the types of research and other conditions for UH IRB oversight.

201.2 Organizational Components of the UH HRPP

The UH HRPP encompasses the HSP, the Office of Research Compliance (ORC) education unit, the Office of Research Services (ORS), Office of Technology Transfer and Economic Development (OTTED), and the Office of the General Counsel (OGC). The HSP is primarily responsible for the administrative, quality improvement, and education units, including serving as the administrative office for the UH IRBs. These functions may be appointed or delegated to other offices or individuals under the ORC umbrella.

Human Studies Program [HSP]

The HSP Administrative Unit:

- Provides administrative support to the UH IRBs;
- Communicates between the Researchers (Investigators and Research Support Staff) and the IRBs; and
- Facilitates the determination of projects that qualify for exemption from IRB review.

The HSP Quality Improvement Unit:

- Conducts on-site post-approval monitoring of UH research;
- Conducts routine review on the knowledge and operations of the HSP administrative office;
- Assesses knowledge and review outcomes of the UH IRBs and its members;
- Manages non-compliance issues of Researchers and IRBs; and
- Reports on deficiencies found from the various HRPP units and makes suggestions for continuous quality improvement.

Office of Research Compliance [ORC] Education Unit

- Develops and conducts educational sessions based on the reported knowledge deficiencies reported by the Quality Improvement Unit (QIU);
- Develops and conducts lecture series, the content of which may depend on the audience, topic, level of research experience, types of research, and the characteristics of the participant population being studied;
- Update educational materials for website postings and required training related to the protection of human participants in research; and
- Coordinate researcher-led lecture series to the IRB, HSP, and other relevant HRPP units on new and controversial issues related to conducting human participant research.

Office of Research Services [ORS]

- Provides contracts and grants administration
- Establishes and administers project accounts, assuring compliance with applicable laws, regulations, policies and award terms and conditions
- Manages significant financial researchers' conflict of interests

Office of Technology Transfer and Economic Development [OTTED]

- Executes contracts and agreement for inventions, patents, copyrights, and technology
- Reviews and approves intellectual property (IP) agreements

Office of Export Controls [OEC]

- Provides administrative review of tasks related to export controlled and/ or classified research;
- Responsible for ensuring compliance with U.S. laws and regulations which regulate strategic information, technology and/or services;

- Reviews and negotiates Non-Disclosure Agreements (NDAs), Confidentiality Agreements (CAs), Material Transfer Agreements (MTAs), etc., as delegated by the Vice President for Research and Innovation.

Office of Risk Management [ORM]

- Identifies, evaluates and manages risks inherent in the operations of the University
- Provides leadership and implements risk management principles and practices and services as a system-wide resource for risk management related issues

Office of General Counsel [OGC]

- Reviews and provides counsel on legal issues arising out of activities of the UH system; and
- Serves as consultants to the UH IRB for legal issues arising out of research activities conducted on behalf of UH.

Information Technology Services [ITS]

- Information Security, within Information Technology Services, is responsible for protection of institutional data assets both electronic and paper

Data Governance

- Focuses on privacy and security of UH Institutional Data (data that is used to meet the University's administrative and academic requirements and primarily involves student, human resource, and financial data).
- Reviews and approves requests involving the use of UH Institutional Data for research
- Provides training on protecting UH Institutional Data

201.3 Delegation of Responsibility for Implementing HRPP

The University President delegates the primary responsibilities for maintaining and overseeing the HRPP to the HSP. The [Executive Policy \(EP\) 12.301](#), approved by the UH President and the [Administrative Procedures \(AP\) 12.301](#), approved by the UH Vice President for Research and Innovation, lay the overarching UH policies and procedures in human participant protection.

The HRPP General Policy Manual (GPM) and its Standard Operating Procedures (SOPs) comprise of the policies and procedures related to human research protection. The GPM and SOPs are written to comply with applicable federal regulations and guidance, including 45 C.F.R. part 46 and 21 C.F.R. parts 50 and 56, and the principles of the Nuremberg Code, the Belmont Report, and the Declaration of Helsinki.

The GPM is a living document that is subject to review and revision, which may be required by amendments in federal regulations, Hawai'i law, federal guidance, or UH policies. The GPM and other related materials, along with any subsequent changes to these materials, are made available on the HSP

website, and distributed/communicated to the UH research community via presentations, educational sessions, and electronic communication.

Human Studies Program (HSP)

Responsibilities of the Office

The UH HSP is the administrative office of the UH IRBs. The primary responsibilities of the UH HSP is to ensure that the rights, safety and welfare of human participants are protected, and that human participant research is conducted ethically, and in compliance with applicable federal regulations, the requirements of state law, federal guidance, and UH policies.

Officials Specifically Responsible for Protecting Research Participants

Designated Institutional Official (IO)

As the Designated Institutional Official (IO), the UH Vice President for Research and Innovation is ultimately responsible for ensuring the protection of human participants involved in UH research. The IO shall maintain open communication channels between the HSP, research investigators, and institutional leadership. The IO receives copies of all approved IRB meeting minutes and notices of serious or continuing noncompliance and unanticipated problems in human participant research.

Director of the HSP (the Director)

The HSP Director is responsible for the day-to-day program operations and oversight, which includes the following:

- Creates, establishes, and maintains the HSP's policies and procedures and related research policies and procedures on behalf of UH;
- Oversees the protection of human participants and regulatory compliance for UH;
- Ensures that open communication channels are maintained between the components of the HRPP;
- Oversees research investigators and staff, and research management;
- Ensures the IRBs independence, including the authority to act without undue influence
- Conducts periodic reviews of the HSP and its IRBs;
- Ensures that the HSP is functional, adequately staffed and funded, involving:
 - Annual review of the resources allocated to the HSP, and
 - Participation in the annual budget preparation for the HSP and incorporation of the HSP budget into the ORC budget; and
- Serves as the conduit between the IO and the IRBs.

201.4 Laws and Ethics Governing Human Participant Research

Ethical Principles

The main ethical principles that apply to research covered by the HRPP, including protocols and proposals, “exempt” under the federal regulations pertaining to human participant research are those set forth by the “*Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of*

Research of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research” (Belmont Report).

The three main principles are:

1. Respect for Persons (e.g., applied by obtaining informed consent, giving consideration to privacy and confidentiality, and adding protections for vulnerable populations)
2. Beneficence (e.g., applied by weighing risks and benefits)
3. Justice (e.g., applied by the equitable selection of participants)

All parties involved in the conduct of research are expected to also adhere to the principles of expertise (“competent to do the work”) and integrity (“faithfully adhere to professional principles”). Ethical principles from other sources (e.g., International Conference on Harmonization) may also apply to research covered by the HRPP, for example:

- To an individual protocol because its particular circumstances raise a type of ethical issue that most other protocols do not;
- When they are recognized by the federal sponsor or other funding source or the state or country where the research will occur; or
- When they have been developed for specific areas or types of subjects (e.g., embryos and fetal tissue, participants who are illiterate);

These principles are also covered in the Collaborative Institutional Training Initiative ([CITI](#)) tutorial for investigators, IRB members, and IRB staff and in the orientation given to new IRB members.

Legal Principles

The following legal principles, covered by the HRPP, govern human participant research and are applicable to individual protocols or proposals are:

- Department of Health and Human Services (HHS) Policy for Protection of Human Subjects in 45 C.F.R. Part 46, which includes:
 - Subpart A (Common Rule), and
 - Subparts B through D (vulnerable populations)
- Food and Drug Administration (FDA) Regulations for the Protection of Human Subjects in 21 C.F.R. Parts 50 and 56
- Standards for Privacy of Individually Identifiable Health Information (HIPAA Privacy Rule) in 45 C.F.R. Parts 160 and 164
- Applicable Hawai`i law

State vs. U.S. Local Law

If a study is conducted in the United States, federal regulations on human participant research must be followed unless the regulations are silent or specifically refer to state or local law on certain issues.

If a study is conducted outside of the U.S.:

1. federal regulations of a U.S. agency control if the study is funded by the U.S. agency;
2. local law controls if the study is not funded by a U.S. agency.

The following issues depend on the state or local law of the location where the research is conducted:

1. The definition of children,¹
2. Guardian of a child who is authorized to give parental permission for the child to participate in research,²
3. Legally authorized representative who is authorized to consent on behalf of a subject to participate in research,³ and
4. The legality of consent⁴.

In most situations, it is not difficult to pinpoint the location where the research is conducted, except research conducted on the Internet (Internet research). In Internet research, research can take place at any location with access to the Internet. The UH IRB adopts the policy that the location of Internet research is where the Investigator is during the research.

Laws Governing Transnational Research

Also known as “international research,” transnational research covers research conducted outside of the United States.

UH Investigators⁵ are responsible for:

- complying with local laws and considering the cultural context of the country where the research is conducted;
- complying with U.S. regulations and guidelines if the research is funded by a U.S. agency;⁶ and
- following applicable international guidelines on biomedical research, e.g., the Declaration of Helsinki⁷, Guideline for Good Clinical Practice (E6)⁸, and International Ethical Guidelines for Biomedical Research Involving Human Subjects⁹.

UH IRB, as the IRB of record, and UH Investigator share responsibility for ensuring that:

- the same or equivalent protections are provided to human participants in research conducted in countries other than the United States;
- the researchers have sufficient knowledge of local laws and cultural context to determine how the research shall be conducted;
- the consent process is appropriate to the population and culture; and
- the researchers have made adequate provisions for data and safety monitoring.

¹ 45 C.F.R. § 46.402(a).

² 45 C.F.R. § 46.402(e).

³ 45 C.F.R. § 46.102(c).

⁴ For Hawaii law on electronic signature, see Haw. Rev. Stat. §§ 489E-1–489E-19 (2013).

⁵ “UH Investigator” means an investigator who is affiliated with UH, i.e., (1) employees who receive paychecks from the UH; (2) students who are currently taking courses for credit at UH; or (3) members of UH Board of Regents.

⁶ 45 C.F.R. § 46.101(a) (2014); 71 Fed. Reg. 38645 (July 7, 2006).

⁷ WMA Declaration of Helsinki—Ethical Principles for Medical Research Involving Human Subject, World Med. Ass'n, 1–2, [http://www.wma.net/en/30publications/10policies/b3/index.html.pdf?print-media-type&footer-right=\[page\]/\[toPage\]](http://www.wma.net/en/30publications/10policies/b3/index.html.pdf?print-media-type&footer-right=[page]/[toPage]) (last visited Aug. 22, 2014) (describing ethical guidelines for physicians engaged in biomedical research).

⁸ ICH Harmonised Tripartite Guideline—Guideline for Good Clinical Practice E6(R1), Int'l Conference on Harmonisation of Technical Requirements for Registration of Pharm. for Human Use, 1 (June 10, 1996), http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf (describing ethical and scientific quality standards for designing, conducting, recording, and reporting clinical trials involving human subjects).

⁹ International Ethical Guidelines for Biomedical Research Involving Human Subjects, Council for Int'l Orgs. of Med. Scis., 10 (2002), http://www.cioms.ch/publications/layout_guide2002.pdf (describing the ethical guidelines for biomedical research involving human subjects).

201.5 Research Covered by HRPP

The University conducts and oversees biomedical, social and behavioral sciences research. Human participant research conducted at each UH affiliated organization is covered by the UH FWA. Regardless of funding sources, all human participant research engaged¹⁰ by UH are governed by subpart A of 45 C.F.R. part 46, and the principles of the Nuremberg Code, the Belmont Report, and the Declaration of Helsinki.

An activity is covered by the UH HRPP when:

1. It is considered “human subject research” – as defined in any of the following regulatory agencies:
 - HHS regulations or other Common Rule regulations
 - FDA regulations
 - Any other applicable state or local regulations, e.g., Hawai`i State regulations, UH policies
- AND
2. UH (or its faculty, staff or students) is engaged in the research
 - UH is engaged in the research if:
 - (1) UH receives a grant or contract under which the research is conducted, and/or
 - (2) UH’s faculty, staff or students obtain:
 1. Data about research participants through intervention or interaction;
 2. Identifiable private information about the research participants; or
 3. Informed consent from research participants.

A non-UH investigator who conducts human subjects research and seeks to access UH resources, such as facilities, personnel, data, or information, must consult with the Human Studies Program (HSP). The HSP will determine whether UH is engaged in the research. If the HSP determines that UH is engaged in the research, the non-UH investigator must seek review by the UH IRB.

See **SOP 103: When Must a Non-UH Investigator Seek Review by the UH IRB? – The Issue of Engagement** for more information.

Approvals Required Prior to Research Commencement

Research involving human participants must be reviewed and approved by an IRB before an Investigator initiates activities of the research.

In addition to seeking approval from the IRB, Investigators may need to seek review and approval from ancillary departments before commencing in research activities:

- Funded research (e.g., industry-sponsored clinical trials, federally-funded research) will need to apply to the ORS through *myGrant*.
- Research involving UH Institutional Data require approval from UH Data Governance Office before the data will be released.
- Research involving primary and secondary schools or offices under Hawai`i Department of Education (HIDOE) need to apply and seek separate approval from the HIDOE Data Governance and Analysis Branch.

¹⁰ "Engaged" means that an institution involves in a human subjects study to such a degree that the institution must have the study reviewed and approved by an IRB before any research activity of the study may be initiated. For details on engagement, see **SOP 103, When Must a Non-UH Investigator Seek Review by the UH IRB?—the Issue of Engagement**.

- Research involving matters covered by U.S. Export Control Laws (ITAR, EAR, OFAC, etc.) may need to seek review and approval from the OEC (matters involving foreign nationals, select agents, etc.)
- Research involving transfer of biospecimen may require additional approval from the UH Biosafety Office.
- Research involving use of animals for research may require additional approval from the Institutional Animal Care and Use Committee (IACUC).

201.6 Scientific and Scholarly Review

When evaluating the scientific and scholarly validity of a research protocol or proposal, the IRB relies on the review provided by different entities:

- For federally sponsored research, the peer review process by the sponsoring agency (e.g., NIH, NCI, DOD) provides scientific and scholarly review.
- For research subject to FDA review, the FDA conducts a rigorous scientific design review during IND or IDE evaluation. Most industry-sponsored research falls within this category. The exception would be for Non-Significant Risk (NSR) device research, in which the IRB serves as the FDA's surrogate in reviewing and approving NSR studies.
- For student-led research, the faculty advisor and the academic committee (e.g., Undergraduate Honors, Graduate Thesis, Dissertation, Plan B project), as appropriate, are responsible for scientific and scholarly review of their student's research project

For research that has departmental funding, gift funding or no funding, or that has not otherwise gone through a scientific review as described above, the UH IRB will review those studies.

See **SOP 104: Ensure Sound Design and Minimize Risk** for details and procedures regarding scientific and scholarly review of research.

201.7 HRPP Resources

Human and Fiscal Resources

UH maintains human and fiscal resources for administrative support to the operation of its HRPP.

The HSP receives its annual budget through the Vice President for Research and Innovation from the University of Hawaii System. The annual budget is established by a three-step process:

1. IRB Chairs and the HSP Director discuss priorities and resources necessary for the new academic year. This includes budget to secure educational materials and training opportunities for IRB members and its collective IRBs for the upcoming year.
2. The HSP Director and ORC budget officers, with input from the ORC Director, prepare income and expense plans for the following year. The yearly expenditure plan takes into consideration:
 - Adequate number of IRBs
 - Adequate staffing

- Adequate technology support
 - Adequate funds for educational opportunities for IRB members and HSP staff, including off-site conferences
 - Adequate funds to provide ongoing office and logistic support
 - Adequate funds to carry out agreed-upon special projects.
3. The HSP Director formulates these plans into a budget, which is then integrated into the ORC budget. The ORC budget is ultimately reviewed and approved by the Vice President for Research and Innovation. This budget is then further integrated by the University Fiscal Office into the University's consolidated budget plan presented to the Board of Regents for approval. Fiscal budget begins July 1st of each year.

Assessment of IRB Workload

The HSP assesses its level of activity at least once a year in order to attempt to maximize the efficiency of workflow to IRB load. It takes into consideration the ratio of applications to staff, the number of transactions generated by each submission, the type of review (full-board, expedited or exempt), and any other appropriate variables. Input from the IRB Chairs regarding the volume of work (i.e., hours to review) and other IRB-related matters are discussed in the HSP annual report that is presented to the Vice President for Research and Innovation. When adjustments are necessary, their financial implications are considered during the budget assessment outlined above. New IRBs, IRB reviewers, or staff positions are appointed or created to meet workload demands.

201.8 Investigator Resources to Ensure Care and Safety of Participants in Human Research

To approve a research protocol or proposal, the IRB must determine that, where appropriate, there are adequate resources to ensure the care and safety of participants throughout the entire conduct of the project. Review of the submitted protocol or proposal is assessed from the information provide in the eProtocol Application (see [GPM 204.2](#) for information about eProtocol) and as necessary, requested by the IRB or HSP staff for additional information (see [GPM 204](#) for information about Review Process). If the protocol or proposal does not provide adequate protection, it will not be approved.

Principal Investigators (PIs) are required to indicate in the eProtocol Application whether investigators:

- will have access to a population that will allow recruitment of the required number of participants;
- will have sufficient time to conduct and complete the research; will have adequate numbers of qualified staff; will have adequate facilities;
- will have a process to ensure that all persons assisting with the research are adequately informed about the protocol and their research related duties and functions; and
- will have medical or psychological resources available that participants might require as a consequence of the research when applicable.

PIs shall 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.

201.9 Communication Between HRPP Components

Communication

The IRB ensures that the communications required by the eProtocol Application takes place. Shared access to eProtocol between various components of the HRPP ensures that situations which require communication and interaction between these components are handled appropriately:

- **Protocols involving biosafety materials** and requiring review by the Institutional Biosafety Committee must be reviewed by this Committee and receive an approval letter in addition to review by the IRB.
- **Protocols involving UH institutional data** and requiring review by the IRB must be reviewed by this Committee and receive an approval letter from the IRB. UH Data Governance Office will not process or approve the request for institutional data until IRB has approved the project to which the data will be needed.
- **Investigator Conflict of Interest disclosures:** All Investigators' conflicting interest is managed via the Conflict of Interest Committee (COIC) under the ORS. The IRB will not approve a protocol or proposal application until any disclosed COI has been reviewed and resolved by the COIC, and as appropriate, a plan or strategy to adequately eliminate, mitigate, or manage the conflict that has been identified by the COIC (See [GPM 203.5](#)).
- **Blood, tissue, or data (slides, X-rays, etc.)** that are being transferred in or out of the institution: The PI must coordinate with the Office of Export Control (OEC) about a Material Transfer Agreement (MTA).
- **Funding Status:** Inquires are made to the ORS to verify whether there is active funding on a particular project. Funding received by ORS for a designated research protocol or proposal will not be released to the PI until IRB approval is secured.

Policies Available to all Parties to Research

This HRPP General Policy Manual and other relevant policies and procedures are available to the sponsors and to the entire UH research community, including researchers, research staff, HRPP staff, IRB members, employees, UH staff, and students through the HSP website.

Structure and Composition of the Institutional Review Boards

GPM 202
Revised Date: December 18, 2015

202.1 Scope of UH IRB Authority

The IRB derives its authority from both regulatory and institutional sources (e.g., EP 12.301 and AP 12.301). IRB provides reports to the Institutional Official through the HSP Director. No UH Human Subjects Research can commence without the approval of the IRB.

The IRBs operating under the HSP have the statutory and institutional authority to take any action necessary to protect the rights and welfare of human research participants involved in research. Along with conducting reviews of human participant research, the IRB authority includes, but is not limited to, the following:

- Assess suspected or alleged deviations from regulations or approved protocol;
- Address participant complaints;
- Investigate violations of external regulations or UH policies; and
- Monitor research conduct and report on noncompliance (45 C.F.R. parts 46.109, 46.112, 46.113)

The IRB has the authority to suspend or terminate the enrollment or ongoing involvement of research participants and research as it determines necessary for the protection of those participants.

Upon request, the IRB shall review and comment on proposed external regulations dealing with human research. When appropriate, the IRB will formulate draft policies and procedures for approval by the appropriate UH administration.

202.2 Composition and Membership

IRB Composition

Each UH IRB meets the following IRB composition requirements¹¹:

1. Has at least five (5) regular members;
2. Possesses varying professional backgrounds to appropriately and adequately review research activities commonly conducted at the UH;
3. Is sufficiently diverse relative to ethnicity, gender, cultural background, and sensitivity to community attitudes;
4. Includes members knowledgeable of institutional commitments, applicable law, and standards of professional conduct to determine the acceptability of a proposed study;
5. Includes both male and female members at any given time;

¹¹ 45 C.F.R. § 46.107; IRB Registration Instructions, HHS (June 15, 200), <http://www.hhs.gov/ohrp/assurances/forms/irbregisinstruct.html>.

6. Includes at least one member whose primary concerns are scientific, and at least one member whose primary concerns are nonscientific;
7. Includes at least one member who, or whose immediate family member, is *not affiliated* with the UH; and
8. If the IRB regularly reviews studies that involve a vulnerable category of participants, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration is given to include one or more individuals who are knowledgeable about and has experience in working with these populations.

Alternate Members

Each alternate IRB member, who votes in the place of a regular member at the IRB meeting when the regular member is absent or recused from voting, has the experience, expertise, background, professional competence, and knowledge equivalent to that of the regular IRB member who the alternate replaces.¹²

Membership: Length of Term, Responsibilities, Attendance, Compensation, and Removal

An IRB consists of regular and alternate members. This section applies equally to regular and alternate members unless stated otherwise.

Appointment

The IRB Chair and the Director nominate and appoint individuals for IRB membership. Investigators and faculty or entities outside the HSP may recommend, but are not involved in the appointment of IRB members.

Members are selected based on the following qualifications:

1. Knowledge of applicable federal regulations;
2. Experience in performing research;
3. Experience in serving on an IRB or other research committees;
4. Knowledge of community values and norms; and/or
5. Other qualifications determined to be important in maintaining a diverse and qualified IRB.

Length of Term

IRB members serve two (2)-year terms, and are eligible for reappointment.

Responsibilities

All IRB members are responsible for reviewing and monitoring research involving human subjects and protecting the rights and welfare of subjects. Members vote to approve, require modifications in, or disapprove research submitted to the IRB. Duties of members and alternate members include:

1. Attending IRB meetings on a regular basis;
2. Reviewing received meeting materials prior to the meetings;
3. Serving as a primary or secondary reviewer as assigned;
4. Serving as general reviewers on all research discussed at convened meetings;
5. Conducting expedited reviews on behalf of the IRB when so designated by the IRB Chair;

¹² [OHRP IRB Registration Form](#).

6. Maintaining confidentiality of IRB decisions and materials;
7. Keeping abreast of regulations and policies on human research; and
8. Completing the necessary orientation and required educational requirements.

Attendance Requirements

Regular IRB members are expected to attend at least six (6) of all convened meetings in a year. If a member cannot attend a scheduled meeting, the member shall notify the Director or the Director's designee at least one week before the meeting.

At least one unaffiliated member must be present in at least six (6) out of twelve (12) meetings in a calendar year.

Compensation

UH IRB members do not receive financial compensation.

Removal

A member may renew their term in the IRB indefinitely until the member steps down voluntarily or involuntarily. A member may be removed because of conflicts in time or interest. A member also may be removed for improper conduct, such as not acknowledging a conflict of interest, not maintaining confidentiality of the proceedings, failure to fulfill training requirements, or lack of regular attendance or meaningful participation in IRB meetings. A decision to remove a member is made collaboratively between the IRB Chair and the HSP Director.

IRB Chair and Vice Chair

IRB Chairs and Vice Chairs are appointed by the HSP Director and the ORC Director.

Selection of the Chair and Vice Chair are based on, but not limited to:

1. Comprehensive knowledge of the human subjects regulations,
2. Experience as an Investigator,
3. Uses sound ethical judgment which can be evidenced by past practices,
4. Experience as a Chair or member of an IRB,
5. Willingness to commit as a Chair/Vice Chair, and
6. Status, experience, or reputation consistent with upholding the independence of an IRB

The Chair and Vice Chair serve a two (2) year term and may be reappointed.

Responsibilities of the IRB Chair and Vice Chair

In addition to the responsibilities as a member, the Chair has primary responsibility for conducting IRB meetings and ensuring that the IRB operates within all applicable regulatory requirements. The duties of the Chair include:

1. working with IRB members, the Director and staff, and Investigators to ensure that the rights and welfare of research participants are protected;
2. ensuring that IRB minutes are recorded accurately;

3. reviewing and approving protocol applications that may be expedited or delegating the authority to experienced members of the IRB;
4. ensuring that IRB members having a conflict of interest with a particular protocol abstain from voting on the protocol;
5. ensuring a quorum is maintained when voting;
6. participating in the resolution of controversial, substantive or procedural matters; and
7. participating in monitoring and improving the operation of the IRB.

The IRB Vice Chair assumes all responsibilities of the Chair when the Chair is unavailable. If the Chair is unable to perform Chair duties, the Vice Chair assumes all responsibilities of the Chair until the Director and the Assistant Vice Chancellor of Research Compliance (AVCRC) appoint a replacement IRB Chair. It is not required for an IRB to have a Vice Chair.

202.3 IRB Member Scientific and Scholarly Expertise

Having the diverse scientific or scholarly expertise, IRB members can review a broad range of UH-engaged research. Policy requires IRB members to be knowledgeable about all relevant regulatory requirements, while remaining impartial and objective to the best of their ability during protocol review, deliberation and voting. The IRB includes members who are particularly knowledgeable about research ethics and the vulnerable research participants included in UH research.

However, in situations where the IRB lacks members who have the expertise in a particular research, outside experts may be consulted. Consultants may provide comments in writing. The written comments are retained in the study files. An IRB may also consult the Investigator about the study.

The consultants may be asked to attend a convened IRB meeting, or assist in providing information to the designated reviewer in an expedited review. Consultants do not vote and are not counted towards a quorum; they are excused from the meeting before the vote. If a consultant attends an IRB meeting, meeting minutes document the attendance and describe the consultant's role in the review.¹³

202.4 Members' Conflicts of Interest

No IRB member participates in the IRB's review of any research where the member has a conflicting interest, except to provide information requested by the IRB.¹⁴ The IRB members, including the Chair, who have conflicting interests in the research, must disclose those conflicts before the IRB's review of the study, and recuse themselves from the deliberation, quorum count, and vote on the research.¹⁵

Individuals responsible for business development¹⁶ do not serve on the IRB as members nor are involved in the day-to-day operations of the IRB. This restriction is to ensure the IRB review process is free of conflicting interests so that the members' obligation to protect participants is not compromised.

See **SOP 106: IRB Member Conflicts of Interest** for procedures for reporting and managing IRB

¹³ Guidance on IRB Continuing Review of Research, OHRP (Nov. 10, 2010), <http://www.hhs.gov/ohrp/policy/continuingreview2010.html>.

¹⁴ 45 C.F.R. § 46.107(e); 21 C.F.R. § 56.108(e).

¹⁵ Note: abstention is not due to conflicts of interest and abstained members may be counted towards quorum. Id.

¹⁶ Examples of individuals responsible for business development are the Director for the Office of Research Services, Vice President for Research, or Vice Chancellor for Research. Those individuals are responsible for raising funds or garnering support for research.

member conflict of interests.

202.5 Training of IRB Chairs and Members

Before assuming responsibility as a voting member of the IRB, newly appointed IRB members participate in an orientation and are given copies of relevant policies and procedures and other documents appropriate to their role.

New members are also paired with experienced members for the first few protocols that are assigned to them as reviewers. New members may seek assistance from HSP staff and experienced IRB members regarding questions about regulations and review process at any time during their term.

Continuing Education

IRB members, the HSP Director and other subject matter experts conduct educational presentations to the convened IRB. Longer policy discussions or special topic seminars are scheduled as needed. IRB members periodically receive copies of books, articles, newsletters and other information in electronic format or through materials distributed at IRB meetings on the most current information on human participant research as it relates to IRB review. Topics, identified by the QIU to require more attention, will be reviewed during special training sessions. The HSP maintains reference materials in its office, which are made available to IRB members.

202.6 IRB Roster and Quorum Requirements

IRB Roster

UH IRB Rosters are created to meet the requirements specified under 45 C.F.R. §§ 46.107 and 108; and 21 C.F.R. §§ 56.107 and 108.

An IRB Member database is maintained by the HSP and used as the data source for all IRB membership roster needs. The IRB Member database includes all information required under the HHS and FDA regulations and Office for Human Research Protection (OHRP) guidance (45 C.F.R. §§ 46.107 and 108; 21 C.F.R. §§ 56.107 and 108) including:

- Members' names
- Names of alternate members (and regular members who whom they substitute)
- Gender
- Earned degrees and licenses
- Scientific status (see definition on “scientist” vs. “non-scientist”)
- Representative capacity (e.g., prisoners, children, pregnant women)
- Affiliation (see definition on affiliation)

Changes to IRB membership are reported to OHRP. The HSP Director (or delegate) revises and registers its membership list to OHRP whenever membership or member information changes occur; and whenever a new IRB is formed or eliminated.

UH graduate students may serve as IRB members to represent the perspective of participants in many social & behavioral sciences research. A UH student may be nominated by experienced IRB members who are also UH faculty or administrators that have witnessed a student's potential to appropriately and objectively review human participant research. Senior IRB administrative staff may also be appointed as an alternate member of the IRBs.

Quorum and Voting Requirements:

The IRB Chair and Vice Chair are voting members of the IRB. The Chair determines that quorum is established and maintained, chairs the meeting discussions, and calls for votes as appropriate.

Maintaining quorum and voting at convened meetings is based on the following for each meeting, unless otherwise indicated:

1. A majority of the (voting) IRB members (or their designated alternates) including at least one member with a non-scientific background must be present to conduct a convened meeting. For research to be approved, it must receive the approval of the majority of members present at the meeting.
2. If an IRB reviews research that involves categories of participants vulnerable to coercion or undue influence such as children or prisoners, one or more individuals knowledgeable about or experienced in working with such participants must be present;
3. If an IRB reviews research involving prisoners, a prisoner representative must be present to vote, and a majority of the members present must have no association with the prison involved.
4. Members recusing themselves from a particular review due to conflicts of interest may not be counted towards quorum for the particular review.

Recusal is due to conflicts of interest while abstention is due to reasons other than conflicts of interest. An IRB may not count recused members, but may count abstained members, towards quorum.

5. Members may participate in meetings by being physically present or via telephone or virtual, synchronous audio-visual teleconference, with the same standards and opportunity to participate fully in IRB discussions. Meeting minutes documents each individual's mode of participation. Use of electronic devices to access meeting materials is allowed and encouraged during the meetings.
6. Individuals who are not listed on the official IRB membership roster may not vote with the IRB. These include non-voting ex-officio members, ad hoc consultants, and HRPP staff.
7. When a member and their alternate both attend a meeting, either person (but not both) may vote on each protocol or proposal.

8. Proxy votes are not allowed.
9. If the quorum is lost during a meeting, the IRB cannot take any further actions or vote until the quorum is restored.
10. The HSP staff is responsible for monitoring the members present at a convened IRB meeting to ensure that at the beginning of the meeting and for each subsequent vote the meeting is appropriately convened.

202.7 IRB Meeting Schedule and Materials

Scheduling of the Meetings

During the academic year (September through May), the IRB meet once a month; during the summer months (June and August), it may convene less frequently.

The annual meeting schedule is distributed about one month before the new calendar year, and posted on the HSP website. Changes in dates, times, and locations of scheduled IRB meetings are communicated to all IRB members before the meeting or at the beginning of a meeting during the announcement portion. Investigators are notified of rescheduling or cancellation of IRB meetings if their application is queued for review.

Review and Preparation Time

Application Materials

The IRB Coordinators assigns applications to the primary and secondary reviewers in sufficient time for them to be reviewed before the meeting, usually at least two weeks prior to the upcoming meeting. All other members are granted access to the presented application materials, usually at least two weekends prior to the upcoming meeting.

The HSP provides materials for IRB members before each scheduled convened meeting. For the list of materials provided to members, see **SOP 105: IRB Meeting Preparation and Conduct**.

Monitoring and Maintaining Compliance

GPM 203
Revised Date: December 18, 2015

203.1 Assurance of Compliance

The UH System and its affiliates covered by the HRPP maintain its FWA under OHRP (45 C.F.R. § 46.103), and is filed and searchable to Investigators and others involved in human participant research on the OHRP website.

203.2 Access to Policies, Procedures, and Other Resources

The HSP has primary responsibility for ensuring the HRPP GPM and related materials are available to the entire UH research community, including:

- Investigators
- Research support staff (e.g., study coordinators, research assistants, etc.)
- HSP staff
- IRB members
- UH administrators, faculty, staff, and students
- Collaborating research sites and their administrators

The HSP maintains the [HSP website](#) which provides access to:

- HRPP GPM
- HRPP SOPs
- Links to relevant federal regulations and guidelines, and ethical principles from various disciplines (e.g., American Psychological Association, American Sociological Association, etc.)
- Links to collaborative research institutions and non-UH IRBs
- Links to other UH departments and offices involved in human participant research
- Information and instructions on required and elective training for human participant research
- Templates and guidelines for consent forms, recruitment material, and other study material
- HSP educational presentations
- Application and report forms and reviewer checklists and worksheets (based on eProtocol application)
- Alerts and updates on revised or new policies and procedures pertaining to human research protection
- Frequently Asked Questions
- Guidelines and checklists to assist Investigators on human participant research determination (e.g., review type, quality improvement vs. research, etc.)
- Information for research participants

203.3 Independence of the UH IRBs

Organizational Structure to Maintain Independence

The IRB operates independently, with HSP administrative support. The duties of the Vice President for Research and Innovation relate to establishing policy for research and oversight of research compliance, particularly as it relates to human participant research.

Delegation to the IRB

The UH IRBs have the authority to:

- Review, approve, disapprove, require to modify research involving human participants;
- Suspend or terminate the enrollment and/or ongoing involvement of human participants in research, as necessary for the protection of those participants (e.g., cases where research has been associated with unexpected serious harm to participants), or
- Suspend or terminate an Investigator's privilege to conduct human participant research (e.g., in situations where research is not being conducted in accordance with IRB requirements),
- Observe or delegate a third party to observe the consent process
- Observe or delegate a third party to observe the conduct of research.

Prohibiting External Entities from Assuming IRB Approval Authority or Using Undue Influence

Officials/administrators, investigators, faculty, staff, students, and sponsors contracting with UH for research are prohibited from:

- Maintaining or claiming IRB approval of research that has been disapproved or not yet been reviewed by the IRB. A decision of any IRB to disapprove a research protocol or proposal cannot be overridden by the State or Institutional Official.
- Attempting to use or using undue influence with the IRB, any of its members or staff, an Investigator or any other member of the research support staff to obtain a particular result, decision or action.

In preventing undue influence of or threat to IRB members, the HSP and the UH IRBs preserve the anonymity of its members. IRB Rosters are kept confidential from Researchers, faculty, staff, students, and contracted sponsors. Only redacted rosters are provided for individuals requesting a copy for purposes of reporting to regulatory departments, funding agencies, etc.

203.4 Regulatory Definition of “Human Subject Research”

Human subject research is defined under 45 C.F.R. §§ 46.102(d) and (f), 21 C.F.R. §§ 50(c), (e), and (j), specifically:

“Human Subject” as defined by DHHS is a living individual about whom an Investigator (whether professional or student) conducting research obtains (1) data through Intervention or Interaction with the individual, or (2) information that is both Private Information and Identifiable Information.

For the purpose of this definition:

- “Intervention” means physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes.
- “Interaction” means communication or interpersonal contact between Investigator and subject.
- “Private Information” means information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).
- “Identifiable Information” means information that is individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the Investigator or associated with the information).

“Human Subject” as defined by the FDA is an individual who is or becomes a subject in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. A human subject includes an individual on whose specimen a medical device is used.

“Research” as defined by the DHHS is a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

“Research” as defined by the FDA is any experiment that involves a test article and one or more Human Subjects, and that meets any one of the following:

- Must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act meaning any use of a drug other than the use of an approved drug in the course of medical practice;
- Must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act meaning any activity that evaluates the safety or effectiveness of a device; OR
- Any activity the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.

The HSP, as designated by its IRB, retain ultimate authority to determine whether an activity meets the definition of “human subject research.” All protocols and proposals involving both “research” and “human subjects” (except those determined to be exempt) must be reviewed and approved by the IRB before any research activity involving human participants commence.

See **SOP 101: Human Subject (Participant) Research Determination** for procedures for making determinations on UH projects.

Exempt Research Determination

As defined per the Common Rule, Subpart A of 45 C.F.R. part 46, exempt research encompasses categories of research that do not require IRB approval and continuing review (see **SOP 111: Exempt Review and Determination**).

Exempt status cannot be granted when:

- Categories (1) through (5) apply and research is subject to FDA regulations.
- The research involves significant physical invasions or intrusions upon the privacy of its participants.
- The research involves prisoners as participants.
- Category (b)(2) applies and research involves children as participants, except for research involving observation of public behavior or when the Investigator(s) do not participate in the activities being observed.

Emergency use of a test article is exempt from prospective IRB review per 21 C.F.R. § 56.104.

See **SOP 111: Exempt Review and Determination**

Managing Conflict of Interest When Making Exempt Determinations

IRB members and HSP staff involved in reviewing and approving the exempt determination of protocol or proposal applications refrain from participating in the review of the research in which they have a conflicting interest (see **SOP 102 IRB Member Conflicts of Interest**).

203.5 Conflicts of Interest

Executive Policies and Administrative Procedures

The University has the following policies and procedures on reporting and managing significant financial and other conflicts of interest for UH research:

- [Executive Policy 12.214](#) on Conflicts of Interest and Commitment
- [Administrative Procedures A5.504](#) on Conflicts of Interest and Commitment
- [Administrative Procedures A8.956](#) on Financial Conflicts of Interest (FCOI) for Public Health Services Grants, Cooperative Agreements and Contracts

The John A. Burns School of Medicine (JABSOM) also provides faculty and staff a policy document “JABSOM Policy on Interactions with Industry (http://jabsom.hawaii.edu/wp-content/uploads/2014/07/COI-draft-10_10_13-changes-excepted.pdf)

Investigator’s Conflict of Interest -- Role of the IRB

Investigators’ Conflicts of Interest regarding research are managed by the ORS, Compliance Section.

See **SOP 107: Investigators’ Conflicts of Interest (COI)** for IRB role and procedures involving Investigator’s conflict of interest in research.

Recordkeeping

Records on all disclosures of financial interests and all decisions to manage, mitigate, or eliminate COI for a particular research protocol or proposal are maintained for three (3) years from that study’s

closure date. This information is made available to HHS upon request while maintaining the confidentiality of all records of financial interest.

Institutional Conflict of Interest

An institutional conflict of interest (ICOI) occurs when an Investigator at UH undertakes human participant research on a drug, device, biologic or other item on which UH has a patent, has licensed the intellectual property, or receives royalties or other fees.

All new human participant research protocols submitted for IRB review must indicate the source(s) of all funding to be used in supporting the research, including unrestricted school, department or individual accounts, as well as the name of the manufacturer when applicable. In addition, the Investigators are required to answer questions about the relationship of their research to their administrative duties. When a protocol lists a manufacturer, or when other information indicates a potential conflict, the issues are handled as outlined in accordance with [Executive Policy 12.214](#). Documentation and reporting is to be conducted in accordance with [APM A5.504](#) and [APM A8.956](#). Decisions are communicated to the IRB and to the relevant academic departments within the University so that the recommendations can be implemented at the level of the individual schools as appropriate.

203.6 Non-Compliance

Any situation of perceived or actual serious or continuing non-compliance jeopardizes the UH's commitment to human participant research protection. It is essential to report any possible non-compliance for accountability and education purposes, correcting non-compliance, and attempting to prevent reoccurrences mitigate any adverse effects on research participants.

In general, "non-compliance" is defined as an action or activity in human participant research that does not follow the IRB-approved protocol or proposal, other requirements and determinations of the IRB, the HRPP GPM and other applicable UH policies and procedures, or relevant state or federal laws. Protocol violations (PVs) or protocol deviations (PDs) are considered non-compliance instances, and need to be reported to the IRB or HSP.

Obligation to Report Non-compliance

The following individuals, or entities, have the responsibility to report observations, evidence or allegations of non-compliance of human participant research to the Human Studies Program:

- Investigators (i.e., Principal Investigator, Co-Investigator, Sub-Investigator)
- Research support staff
- UH administrators, faculty, staff, or students
- IRB member
- HSP staff
- Study monitor, auditor or sponsor either directly or through the Investigator

Research participants and individuals not directly involved with conducting or overseeing the research are also encouraged to report suspected non-compliance to the Human Studies Program.

Reports of possible non-compliance may also be directed to the following individuals, who in turn forward them to the HSP staff:

- Principal Investigator
- The Vice President for Research and Innovation (Institutional Official)
- The Office of Research Compliance

HSP staff may also uncover possible non-compliance or evidence of non-compliance during the course of their normal duties.

Non-Compliance – Allegations or Findings

Reports of noncompliance are received in one of two forms: (1) allegations or (2) findings. Allegations of noncompliance have yet to be proven and are reviewed and investigated. Once an allegation is determined to be true based on the preponderance of the evidence, it is then considered to be a finding. Generally, self-reported incidents of non-compliance incidents by the Investigators via appropriate forms (e.g., protocol violation report, continuing review, etc.) will be accepted as findings of noncompliance.

Handling Non-Compliance

The HSP handles non-compliance in the following order: (1) receipt of an allegation, (2) inquiry, (3) formal investigation, (4) appeals, (5) dissemination of findings, and (6) reporting to IOs and general agencies.

See **SOP 108: Determining and Reporting Non-Compliance and Protocol Violations** for definitions and reporting procedures.

Some cases of non-compliance may involve other allegations, such as academic misconduct or financial mismanagement. The HSP and the IRBs cooperate with other entities in their review of those allegations to avoid duplicated effort and minimize competition for resources. The HSP may also report those allegations to appropriate institutional officials.

IRB members, and other individuals involved in the review process of a non-compliance case must recuse themselves from the review if they have a conflict of interest in the matter.

It is against UH policy to retaliate against good faith whistle-blowers. Prompt reporting of non-compliance and fair review of allegations are critical for the HSP to protect human participants, and require a climate free of fear from retaliation. Generally, the Investigator under review will have access to the identities of the persons who have filed an allegation against the Investigator or provided information on the allegation. However, for those individuals subordinate to the Investigator who wish to maintain anonymity, the HSP strives to protect their identities while providing the Investigator access to relevant information regarding the allegations. Note, that the HSP cannot guarantee absolute anonymity.

IRB Actions to Protect Human Participants in Research

At any time during the review of an allegation, the IRB may take one or more of the following actions to ensure the safety and welfare of human participants in research:

1. Suspending the study;
2. Requiring the Investigator to submit a corrective action plan;
3. Requiring the Investigator or Research Support Staff to complete additional training;
4. Requiring that currently- or previously-enrolled subjects to be contacted and provided with additional information or be re-consented;
5. Requiring more than one review annually;
6. Initiating an audit of the study;
7. Reporting to UH IOs and federal agencies;
8. Initiating sanctions against the Investigator; and
9. Terminating the study.
10. Any administrative action that is appropriate under the circumstances.

203.7 Unanticipated Problems and Other Reportable Information

Both DHHS and FDA regulations require Unanticipated Problems (UPs) to be reported to the IRB.

See **SOP 116: Reporting and Reviewing Unanticipated Problems** for further information on procedures regarding UPs.

Reporting UPs to the IRB

When reporting UPs to the UH IRB, the Investigator shall:

- notify the IRB of each event that qualifies as a UP by contacting HSP within 24 hours of when the Investigator becomes aware of the event,
- report the event to the IRB using the appropriate form on reporting unanticipated problems no later than ten (10) working days after the Investigator becomes aware of the event, and
- file a follow-up report to the HSP if appropriate.¹⁷

An Investigator shall report UPs to the IRB, regardless of whether it is an internal or external event. The UH IRB only reviews a UP report on internal events, and external events where UH IRB is the IRB of record.

However, an Investigator is not required to report every adverse event to the IRB unless the event qualifies as a UP. Information on the distinction between “unanticipated problems” and an “adverse event” can also be found in the **SOP 116: Reporting and Reviewing Unanticipated Problems**.

The HSP fulfills the reporting requirements to institutional administrators, the sponsor and/or to the appropriate regulatory agency (FDA or OHRP) on UPs within two (2) months after the IRB or the IRB Chair recognizes that the event is an unanticipated problem.

Reviewing UPs

Unanticipated Problems are always reviewed by a convened IRB.

In the process of reviewing a UP report, the IRB may take the following actions to address the problem:

¹⁷ See OHRP Guidance on UPs, *supra* note **Error! Bookmark not defined.** at V.

- accept the report as submitted;
- request additional information from the Investigator;
- require modifications to the risk section of the consent form;
- require that a written communication be sent to all enrolled participants about the newly-recognized risk;
- require provisions of additional information to past participants;
- require current participants to re-consent to participation;
- modify the schedule of continuing review;
- require changes to the protocol initiated by the Investigator before obtaining IRB approval to eliminate apparent immediate hazards to participants;
- require a change in the study inclusion or exclusion criteria;
- require additional education and/or training for the research team;
- require the research site to develop procedures designed to prevent the reoccurrence of the UP;
- require changes to the protocol designed to reduce or eliminate the risk;
- require temporary or permanent suspension of enrollment of participants;
- require more than one review annually;
- suspend or terminate the research;
- suspend or terminate funding;
- notify the sponsor of action taken;
- require that the Investigator report the event to the sponsor, regulatory agency, or both; or
- other action determined to be appropriate by the IRB.

Studies Regulated by FDA

Reporting Requirements for UPs in Investigational Drug (IND) Studies

Investigators must promptly report all UPs to the IRB¹⁸ and report to sponsors any Adverse Events (AEs)¹⁹ related to the study they are responsible. In a multicenter study, the Investigator may rely on the sponsor's assessment of AEs and provide the IRB with a UP report prepared by the sponsor.²⁰

Reporting Requirements for UPs in Investigational Device (IDE) Studies

The reporting requirements on IDE studies are different from those on IND studies.²¹ An Investigator must submit to the IRB and the sponsor any unanticipated adverse device effect occurring during an investigation as soon as possible, but no later than ten (10) working days after the Investigator first learns of the effect.²²

¹⁸ 21 C.F.R. §§ 312.66, 312.53(c)(1)(vii); 56.108(b)(1).

¹⁹ 21 C.F.R. § 312.64(b).

²⁰ [FDA Guidance Adverse Event Reporting to IRBs – Improving Human Subject Protection](#).. Section III. Reporting AEs to IRBs in clinical trials of drug and biological products conducted under IND regulations.

²¹ [FDA Guidance Adverse Event Reporting to IRBs – Improving Human Subject Protection](#).. Section IV. Reporting AEs to IRBs in clinical trials of devices under IDE regulations.

²² 21 C.F.R. § 812.150(a)(1).

Internal and External Reporting

Reportable Decisions

If the convened IRB:

- determines that serious or continuing non-compliance has occurred as specified in Section 203.5, or
- determines that an unanticipated problem involving risks to participants or other (UP) or some other reportable event has occurred as specified in [Section 203.6](#), or
- suspends or terminates the approval of a protocol or proposal pursuant to [Section 206.5](#)

The IRB Chair and the HSP Director will notify the determination and IRB actions to the Institutional Official. Written procedures for reporting unanticipated problems, non-compliance, suspension and termination follow the OHRP and FDA regulations (45 C.F.R. § 46.103(5); 21 C.F.R. § 56.108(b)).

203.8 HRPP Quality Improvement

The UH supports quality improvement activities to foster ethical research conduct and compliance with institutional policies and procedures, including applicable federal and state regulations and guidance. The HSP Quality Improvement Unit (QIU) assesses and improves the compliance, efficiency, and effectiveness of the UH HRPP.

The objectives of these quality improvement activities are to:

1. Improve compliance of Investigators with their responsibilities.
2. Improve compliance of IRB meeting minutes with regulatory compliance
3. Increase efficiency of recording and finalizing IRB meeting minutes.

The QIU conducts reviews of records, interviews and observation of activities and facilities, and conducts surveys and other assessments for the following groups:

1. Investigators and research personnel participating in the design, conduct, data collection and/or analysis of human participant research (exempt and non-exempt) on behalf of UH;
2. UH IRBs;
3. HSP staff; and
4. Individuals involved in HSP education and outreach on human research participant protection.

See **SOP 110: Quality Improvement Activities** for specific activities and procedures in conducting and assessing quality improvement activities.

Additional Requirements

See **GUIDE 617: Other Federal Agencies – Additional Requirements** for other requirements depending on the sources of support/funding.

External Compliance Monitoring

On-Site Visit

Pursuant to 45 C.F.R, 46.109(e), the IRB have the authority to observe or have a third party observe the consent process and the research. Delegated by the UH IRB, select UH research projects may be audited by the QIU to assess its compliance with HHS regulations. Research is selected based on the criteria listed under the **SOP 110: Quality Improvement Activities** and monitored based on one of four categories: (1) routine, (2) for-cause, (3) Investigator-requested, or (4) observation of the informed consent process.

Reporting Outcomes

Outcomes of compliance monitoring activities are documented and reported to the HSP Director, the UH IRB, the ORC Director, the Institutional Official and other units within UH, as appropriate. These findings, supplemented by other review results when available, provide a qualitative and quantitative measurement of compliance with the HRPP. The HSP Director prepares and submits an HSP Annual Report that includes a summary of the compliance monitoring outcomes to the Office of the Vice President for Research and Innovation each year.

Research Community Feedback

The QIU tracks comments, inquiries and concerns received from UH Investigators, research personnel and participants to identify areas for potential improvement in the effectiveness of HRPP policies and procedures and for ensuring the protection of human research participants.

There are a variety of mechanisms available to Investigators for contacting relevant individuals to bring concerns and suggestions, including:

- Reporting possible non-compliance
- Reporting possible unanticipated problems
- Making general comments and suggestions and expressing concerns about other matters, issues or processes involving the HRPP, including IRB review and operations to any person in the HSP or in the ORC.

Additionally, input from researchers are actively sought for each protocol or proposal review on a continuing basis, via an online anonymous feedback survey about the service provided by the HSP and its IRBs; researchers may comment or provide suggestions on any aspect of the IRB or HRPP, by emailing the HSP through their website (<https://manoa.hawaii.edu/researchcompliance/human-studies>), directly emailing to HSP (uhirb@hawaii.edu), or by making an appointment with the HSP.

The HSP Director receives and evaluates the input from any of these sources, with review by other individuals, as necessary (e.g., OGC). The researcher receives a direct response for the input submitted, unless the researcher wishes to remain anonymous.

The Assistant Vice Chancellor for Research Compliance handles any concerns or complaints related to the HSP Director.

Systematic Review

GPM 204
Revised Date: December 18, 2015

204.1 Protocol Review

The UH IRBs and the HSP, as delegated by its IRBs, oversee only human participant research in which UH is engaged or for research that has entered into an agreement with UH for UH IRB to be its “IRB of Record.”

All UH new human participant research (as defined in Section 201.5) and modifications to approved research (except to remove apparent immediate hazards to participants) must be prospectively reviewed and approved by the IRB, before research activities take place. Approved protocols and proposals must undergo continuing review if research activities are expected to continue beyond the approval period set by the IRB.

204.2 IRB Protocol Applications (eProtocol)

Most protocol and proposal submissions to the IRB are completed via an online web-based system called “eProtocol.” Forms available for online submission include:

- Protocol or proposal applications for:
 - New research
 - Modifications
 - Continuing Review
- Reports
 - Unanticipated Problems and Serious Adverse Events
 - Protocol Violations or Deviations
- Final Reports

See [UH eProtocol Quicklink](#) for more information on the UH eProtocol system for submitting research protocols and proposals.

Protocol applications include, but are not limited to, the following sections to be completed by the Investigator or Investigator’s designee:

- Research Personnel
- Study Location
- Funding
- Resources
- Collaboration/Multi-site
- Participant population
- Purpose, procedures, background
- Use of Drugs or Devices
- Recruitment methods and screening procedures

- Inclusion and exclusion criteria
- Vulnerable populations
- Potential risks and benefits
- Privacy and confidentiality
- Conflict of Interest
- Consent and assent
- HIPAA

Review Type

New protocol and proposal submissions are processed according to one of three levels of review:

1. **Exempt:** UH requires protocols and proposals qualifying for exemption from applicable, federal, state and local regulations to be submitted for IRB review and confirmation. Exempt review is performed by HSP staff who have the knowledge and authority to confirm exemption or refer the protocol or proposal for expedited or convened IRB review.
2. **Expedited:** Protocols that qualify for expedited review must meet the requirements set forth in 45 C.F.R. § 46.110 (i.e., the research involves not more than minimal risk and falls within the categories published in the November 9, 1998, Federal Register 63 F.R. 60367; F.R. 60356 HHS-FDA list of research eligible for expedited review).
3. **Convened IRB:** Research that does not qualify for exempt or expedited review is subject to convened IRB review.

Other Research or Special Situations

Additional Requirements – Other Federal Agencies: Depending on the source of support for the research, regulations from other agencies might apply. See **GUIDE 617: Other Federal Agencies – Additional Requirements** for these special considerations and for links to checklists to help ensure that all special considerations are met.

Emergency Use of a Test Article: SOP 121: Emergency Use of a Test Article describes the requirements for the emergency use of an investigational drug, device, or biologic under FDA regulations 21 C.F.R. § 56.104(c), and documentation to be submitted to the IRB.

204.3 Assignments of Protocols or Proposals For Review

Reviewer assignments are made with the objective of matching reviewer expertise and experience with the research subject matter (See [Section 202.3](#)). IRB members who are “non-scientists” assigned to review research are valued for the community perspective they bring to the review process for ensuring the protection of research participants.

Attempt is made to assign any modification requests and continuing review submissions to the same primary reviewer who reviewed the research when it was initially approved.

Full-Board -- Primary Reviewer System

The IRB utilizes a primary reviewer system, in which new protocols or proposals qualified for full-board review are assigned a primary reviewer who is responsible for performing a comprehensive review and presenting an assessment of the study at the convened meeting.

A secondary reviewer is also assigned. The secondary reviewer reviews the study and may present an assessment on the study. The secondary reviewer serves as the primary reviewer when the primary reviewer is absent at the meeting. The reviewers may contact the Investigator for any additional information, as necessary. HSP staff maintains anonymity of their Reviewers from the Investigators of research they are assigned, but Reviewers may waive their anonymity by contacting the Investigator.

Expedited Research – Reviewer Qualifications

Only the IRB Chair or an experienced IRB member designated by the Chair may review research under an expedited review research. An IRB member is considered “experienced” when he/she has served the IRB for at least the last 6 months at the time of assignment and/or has had experience conducting human subjects research, or any other equivalent experience or expertise.

Administrative Changes to Expedited Research

Request for administrative changes to expedited research may be reviewed and approved by designated HSP staff. Examples of administrative changes to research include:

- Change in Project Title
- Principal Investigator’s contact information
- Changes to version number and/or revision date of study documents

204.4 Protocol/ Proposal Review

Criteria for Approval by an IRB

All proposed research must meet UH HRPP ethical standards governing the conduct of research (e.g., acceptable risk vs. benefit relationship, equitable selection, informed consent, protection of privacy, maintenance of confidentiality, and protections for vulnerable populations). The reviewers follow the approval criteria set forth in 45 C.F.R. § 46 and 21 C.F.R. § 50 in reviewing and approving a new protocol/proposal, continuing review, or review of a modification when the modification affects a criterion for approval. The IRB confirms that proposed Research Application, informed consent documents, and recruitment materials are accurate and complete.

The reviewers consider the regulations in reviewing and approving a protocol or proposal. They are facilitated in their consideration by the following several of HSP’s regulatory guidance and reviewer worksheets.

To approve research, an IRB must determine whether the following criteria are met²³:

1. *Risks to subjects are minimized*
 - (i) *by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and*
 - (ii) *whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes;*
2. *Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB shall consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB shall not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility*
3. *Selection of subjects is equitable. In making this assessment the IRB shall take into account the purposes of the research and the setting in which the research will be conducted and shall be particularly cognizant of the special problems of research involving members of vulnerable populations such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons;*
4. *Informed consent will be sought from each prospective subject or the subject's legally authorized representative according to Title 45, Section 46.116 in the Regulations;*
5. *Informed consent will be appropriately documented according to Title 45, Section 46.117 of the Regulations;*
6. *When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects; and*
7. *When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain confidentiality of data.*

Review of Exempt Research

Continuing review is not required for exempt research. Modifications, however, are subject to review by HSP staff delegated by the IRB to conduct exempt review. Approval of the modification is required before implementing the change to the research. If a modification to an exempt research changes the review type appropriate for the research, the HSP staff will move the protocol or proposal to the appropriate review type status.

See [Section 203.4](#) for information on exempt categories.

Continuing Review

The IRB applies the same criteria for approval at continuing review as at initial review of new protocols or proposals.

²³ 45 C.F.R. § 46.111(a).

Submission of a protocol or proposal for continuing review is required on all non-exempt approved research where its activities are ongoing, including but not limited to:

- Continuing recruitment and enrollment of participants;
- Research tests, procedures, and other interactions and interventions;
- Review of identifiable information;
- Data analysis; and
- Follow-up of previously enrolled participants.

The IRB determines whether the protocol or proposal needs verification from sources other than the researchers that no materials changes had occurred since previous IRB review.

Continuing review is not necessary only when:

- The research is permanently closed to the enrollment of new participants,
- All participants have completed all research-related interventions, and
- Collection and analysis of private identifiable information has been completed.

The continuing review application must be accompanied by the previously approved versions of the protocol or proposal's supporting documents. (e.g., consent forms, advertisements, sponsor protocol). Modifications to the research at the time of continuing review shall be submitted separately as a modification request, and the continuing review shall reflect the protocol or proposal without the modification being requested.

Modifications

No modification to protocols may be implemented without prior approval of the IRB, except where necessary to eliminate apparent immediate hazards to participants. Investigators are required to complete a Modification request application that includes a summary of the proposed modification and indicate the change in the risks to participants associated with the modification (e.g., increase, decrease, no change).

Modifications involving changes to previously approved or submitted documents (e.g., consent forms, advertisements, and protocols) or the addition of new documents must be accompanied by the new documents and/or the proposed revised versions of the previously approved or submitted documents. Revised versions of previously approved documents must show its changes in track format.

In circumstances where a modification is made without prior IRB approval because it is necessary to eliminate apparent immediate hazards to participants, the Investigator must report this change to the IRB (see **GUIDE 614: Events and Information that Require Prompt Report to the IRB**). The IRB will determine whether the change was consistent with ensuring the participants' continued welfare.

If significant new findings or information are submitted as part of a modification or continuing review, the IRB may require the reporting of this information to participants if the information could reasonably affect participants' willingness to continue their participation.

See **SOP 115: Submitting Modification Requests to the IRB** for more information on the procedures for requesting approval of modification requests to IRB-approved research.

Status/Final Reports

Upon completion of a research project Investigators may be required to submit a Final Report notifying the IRB of the completion of the project.

Final Reports are required for:

- Research that was subject to a full-board review and involved enrolled participants.

Final Reports are not required for:

- Research subject to expedited or exempt review, or
- Research projects subject to full board review but never commenced or never enrolled participants.

204.5 Full-Board Review

New Protocol or Proposal

Along with assigning a new protocol or proposal to a primary and secondary reviewer, external expert reviewers may be asked to review to the research, when applicable (e.g., Data Governance if project involves request and use of institutional data). The primary reviewer may also contact a consultant to assist with the review of a study prior to the convened meeting.

If there is not at least one person on the IRB with the appropriate scientific or scholarly expertise, or other expertise or knowledge, to adequately conduct an in-depth review of the research, the IRB defers the application to another meeting or to another IRB, or obtains consultation. The convened IRB can determine whether a consultant is needed.

Modification Requests

The following modifications are subject to full-board review and are assigned by the IRB Coordinator to one reviewer who reviews and presents the modification request at the convened meeting:

- **Major (or “substantive”) modification** is a change that may increase the level of risk to participants or a greater than minor modification in any of the following:
 - Informed consent
 - Research design or methodology
 - Participant population enrolled in the research
 - Qualifications of research personnel
 - Facilities used to support the safe conduct of research
 - Any other issues that would warrant review of the proposed changes by the full-board IRB
- **Substantive modifications or clarifications** are requested by the convened IRB, and are directly relevant to required IRB determinations.

Continuing Review

For all protocols or proposals initially subject to full-board review, the continuing review application undergoes full-board review, unless it meets the criteria for expedited review (see below). Those that must undergo full-board review are assigned to one reviewer who reviews and presents the continuing review application at the convened meeting.

Other Reports

See [Section 203.7 on Unanticipated Problems](#), and
See [Section 203.6 on Non-Compliance](#)

IRB Notification to Organizational Offices and Officials

The HSP notifies organizational offices and officials in writing, of the IRBs' findings and action and provide a copy of the minutes to the Vice President for Research and Innovation.

204.6 Expedited Review

See OHRP Guidance [Categories of Research That May Be Reviewed by the Institutional Review Board \(IRB\) through an Expedited Review Procedure](#) for human participant research that qualifies for expedited review.

Additional requirements may apply depending on the type of research project, or the sources of support or funding for the project or institution at which the study will be conducted. See **GUIDE 617: Other Federal Agencies – Additional Requirements**.

Only the IRB Chair or an experienced IRB member designated by the Chair may review research under an expedited review procedure. See [Section 204.3](#) for information on reviewer qualifications.

New Protocol or Proposal

Protocols and proposals subject to expedited review follow a single reviewer process and are assigned by the IRB Coordinator either to the IRB Chair or to a qualified IRB member.

Modification Requests

Modifications (minor) eligible for expedited review must meet all of the following criteria, based on the judgment of the IRB reviewer:

1. Any increase in risk is less than minimal risk.
2. All additional activities or procedures would have been eligible for expedited review had they been included in the initial protocol or proposal review.
3. Either the research is minimal risk or the proposed changes do not alter the study design.

If the modification changes the review type appropriate for the research, the HSP staff will move the protocol or proposal to the appropriate review type status. The IRB reviewer makes the final determination of whether changes to the research are “major” or “minor.”

Continuing Review

Protocols and proposals subject to expedited continuing review are assigned to one reviewer and are not presented at a convened meeting.

For Protocols or Proposals Initially Subject to Full-Board Review

For a protocol or proposal initially subject to full-board review, the continuing review undergoes expedited review if:

- Under Expedited Category 8:
 - (i) The research is permanently closed to enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long term follow-up of subjects; OR
 - No subjects have been enrolled and no additional risks have been identified; OR
 - The remaining research activities are limited to data analysis,
- Or under Expedited Category 9:
 - For continuing review of research, not conducted under an investigational new drug (IND) application or investigational device exemption (IDE) where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

For Protocols or Proposals Initially Subject to Expedited Review

For a protocol or proposal initially subject to expedited review, the continuing review undergoes expedited review if:

- It does not include any modifications, OR
- If modifications are included, the proposed modifications would have been eligible for expedited review had they been part of the initial protocol or proposal.

Final Reports

Final Reports prior to closure of research project are subject to expedited review and are assigned by the IRB Coordinator to one reviewer and are not presented at a convened meeting (see **APP 08: Study Closure Form**).

204.7 IRB Decisions

Protocols/ Proposals Subject to Full-Board

The IRB systematically evaluates each protocol or proposal to ensure the protection of research participants and reach a decision. The IRB consider the approval criteria set forth in 45 C.F.R. § 46.111 and 21 C.F.R. § 56.111 in reviewing a research protocol or proposal.

The possible decisions are:

1. **Approval** means approval of the study as submitted. The study may commence once the Investigator receives the approval letter from the HSP.
2. **Approval with Stipulations** is acceptance of the study with requests for clarification or modifications as a condition for final approval. The IRB adopts this action only when minor changes are requested. The Investigator may not begin the study before the approval date on the final written approval from the HSP.
3. **Recommendations.** The IRB may make recommendations to the Investigator, often to clarify the protocol or informed consent documents. Unlike stipulations, they are NOT required changes.
4. **Deferral** of an application requires a written response from the Investigator to substantive questions raised by the IRB during its review. Those questions are directly related to the [Criteria for Approval by an IRB](#). The response from the Investigator must be reviewed by a convened IRB. An IRB adopts this action when substantive changes are required.

An IRB votes on the action of deferral because deferral is one of the allowable actions by an IRB besides approval, which includes approval without and with stipulations, and disapproval.

5. **Disapproval** of an application indicates that the study does not meet the Criteria for Approval by an IRB and the study, as presented, may not be performed at the UH or by a UH faculty member, staff, or student. This action does not apply to a study under expedited review.
6. **Tabled** applications are deferred to a future convened meeting for review, and are usually done because the IRB lacks the appropriate expertise to adequately review the protocol or proposal or the IRB finds it necessary to seek external consultation. Tabled applications do not require voting, as this is not an official IRB action.

Protocols/ Proposals Subject to Expedited Review

The reviewer(s) of protocols or proposals subject to expedite review act on behalf of the IRB and have the authority to approve, require modifications (to secure approval) or request full-board review of the research. Expedited reviewers consider the approval criteria set forth in 45 C.F.R. § 46.111 and 21 C.F.R. § 56.111 in reviewing a research protocol or proposal.

The possible decisions are:

1. **Disapproval Not Allowed.** An expedited reviewer may not disapprove research. Research may be disapproved only after a convened IRB review. It can be returned to the Investigator if incomplete, or referred to the convened IRB if the reviewer does not approve the research.
2. **Allowable Types of Actions.** An expedited reviewer may adopt one of the following actions:
 - a) **Approval** if all criteria for IRB approval are met,
 - b) **Approval with stipulations** (equivalent to “approval with conditions” as termed by federal regulations) in which the Investigator must address certain questions or concerns about the application prompted by the expedited review; application is not approved until reviewer has reviewed and approved the Investigator’s response, or
 - c) **Referral** to the convened IRB if the expedited reviewer finds that the protocol or proposal warrants a full-board review or disapproval.

204.8 Approval Date and Determination of Expiration Date

Approval Date

The “approval date” is the date when the Investigator may start to conduct the study.

How Is the Approval Date Determined?

- **If the Study Is Approved Without Stipulations**, the approval date is the date when the research is approved by expedited review or the date of the convened review.
- **If the Study Is Approved With Stipulations**, the approval date is the date when the Chair or the Chair's designee determines the stipulations have been met.

Expiration Date

The HSP does not fix the anniversary date of research. The IRB sets the expiration date at the time of approval.

Definition:

The expiration date is the last day that the study is approved, which means the Investigator may conduct the study on the expiration date. Continuing review of the study must occur by or on the expiration date.

How Is the Expiration Date Determined?

The Regulation. An IRB must conduct continuing review of a study not less than once a year.²⁴

²⁴ 45 C.F.R. § 46.109(e).

Projects Requiring More Frequent Review. In determining which projects require review more often than annually, the IRB will consider the degree of risk of the study, the risk/ benefit ratio (i.e., the higher the perceived risk, the earlier the IRB may set the expiration date of the approval), the participation of vulnerable subject populations (if any), investigator experience, and other pertinent factors including, but not limited to, whether:

- The study involves unusual levels or types of risk to the participants;
- The investigator has failed previously to comply with HRPP policies and procedures, applicable federal regulations or IRB requirements;
- The IRB has concerns about possible material changes occurring without IRB approval.

Initial Review.

- **Approval Period.**²⁵ If the study is approved during the initial review, the approval period will be counted from the approval date.
- **The expiration date.** If the study is approved for one year, the expiration date is the day before the approval date in the next calendar year. If the approval period is less than a year, the expiration date is the last day within the approval period from the approval date.

Continuing Review.

- **Approval Period.** If the study is approved during continuing review, the approval period will be counted from the date of review, the date of expedited review if the study was under expedited review or the convened-IRB meeting if the study was under convened-IRB review.
- **The Expiration Date.** Counting approval period from the date of review makes a difference in the expiration date only when the study is approved with stipulations during continuing review. If a study is approved with stipulations for one year during continuing review, the expiration date is one year from the date of review, not the approval date. The next continuing review must occur by or on the expiration date.

Notification from the HSP about Expiration of Approval

About sixty (60) days before the expiration date, the HSP notifies the Investigator by email that the research's expiration date is approaching and the research would be closed if the Investigator fails to apply for continuing review within three (3) months after the expiration date. This notification is considered a courtesy provided to Investigators. Investigators are expected to track their study approval and to promptly apply for re-approval to avoid a lapse.

Lapse of Research

In general, a lapse occurs when the IRB has not approved the research by or on the expiration date. If research lapses,²⁶

- **all research activities involving human subjects must stop until the IRB reapproves the research, with the exception of already-enrolled participants described below; and**
- **the Investigator may not enroll new participants.**

Note: The Regulations only governs [research involving human subjects](#). Thus, when research lapses,

²⁵ [OHRP Guidance on Continuing Review](#).

²⁶ *Id.* at H.

all research activities involving human subjects must stop, but it does not mean all research activities must stop.

The HSP will close the research file if the Investigator fails to apply for continuing review within three months after the expiration date.

If research lapses, the Investigator must stop all research activities involving human subjects until the IRB reapproves the research, except if the Investigator determines to be in the best interest of already-enrolled participants for them to continue participating in the research. The exception applies, for example, when the research interventions hold out the prospect of direct benefit to the participants or when withholding those interventions poses increased risk to the participants. The Investigator, in consultation with the participants' treating physicians if the Investigator is not the treating physician, may determine whether continuing the research is to the best interest of the subjects. The Investigator shall submit the determination as soon as possible to the IRB to seek confirmation. The IRB Chair, a member or group of members designated by the IRB Chair, or the convened IRB may make the confirmation. If the IRB does not confirm the determination, the Investigator must stop all research activities involving human participants.

A research lapse does not warrant reporting to OHRP or other federal agencies, but, if an Investigator frequently fails to submit applications for continuing review or an IRB frequently fails to approve research before the expiration date, the HSP Director and IRB Chair, as appropriate, determine whether noncompliance exists and needs to be reported to the IO, funding agencies, and the OHRP.²⁷

Communication of IRB Actions

Notifying the Investigator

The HSP notifies IRB actions to the Investigator in writing.

If the IRB defers the research, the IRB must provide the Investigator the questions raised by the IRB during the review that require the Investigator's response.

If research is approved, the notification must clearly state²⁸:

- the approval date;
- the approval period;
- the expiration date by or on which continuing review must occur, and
- stipulations of the approval, if any.

If the IRB disapproves research, the IRB must include a statement regarding the reasons for the decision and provide the Investigator an opportunity to respond in person or writing.²⁹ Any response from the Investigator will be reviewed by a convened IRB. The Investigator is allowed to revise the protocol/ proposal and resubmit for IRB review and approval as a new application.

Notifying the Institutional Official (IO)

The HSP notifies the IO of the IRB findings by emailing meeting minutes to the official.

²⁷ 45 C.F.R. § 46.103(b)(5); [OHRP Guidance on Continuing Review](#), at H.

²⁸ [OHRP Guidance on Continuing Review](#), at I.

²⁹ 45 C.F.R. § 46.109(d); [OHRP Guidance on Continuing Review](#), at I.

Documentation of IRB Activities

GPM 205
Revised Date: December 18, 2015

205.1 IRB Records

The Human Studies Program maintains adequate documentation of IRB activities.³⁰ The HSP utilizes an electronic protocol application system called “eProtocol.” Copies of certain documents are also maintained in hard copy files and electronic files stored outside the eProtocol system.

205.2 IRB Research Files

Electronic Protocol System (eProtocol)

The eProtocol system maintains electronic records of all documents submitted through the system for every protocol event. The eProtocol system contains a search function for locating and retrieving application by protocol number, project title, name of the Principal Investigator (PI), names of co-Investigators, review type, meeting date, HSP file number, reviewer or any combination of the above categories.

Electronic copies of all materials submitted to the IRB can be accessed through eProtocol on an event-by-event basis through the eProtocol Event History function, thus all documents supporting each protocol event are accessible to reconstruct the entire history of an application.

Each research file contains, as applicable to the research:

1. **Application Form(s).** The research file includes one or more of the following application types:
 - New Application for biomedical, social & behavioral sciences, and cooperative research (Full-board, Expedited and Exempt review) submitted for all new research projects;
 - Modification Request Form, submitted for modifications to approved research;
 - Continuing Review Form, submitted for continuing review research;
 - Reports submitted for reportable events and information per **GUIDE 614: Events and Information that Require Prompt Reporting to the IRB.**
 - Status/Final Report Form, submitted for continuing review of research with less than one year approval period and for closing full-board review research.

IRB and HSP reviewer comments and Investigator responses that occurred during IRB review are included with each application. Comments and responses exchanged via email are also included as attachments, or are stored in electronic copy files.

³⁰ 45 C.F.R. § 46.115.

2. **IRB-approved research protocol or proposal**, as applicable. The protocol or proposal shall include information about the research aims/ hypothesis, literature review or background, procedures or methodologies, description of study instruments, data analysis, etc.
3. **IRB-approved informed consent document(s)**. The research file includes all approved consent forms, including the currently approved consent form.
4. **IRB-approved assent form(s)**. If a study involves children or adults with diminished capacity, when appropriate, from whom the Investigators will obtain assent, copies of approved assent forms are included in the research file.
5. **Scientific evaluations of the proposed research**. Documentation of scientific review is included in the research file. See [Section 201.6](#) for information on scientific and scholarly review.
6. **Sponsor Materials**. For investigational drug studies, the Investigator's Brochure and Sponsor's Protocol, including current amended editions of these documents and all previous versions are included in the research file.

For investigational devices, a report of prior investigations and the Sponsor's Protocol are filed.

7. **Application for federal grant support**. For research supported by federal funds, a copy of the grant proposal is included in the research file. If the federal funding is subcontracted through another institution, the sub-contract with that institution is noted in the research file.
8. **Advertisements, recruitment scripts** which include phone screening scripts and non-medical oral scripts, flyers, website and other recruitment materials. See Section 207.2 Review of Recruitment Plan, Advertisements, and Compensation.
9. **Questionnaires, surveys, interview scripts, diaries** or other documents used in the course of the study.
10. **Participant informational sheets, brochures, and research newsletters**.
11. **Reports submitted for reportable events and information** per guidance (**GUIDE 614 Events and Information that Require Prompt Reporting to the IRB**).
12. **Status Reports and Final Reports** submitted for full-board review research.
13. **Data and Safety Monitoring Board (DSMB) reports, Annual Progress Reports**.
14. **Conflict of Interest (COI) documents**, when COI or ICOI is applicable.
15. **Correspondence and communication** between IRB members, HSP staff and researchers (Investigators and research support staff).
16. **Other IRB correspondence** related to the research.
17. **Documentation of all actions** including approvals, disapprovals, waivers or alterations of consents and HIPAA authorizations (as documented in the application forms).

18. **Approval letters.**
19. **Documentation of research closure** if any, including Final Report forms for full-board research.
20. **Expiration notices** sent.
21. **IRB Authorization Agreement (IAA) and, if applicable, Memorandum of Understanding (MOU)/ Memorandum of Agreement (MOA)** for studies in which either UH IRB cedes oversight to a non-UH IRB or becomes the relying IRB for collaborative or multi-site studies.
22. **IRB approvals from collaborating institutions** are requested and included in the research file.
23. **IRB reviewer checklists and worksheets** used to determine IRB decision.

205.3 Minutes of IRB Meetings

The HSP documents discussions, decisions, and findings either through the IRB meeting minutes or for research subject to expedited review through documentation in the research file or other records.

The minutes of the IRB meetings includes the following:

1. **Meeting attendance** with the following details:
 - a. Names of IRB members in attendance (voting, non-voting, and ex-officio). Non-voting members include alternate members not substituting for a regular, voting member, and ex-officio members,
 - b. When an alternate member replaces a regular member in attendance and voting at the convened meeting,
 - c. Continued presence of quorum for all votes, including a member of non-scientific background,
 - d. Names of IRB members who recuse themselves from the meeting or discussion of a protocol or proposal due to a conflict of interest and indication as such,
 - e. Attendance of members (regular or alternate) who participate through video- or tele-conference,
 - f. Names of IRB members who leave the meeting briefly, are not present during a vote, and are not counted as part of the quorum,
 - g. Names of IRB members who arrive late or leave early from the meeting and their relative arrival or departure times relative to the sequence of protocol/ proposal review,
 - h. Names of HSP staff present, and
 - i. Any other individuals present (e.g., invited guests, Investigators invited to address the IRB, and consultants);
2. **Actions taken by the IRB and separate deliberations** for each action that includes:
 - a. Discussion on protocol events – new, continuing review, modifications, reports of

- b. unanticipated problems and events and information requiring prompt review,
 - c. Approval of research, including approval period for initial and continuing review, and as appropriate based on the degree of risk determined, approval period of less than one year,
 - d. Approval of research with stipulations on specific minor issues, and the designee (HSP staff or IRB reviewer) appointed to sign off on the condition when met,
 - e. Suspensions and terminations of previously approved research,
 - f. The basis for requiring changes in or disapproving research,
 - g. Written summary of discussion of controverted issues and their resolution;
 - h. Requests for consultant review,
 - i. Actions resulting from review of reports of unanticipated problems involving risks to participants or others, or other reportable events and information, and
 - j. Actions resulting from determinations of serious or continuing non-compliance;
3. **Required determinations** and protocol-specific findings justifying those determinations for:
- a. Waiver or alteration of the consent process³¹,
 - b. Waiver of documentation requirement during consent process³²,
 - c. Research involving pregnant women, fetuses, and neonates³³,
 - d. Research involving prisoners³⁴,
 - e. Research involving children³⁵,
 - f. Research involving participants with diminished capacity to consent,
 - g. Waiver or alteration of HIPAA authorization³⁶,
 - h. Waiver of HIPAA authorization for recruitment or screening³⁷,
 - i. Significant risk and non-significant risk device determinations³⁸,
 - j. Determination of the level of risk,
 - k. Determination of serious or continuing non-compliance, and
 - l. Unanticipated Problems and Unanticipated Device Effect;
4. **Vote on actions** as numbers *for*, *against*, or *abstaining*; and
5. **Other issues requiring convened IRB review** such as but not limited to:
- a. Announcements prior to convened meeting,
 - b. DSMB reports,
 - c. Approval of minutes prior to convened IRB meetings,
 - d. Educational sessions for IRB members prior to convened IRB meetings,
 - e. Presentation of information from consultants or experts as previously requested by the IRB,
 - f. Names of IRB members who abstain for reasons other than conflict of interest, and
 - g. Other issues as applicable

Disposition of the IRB Minutes

The HSP staff document minutes and makes them available for IRB review at least four business days prior to the next convened meeting. Minutes may not be altered by anyone once approved by the IRB

³¹ 45 C.F.R. §§ 46.116(c), 46.116(d), 46.117(b)(2); 21 C.F.R. § 50.27(b)(2)

³² 45 C.F.R. § 117(c), 21 C.F.R. § 56.109(c)(1)

³³ 45 C.F.R. §§ 46.204, 46.205, 46.206, and 46.207

³⁴ 45 C.F.R. 46.305, 45 C.F.R. 46.306

³⁵ OHRP: 45 C.F.R. § 46.404-408; FDA: 21 C.F.R. § 50.51-55

³⁶ 45 C.F.R. § 164.512(i)(2)(ii)

³⁷ 45 C.F.R. § 164.512(i)(2)(ii)

³⁸ 21 C.F.R. § 812.2(b), 21 C.F.R. § 812.150(b)(9), and FDA Information Sheet Significant and Non-significant Risk Medical Device Studies.

members but a subsequent IRB meeting. Meeting minutes must be approved by a majority of the convened IRB.

IRB meeting minutes are considered confidential, and access to them is restricted and secured to the extent allowed by law. A copy of approved minutes to the IO is the primary mechanism that the HSP conveys IRB decisions to UH leadership.

205.4 Other Documentation

Information Specific to Certain Types of Research or Special Situations

118 Designation

Certain types of applications for grants, cooperative agreements, or contracts may be submitted to federal departments or agencies with the knowledge that human participants may be involved within the period of support, but definite plans would not normally be described in the applications. Under the federal regulations, e.g., 45 C.F.R. § 46.118, those applications need not to be reviewed by an institutional review board (IRB).³⁹ Principal Investigators submit a request form to the Human Studies Program (HSP) to designate the applications as under 45 C.F.R. § 46.118. Such designation is called Section 118 designation for short and further described in **SOP 123: Section 118 Designation**.

The HSP Director reviews the materials submitted to verify conditions of 45 C.F.R. § 46.118 have been met. The Request for 118 Designation, annual reports, and other documentation exchanged between the PI and HSP staff regarding 118 Designation (i.e., approval letter of 118 designation) are retained in a separate file with the Human Studies Program.

Human Subject Determination

Human Subject Determination applications, Not Human Subjects Research verification letters and any other materials acquired in the process of review of proposed research that has been found to not meet the definition of Human Subject Research are kept in a separate file with the Human Studies Program.

Emergency Use of a Test Article

Activities involving the emergency use of a test article under FDA regulations 21 C.F.R. § 56.104(c) is described in [Section 209.5](#) and **SOP 121: Emergency Use of a Test Article**. Documentation of the emergency use of a test article is submitted to the IRB within five (5) days of the use of the test article and includes the following documents:

- Emergency Use of a Test Article Notification Form
- Consent form, if applicable

The IRB Chair of a biomedical IRB reviews the materials submitted to verify conditions of 21 C.F.R. § 50.23(c) have been met, including requirements for informed consent unless the conditions of 21 C.F.R. § 50.23(a)-(b) have been met. IRB review is documented by **WKSH 321: Emergency Use of a Test Article, Review and Determination**.

³⁹ 45 C.F.R. § 46.118 (2013).

Other IRB-related Information

Other information are maintained by the Human Studies Program, such as correspondence between the IRB and outside agencies and institutions, IRB convened meeting documentation (e.g., meeting agendas, detailed IRB member information and CVs, etc.), IRB member COI disclosure and confidentiality agreements, Institutional IRB Authorization Agreements and MOUs/MOAs, etc.

205.5 Record Retention

In accordance with the Common Rule and FDA regulations, IRB records are retained for at least three (3) years after the completion of the research, either electronically or as hard copy. Therefore, all UH IRB records are retained for three (3) years after completion or termination of a study. This requirement does not apply to research exempt from IRB review. Sponsored grants and contracts may require additional periods for record retention. It is UH policy to retain records for the maximum period around of mandated time.

Other documents, such as meeting agendas and meeting minutes for the last three years are maintained in the Human Studies Program office. Older documents longer than three years may be archived into electronic files and stored in the HSP shared server.

General correspondence from Investigators and other documents not specific to a particular research file are maintained indefinitely with the HSP.

Maintenance of and Access to IRB Records

All hard copy IRB records of active protocols and proposals are secured in closed filing cabinets in locked buildings with regular security patrols. Electronic IRB records submitted and maintained through the eProtocol system reside in a secured server, with password protection access.

Access to IRB records is routinely provided to the Vice President for Research and Innovation, the ORC Director, IRB Chairs, IRB members, HSP staff, and authorized non-UH IRB and regulatory offices (e.g., The Queens Medical Center Research Regulatory Office, Hawai'i Pacific Health Research Institute's Regulatory Office). All other UH access to IRB records is limited to those with a legitimate need for access, such as the University's ORS, OTTED, OGC, and Data Governance.

All records are accessible for inspection and copying by authorized representatives of federal departments or agencies at reasonable times and in a reasonable manner.⁴⁰ The HSP may allow access to IRB records by outside entities (e.g., monitors of sponsors of clinical trials) and agencies (e.g., regulatory agencies).

⁴⁰ 45 C.F.R. § 46.115(b).

Risks to Research Participants

GPM 206

Revised Date: December 18, 2015

206.1 What is “Risk”?

Risk in the context of human participant research refers to the combination or the probability and magnitude of some future harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary independently and result in risks that range from “high” to “low” depending on whether they are more (or less) likely to occur, and whether the potential harm is more (or less) serious.

Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life of during the performance of routine physical or psychological examinations of tests.⁴¹

When following Department of Defense requirements, the definition of the minimal risk based on the phrase “ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests” must not be interpreted to include the inherent risks certain categories of research participants face in their everyday life. See **GUIDE 617: Other Federal Agencies—Additional Requirements** for additional regulations, funding agency requirements and guidance on risk (and minimal risk) applicable to specific situations or populations (e.g., children, prisoners).

206.2 Minimizing Risk in Human Participant Research

There are multiple steps to minimize risk in human participant research. Both the Investigator and the IRB have the responsibility to ensure risks are minimized and reasonable relative to the anticipated benefits before a research secures approval.

Identifying Potential Risk and Analyzing Level of Risk (Investigator)

The Investigator documents in the Protocol/Proposal Application information that would allow the IRB to conduct an analysis of the risks and potential benefits on a particular research study:

- Purpose of the research.
- Scientific or scholarly rationale for conducting such research.
- Research procedures including procedures already performed for treatment or diagnostic purposes.
- Potential risks to participants.
- Procedures for protecting against or minimizing potential risks, including risks to confidentiality and privacy.
- When requesting changes to the research, the Modification Request form includes description of the proposed changes and potential impact on the level of risks to participants.

⁴¹ 45 C.F.R. § 46.102(i); FDA 21 C.F.R. § 56.102(i)

In an Initial Application, Modification or a Continuing Review submission, the Investigator indicates level of risk (little to no risk, minimal risk, greater than minimal risk) to participants by declaring the review type on their submission (exempt, expedited, full-board).

Ensuring Risks are Minimized (IRB Determination)

The IRB considers the overall level of risk to participants in reviewing the proposed research in accordance with the conditions described in 45 C.F.R. §§ 46.111(a)(1-7), 21 C.F.R. 56.111(a)(1-7) and the ethical principles outlined in the Belmont Report. The IRB utilizes its armory of scientific and scholarly expertise, and seek consultants when expertise is needed, to critically assess the research when reviewing risks to participants.

The IRB must determine that risks (or burden to participants) are minimized before approving a research. This includes:

- Ensuring that the proposed research has sound (scientific and scholarly) research design and purpose⁴²;
- The research does not expose participants to unnecessary risks⁴³; and
- When appropriate, the research uses procedures that are already being performed on the participants for diagnostic or treatment purposes⁴⁴.

Appropriate plans to minimize risk to participants may include having an adequate data monitoring plan, coding data to protect confidentiality of participant information, or providing medical or psychological resources to participants as a potential consequence of involvement in the research. If risks are not minimized, the research will not be approved as written.

The IRB also considers the professional qualifications and resources (including time, equipment, support services) of the research personnel to protect participants and minimize potential harm. Research personnel must receive appropriate training, and clinicians involved in the research must maintain the professional credentials and/or licenses appropriate to their role in the research.

Anticipated Benefits (Investigator)

The application requires that the Investigator includes information about the potential benefit(s) to participants (if any), and how the knowledge gained may benefit the participants, future participants or society. Compensation for participation is not considered a benefit.

The Investigator must explain how these potential benefits to the participant or society outweigh the risks inherent in the research.

Potential Risks vs. Anticipated Benefits (IRB Determination)

The IRB determines whether the risks of the research are reasonable in relation to the anticipated benefits (if any) to research participants and the importance of the knowledge that may reasonably be expected to result.⁴⁵

⁴² 45 C.F.R. § 46.111(a)(1)(i), 21 C.F.R. § 56.111(a)(1)(i)

⁴³ *ibid.*

⁴⁴ 45 C.F.R. § 46.111(a)(1)(ii), 21 C.F.R. § 56.111(a)(1)(ii)

⁴⁵ 45 C.F.R. § 46.111(a)(2), 21 C.F.R. § 56.111(a)(2)

The IRB bases its risk/benefit analysis on the information provided by the Investigator and by the expertise of its members and consultants who utilize the most current information about the risks and benefits of the interventions involved in the research.

The IRB considers only those risks that result from the research. It does not consider long-term effects (e.g., public policy implications) of applying the knowledge gained in the research. The IRB does not consider those risks and benefits that participants would otherwise receive if they do not participate in the research.⁴⁶

206.3 Data and Safety Monitoring

When appropriate, the IRB must determine that the research plan includes adequate provisions for monitoring the data to ensure the safety of research participants, prior to approval of the research.

For research (e.g., if more than minimal risk) that requires a Data and Safety Monitoring Plan (DSMP):

- The DSMP must be commensurate with the level of risk, size and complexity of the study.
- The DSMP may need a Data Safety Monitoring Board (DSMB).

Investigators must include a discussion of the DSMP, if applicable, on the Protocol Application.

For guidance, see:

- [Data Monitoring Committees – FDA March 2006 “Guidance for Clinical Trial Sponsors”](#)
- Data Monitoring Plans and Data Monitoring Committees – NIH and NCI policies:
 - [NIH: Policy for Data and Safety Monitoring](#)
 - [NIH: Further Guidance on Data and Safety Monitoring for Phase I and Phase II Trials](#)

IRB Review of the Data and Safety Monitoring Plan

The IRB primary reviewer reviews the proposed DSMP, and the administration and composition of the monitoring entity, when applicable. External experts are consulted when needed to assist with the review.

Reporting DSMP Outcomes

Investigators are expected to submit all reportable findings from the DSMB to the IRB within the prescribed timeframe. See **SOP 116: Reporting and Reviewing Unanticipated Problems**.

Investigators must also including in the continuing review application the outcomes of data and safety monitoring including a summary of adverse events, any unanticipated problems, and any new information pertaining to the research – either from the research itself or from other sources, which have occurred since the previous IRB review. This includes audit, inspection, multi-center trial, and DSMB reports

⁴⁶ 45 C.F.R. § 46.111(a)(2), 21 C.F.R. § 56.111(a)(2)

received by the Investigator and copies of these reports shall be attached to the continuing review application.

206.4 Risks to Vulnerable Populations

The IRB takes into special consideration the Common Rule and FDA regulations in protecting the welfare of vulnerable participants (i.e., children, pregnant women and neonates, and prisoners) involved in research.

To approve research involving vulnerable populations, the IRB must determine, as applicable, that additional safety measures have been placed to protect the rights and welfare of participants who are likely to be vulnerable to coercion or undue influence, such as:

- Pregnant women, human fetuses, or neonates (45 C.F.R. 46 Subpart B)
- Prisoners (45 C.F.R. 46 Subpart C),
- Children (45 C.F.R. 46 Subpart D; 21 C.F.R. 50 Subpart D),
- Individuals with mental disabilities,
- Economically or educationally disadvantaged persons, or
- Socially marginalized persons.

Reviewing Research Involving Vulnerable Participants

When reviewing research involving vulnerable participants, the IRB considers the following elements in the protocol or proposal:

- Method of recruitment and enrollment of participants (i.e., use of exclusion/inclusion criteria; informed consent process; coercion and undue influence; confidentiality of data).
- Group characteristics (e.g., economic, social, physical, and environmental conditions)
- Participant selection to prevent over-selection or exclusion of certain participants based on perceived limitations or complications associated with including those participants.
- Application of state or local laws regarding decision-making abilities of potentially vulnerable populations (e.g., age of majority for providing consent).
- Procedures for assessing and ensuring participants' capacity to understand and provide consent or assent.
- Any other additional safety measure necessary to protect potentially vulnerable populations.

Pregnant Women, Fetuses and Neonates

Under 45 C.F.R. part 46, subpart B, special protections are provided for research involving pregnant women, fetuses and neonates. Research involving women who are or may become pregnant shall receive special attention because of additional health concerns for pregnant women and because of the need to avoid unnecessary risk to the fetus.

Subpart B requires that research involving pregnant women, fetuses, and neonates shall involve the least possible risk. Those engaged in the research may have no involvement in the timing, method, or procedures used to terminate the pregnancy, or to determine the viability of the fetus. No inducements may be offered to terminate a pregnancy.

Each of the four following conditions has their own requirements and IRB determinations:

1. **Research Involving Pregnant Women or Fetuses.** No pregnant women may be involved as a research participant unless either of the following conditions are met⁴⁷:
 - a. The purpose of the research activity is to meet the health needs of the mother, and the fetus is placed at risk only to the minimum extent necessary to meet such needs; OR
 - b. The risk to the fetus is minimal.

Consent: The mother and the father must be legally competent and provide consent, unless the purpose of the research is to meet the health needs of the mother, or the father is not reasonably available, or the pregnancy resulted from rape.

2. **Research Involving Human Fetuses.** For research directed at human fetuses:
 - a. The purpose of the research needs to meet the health needs of the individual fetus and shall be conducted in a way that minimize risk; OR
 - b. The research will pose no more than minimal risk to the fetus, and the purpose of the research activity is to ascertain important biomedical information that is unobtainable by other means.

Consent: The mother and the father are legally competent and have provided consent, unless the father is not reasonably available or the pregnancy resulted from rape.

3. **Research Involving Viable Neonates.** A neonate, after delivery, that has been determined to be viable is considered a “child” and may be included in research only to the extent permitted by and in accordance with the requirements of subparts A and D of 45 C.F.R. part 46.

4. **Neonates of Uncertain Viability.** Neonates of uncertain viability may not be involved in research unless one of the following conditions applies:
 - a. There is no added risk to the neonate and the purpose of the research is to obtain important biological information that cannot be obtained by other means; OR
 - b. The purpose of the activity is to enhance the probability of survival of the individual neonate.

Consent: Research involving neonate of uncertain viability is allowed only if either parent or the parent’s legally authorized representative provides their consent.

5. **Nonviable Neonates.** Nonviable neonates maybe not be involved in research unless all of the following are met:
 - a. The vital functions of the neonate are not artificially maintained;
 - b. Experimental activities that would of themselves terminate the heartbeat or respiration are not used; AND
 - c. The purpose of the research is development of important biomedical information that cannot be obtained by other means.

Consent: Research involving a non-viable neonate is permitted only when both parents have given their informed consent, unless one parent is not reasonably available or the pregnancy resulted from rape or incest. Consent by a parent’s legally authorized representative is not permitted.

⁴⁷ 45 C.F.R. § 46.204.

Prisoners

Under 45 C.F.R. part 46, subpart C, special protections are provided for research involving prisoners. The incarceration could affect the Prisoners' ability to make a truly voluntary decision on whether to participate as subjects in research. To protect prisoners' rights and welfare, the Investigator and the IRB shall take extra measures to meet the ethical and regulatory requirements on research involving prisoners.

Definition of minimal risk in research involving prisoners is different from minimal risk in research involving individuals from the general population. Minimal risk specific to prisoners is measured by the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.⁴⁸

When reviewing research that involves prisoners, the IRB must include at least one member who was a prisoner, or is a prisoner representative with appropriate background and experience to serve in that capacity, except that, where a particular research project is reviewed by more than one IRB, only one IRB needs to satisfy this requirement.⁴⁹ Examples of such members are former or present prisoners, prisoner psychologists, prison social workers, or prison chaplains.⁵⁰ A majority of the IRB, excluding prisoner members, must not be associated with the prisons involved⁵¹ (see [Section 202.2: IRB Member Composition and Structure](#)).

Except certain types of epidemiologic research, research involving prisoners must be in one of the following four categories⁵²:

1. Research on the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the participants;
2. Research on prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the participants;
3. Research on conditions particularly affecting prisoners as a class provided that the study may proceed only after the Secretary of HHS has consulted with appropriate experts; or
4. Research on practices, innovative or accepted, which have the intent and reasonable probability of improving the health or well-being of the participant.

Certain types of epidemiologic research conducted or supported by HHS does not need to be in one of the above four categories listed under 45 C.F.R. § 46.306(a)(2).⁵³ But the epidemiologic research must meet the following requirements before it may proceed:

1. The sole purposes of the research are:
 - (a) to describe the prevalence or incidence of a disease by identifying all cases, or
 - (b) to study potential risk factors associated with a disease, and

⁴⁸ 45 C.F.R. § 303(d).

⁴⁹ 45 C.F.R. § 46.304(b).

⁵⁰ [OHRP IRB Membership Video](#).

⁵¹ 45 C.F.R. § 304(a).

⁵² 45 C.F.R. § 306(a)(2); see Waiver of the Applicability of Certain Provisions of Department of Health and Human Services Regulations for Protection of Human Research Subjects for Department of Health and Human Services Conducted or Supported Epidemiologic Research Involving Prisoners as Subjects, 68 Fed. Reg. 36,929 (June 20, 2003).

⁵³ 68 Fed. Reg. 36,929.

2. the institution responsible for the conduct of the research certifies to OHRP that an IRB:
 - (a) approved the research and made the findings under 45 C.F.R. § 46.305(a)(2)–(7); and
 - (b) determined and documented that:
 - (i) the research presents no more than minimal risk and no more than inconvenience to the prisoner-subjects, and
 - (ii) prisoners are not a particular focus of the research.

See **GUIDE 629: Research Involving Vulnerable Populations** for more information about research involving prisoners. See **SOP 124: Research Involving Prisoners** for procedures in reviewing and reporting research involving prisoners.

Children

If research involves children, the IRB follows subpart D of 45 C.F.R. part 46 in its review of the research, except when the research is regulated only by FDA.⁵⁴

Only the following four categories of research involving children are allowed:

1. **Research Not Involving More than Minimal Risk.** If the IRB finds that the research involves no more than minimal risk to children, the IRB may approve the proposal only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.⁵⁵
2. **Research Involving Greater than Minimal Risk but Presenting the Prospect of Direct Benefit.** If the IRB finds that more than minimal risk to children is presented by a research intervention or procedure that holds out the prospect of direct benefit to the individual subject, or by a monitoring procedure that is likely to contribute to the individual subject's well-being, the IRB may approve the research only if it finds that
 - (a) the risk is justified by the anticipated benefit to the subjects;
 - (b) the ratio of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
 - (c) adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.⁵⁶
3. **Research Involving Greater than Minimal Risk and Presenting No Prospect of Direct Benefit.** If the IRB finds that more than minimal risk to children is presented by a research intervention or procedure that does not hold out the prospect of direct benefit to the individual subject, or by a monitoring procedure that is not likely to contribute to the well-being of the individual subject, the IRB may approve the research only if the IRB finds that
 - (a) the risk represents a minor increase over minimal risk;
 - (b) the intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
 - (c) the intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is vitally important for the understanding or amelioration of the subjects' disorder or condition; and
 - (d) adequate provisions are made for soliciting assent of the children and permission of their

⁵⁴ See 21 C.F.R. §§ 50.50–50.56 (2014).

⁵⁵ 45 C.F.R. § 46.404.

⁵⁶ 45 C.F.R. § 46.405.

parents or guardians.⁵⁷

4. **Research Not Otherwise Approvable but Presenting an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Children.**

For more information on research involving children, see **GUIDE 629: Research Involving Vulnerable Populations**.

Individuals with Diminished Decision-Making Capacity

When research involves individuals with psychiatric, cognitive, or developmental disorders, or who are substance abusers, the predominant ethical concern is that their disorders may compromise their decisional capacity, i.e., their capacity to understand the presented information and their ability to make a reasoned decision. Also, many of those individuals are residents of institutions responsible for their care and treatment. Institutionalization may further compromise their ability to exercise free choice.

Research involving persons with diminished capacity shall bear a direct relationship to their condition or circumstances.

UH Students and Employees

Students and employees⁵⁸ at UH and other facilities under the purview of the IRB are considered vulnerable participants mainly because of the risk of coercion and undue influence.

Students may volunteer out of a belief that doing so will place them in good favor with faculty such as better grades, recommendations, or employment, or that failure to participate will negatively affect their relationship with the Investigator or faculty in general such as seeming “uncooperative” or not being part of the scientific community.

Employee participation raises questions about the ability of employees to exercise free choice because employees are likely to view their employers as authority figures to whom they must show deference. Employees may also fear that a decision to participate could affect performance evaluations or job advancement even if it is only the employee’s perception, or refusal to participate may result in a loss of benefits.

Safeguards will be placed to reduce or minimize undue influence or coercion when recruiting and enrolling participants who are students or employees.

206.5 Suspension and Termination of IRB Approval

The IRBs have the authority to suspend or terminate a previously approved research⁵⁹

⁵⁷ 45 C.F.R. § 46.406.

⁵⁸ What Constitutes Coercion or Undue Influence when Employees Are the Subjects of Research?, HHS, <http://answers.hhs.gov/ohrp/questions/7254> (last reviewed Dec. 30, 2010).

⁵⁹ See 45 C.F.R. § 46.113; 21 C.F.R. § 56.113.

The IRB may decide to suspend or terminate a protocol or proposal for any of the following reasons including but not limited to:

- (a) When an Investigator does not comply with the IRB requirements, the Regulations, or both;
or
- (b) When the study poses unexpected serious harm to research participants. This category includes suspension or termination on an urgent basis.
 - (i) Suspension or termination on an urgent basis means that a study poses imminent high risk to participants such that it becomes necessary to immediately suspend or terminate the study.
 - (ii) The Director or the IRB Chair is authorized to suspend or terminate a study on an urgent basis.

Who Is Authorized to Suspend or Terminate a Study?

The Director, the IRB Chair, and the IRB are authorized to suspend a previously approved research. Only a convened IRB may terminate a previously approved research. The Institutional Official may also suspend a study, but must provide strong justification for the decision. The Institutional Official does not have the authority to terminate a study, but may request to the convened IRB that a study be terminated if there is reason for termination.

Voluntary Suspension or Termination

The sponsor or the Principal Investigator (PI) of a study may voluntarily decide to suspend or terminate the study due to various reasons, including but not limited to:

- (a) an unanticipated problem,
- (b) serious noncompliance, or
- (c) continuing noncompliance.

If this occurs, the PI must notify the HSP in writing no later than *three (3) working days* after the suspension or termination, describing

- (a) the steps taken or to be taken to protect the welfare of currently enrolled participants, and
- (b) corrective actions, if appropriate, to address the cause for the suspension or termination.

This report will be reviewed at a convened IRB meeting. After reviewing the report, the IRB will decide whether to officially suspend or terminate the IRB approval.

Reporting Suspension and Termination of IRB Approval

The HSP staff fulfills the regulatory reporting requirements on suspension and termination no later than two (2) months after the IRB's decision to suspend or terminate IRB approval, including reporting to federal agencies as appropriate.

See **SOP 109: Suspension or Termination of Research** for procedures for suspending or terminating IRB approved research protocols or proposals.

Protecting Participants Who May Be Affected by IRB Action

If the suspension or termination will affect participants in the research (e.g., requires withdrawal of participants), the IRB may require additional actions, taking into consideration the impact on the participants' health and safety. This shall occur before the suspension or termination, when it is feasible and delay will not compromise participants' welfare. Actions the IRB may require include, but not limited to:

- Require the Principal Investigator to submit proposed procedures for any withdrawal of participants.
- Allowing participants to continue with the research (e.g., continuing treatment of investigational drug) if the IRB determines that it is in the best interests of the participants
- Requiring IRB review and approval of any PI correspondence material to participants about the IRB action
- Requiring the reassignment of a new PI to the research

Participant Recruitment and Selection

GPM 207
Revised Date: December 18, 2015

207.1 Equitable Selection

Guidance and information is made available to Principal Investigators (PIs) and research support staff to assist them in creating recruitment materials and participant selection procedures that are fair and equitable. Guidance and information can be found here:

- **GUIDE 619: Recruitment Guidelines**
- **TMP 475: Model Recruitment Flyer**

Investigators shall provide detailed information on how participants will be identified and recruited in response to questions in the Research Application. This information shall include a description of the target study population (including age range, gender, and ethnic background), the inclusion and exclusion criteria and whether compensation for participation will be offered. Additionally, Investigators are required to justify the inclusion of targeted persons (e.g., healthy participants, students or participants with certain medical conditions).

In determining if the selection and recruitment of participants is equitable, the IRB takes into consideration the purpose of the research, the setting in which the research will be conducted, whether potential participants will be vulnerable to coercion or undue influence, the selection criteria, participant recruitment and enrollment procedures, and the influence of compensation to participants. The IRB also reviews whether the study imposes fair and equitable burdens and benefits – such that one group of persons does not disproportionately receive the benefits compared to another group assuming only the risks.

The HSP staff and IRB members review this information and confirm the recruitment and selection methodologies are fair and equitable. If the methodologies for recruitment and selection are not fair and equitable, the Investigator will be asked to revise the recruitment and enrollment plan accordingly, as a condition for approval.

Vulnerable Participants

Investigators must provide justification for involving participants belonging to a vulnerable population, such as children, prisoners, pregnant women, persons of disadvantaged social and economic status, persons with diminished decision-making capacity and homeless people. There must be substantial rationale provided in the research plan on the decision to involve a vulnerable population and why a less vulnerable population would not serve the purpose of the research.

When vulnerable populations are used for enrollment, the IRB assesses the additional safeguards proposed by the Investigator to minimize the possible risks and harm to these populations. Though pregnant women are considered vulnerable participants, women of reproductive age shall not be arbitrarily excluded from participation in research. If such women are excluded, the Investigator must provide a rationale for this decision.

Non-English Speaking Participants

Non-English speaking participants shall not be excluded from research due solely to language barriers. The IRB encourages the inclusion of non-English speaking participants and permits such individuals to be enrolled via informed consent in their primary language or the use of the short form consent process consistent with 45 C.F.R. § 46.117(b)(2) and 21 C.F.R. § 50.27(b)(2). See [Section 209](#) on Informed Consent.

207.2 Review of Recruitment Plan, Advertisements and Compensation

Recruitment Plan

The research plan must include a description on all methods of recruitment proposed on a project, including how participants will be identified for recruitment. Guidance on recruitment is available on the Human Studies Program website, as well as sample recruitment materials (e.g., flyers, recruitment script).

Advertisements

The use of advertisements initiates the informed consent process, and, consistent with the consent process, the IRB reviews those materials for coercion and undue influence during recruitment. The Investigator will be asked to revise the advertisement materials accordingly, as a condition for approval, if the submitted materials are found to be coercive or pose undue influence.

Mode of advertisement (flyers, radio, newspaper, or internet), and information contained in the advertisement must be reviewed and approved by the IRB before use. As appropriate, information on where the advertisement material will be posted and/or the specific vehicle of advertisement (i.e., blog, Facebook, type of magazine) may also be reviewed by the IRB before approval.

- **Printed advertisement:** The IRB reviews the final copy. If posting on the internet or newspaper, the IRB may request to receive the copy within its planned placement (i.e., screenshot), when appropriate.
- **Audio and video advertisement:** The IRB may review and approve the script prior to taping to avoid the chance of re-taping due to inappropriate wording. The IRB reviews the final version of the advertisement.

See:

- Guidance on Recruitment, **GUIDE 619: Recruitment Guidance**
- **GUIDE 620: Advertisements Appropriate Language for Recruitment Material**
- **TMP 475: Model Recruitment Flyer**

Compensation

Compensation, defined as remuneration in the form of cash, gift cards, extra credit, etc., intended to compensate human participants for their time and effort, must be reasonable in relation to the level of

effort required to participate in the research. Financial or other forms of compensation are not considered a benefit from research participation, and therefore cannot be described as a benefit of participating in the research in the consent form. The UH IRB does not permit the use of the term “payment” for compensating participants for their time and effort in the research, since participation in research is voluntary. Instead, “compensation” is often the label used in lieu of “payment.”

Although financial compensation can be perceived as an incentive to a participant, it will not be used in the IRB’s analysis of the risks and benefits of a study. For review of non-exempt research, the reviewer or convened IRB evaluates the amount and the form of compensation to ensure that it is:

- Not coercive nor poses undue influence; and
- Equitable in distribution.

If research involves multiple visits in which compensation is given, compensation shall be prorated throughout the duration of the study to provide partial payment to persons who withdraw before completing the entire study. The Investigator shall also take into consideration how participants shall be compensated if certain procedures within a given visit are not completed, either as a result of the Researchers’ determination or the participant’s choice.

All information regarding compensation for participation, including the amount and the schedule of remuneration, must be included in the informed consent.

Lotteries

The UH IRB *prohibits* lotteries, or other types of chance-based drawings. This is because lotteries or other types of chance-based drawings do not compensate each research participant equally for their involvement and, thus, are not equitable in distribution. Such activities may also pose undue influence in inducing participation.

Referral Payments

The UH IRB may allow finder's fees or referral fees that are made in exchange for referrals of prospective participants. Approval is made on a case-by-case basis. Referral fees may be allowed for research in which recruiting potential participants qualified for the research may be difficult or unreliable through more traditional means.

However, the UH IRB *prohibits* bonus payments to those referring participants that are designed to accelerate recruitment by tying payment to the rate or timing of enrollment.

Privacy and Confidentiality

GPM 208

Revised Date: December 18, 2015

In order to approve research, the UH IRB must be satisfied that, “when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of the data⁶⁰” regarding research involving human participants.

The IRB reviews each protocol and proposal, based on the information provided in the Application, and assesses the type and volume of private information to be collected, how the information is collected, and plans for its use, storage and disclosure. When necessary, the IRB will request more information during its review.

The terms privacy and confidentiality are often misinterpreted. Privacy refers to persons and their interest in controlling the access of others to themselves. On the other hand, confidentiality refers to maintenance of the researcher’s agreement with the participant about how the participant’s identifiable private information will be handled, managed, and disseminated.

For a detailed definitions of “privacy” and “confidentiality,” see [Definitions](#).

208.1 Protecting Participants’ Privacy

Privacy may be a concern if, based on their privacy interests, people want to control:

- (i) The time and place where they give information;
- (ii) The nature of the information they give;
- (iii) The nature of the experiences that information is given to them; and/or
- (iv) Who receives and can use the information.

To approve research, the IRB must determine that, where appropriate, there are adequate provisions to protect the privacy interests of potential or active participants, from the screening and recruitment through all stages of research. If the research plan does not include adequate provisions to protect the privacy interests of participants, the IRB will not approve the research as written.

Provisions to protect privacy interests of participants shall include:

- Ensuring that the conditions under which a procedure is conducted or information is collected (e.g., physical locations, telephone contact, mail or email solicitations) provides protections against interactions with participants being seen, overheard, or inadvertently intercepted or viewed.
- Limiting the information being collected to only the minimal amount of data necessary to meet research purposes.

See [Definition](#)s section on “Private Information.”

⁶⁰ 45 C.F.R. § 46.111(a)(7); 21 C.F.R. § 56.111(a)(7)

208.2 Protecting the Confidentiality of Participant Information

To approve research, the IRB must determine that, where appropriate, there are adequate provisions to protect the confidentiality of information related to potential and active participants, throughout the research life, including data analysis and retention of records. It is the responsibility of the Investigator to design studies that maximizes confidentiality measures to avoid unintentional and unauthorized release or other disclosures.

The Investigator must provide a description of the provisions to protect the confidentiality of data in the Protocol Application. The IRB evaluates the information provided in the application during the review process and at convened meetings. The IRB may request more information during its review, depending on the sensitivity of the information being used, maintained or disclosed. In general, the greater the sensitivity of the information, the more stringent the security measures are needed. For more information on what is considered “sensitive information,” see [Definitions](#).

Evaluation of confidentiality measures takes into account the nature, probability, and the magnitude of harms that would be likely to result from an unauthorized release of the collected information. The IRB evaluates the proposed methodologies for maintaining anonymity (e.g., de-identification, coding), storage plans, access restrictions, data security measures (e.g., encryption, password protection) and other pertinent factors in making its final determination concerning the appropriateness and adequacy of confidentiality measures. See the **APP 04: New Research for Initial Approval, Non-Exempt Application** for the information requested by the IRB for this review.

Changes to confidentiality protection measures on an active study shall first be requested for review and approval by the IRB before implementation of these changes. Request for these changes shall be submitted to the IRB using the **APP 05: Modification Request Application**. These changes are reviewed according to the same requirements described above for new research.

Methods to Maintain Confidentiality

Certificates of Confidentiality (CoC)

Where a protocol or proposal involves the collection of sensitive information, the IRB may determine that special procedures are necessary to protect participants from the risks of external investigative or judicial processes (legally mandated release of information for use in federal, state, or local civil, criminal, administrative, legislative, or other legal proceedings). In such situations, the IRB may require that the PI obtain a DHHS Certificate of Confidentiality (CoC) pursuant to Section 241(d) of Title 42 of the U.S.C. Funding through HHS or other federal funding is not a requirement for obtaining a CoC.

When the PI obtains a CoC, the IRB requires that participants be notified about the protections and limitations under the CoC, through the consent document or HIPAA authorization. In order that a participant may weigh the risk of such release of information and not expect more confidentiality protection than is actually provided by the CoC, the IRB requires that the possibility of release for those purposes be stated clearly and explicitly in both the protocol and the consent form. The IRB also requires that any participant enrolled after expiration or termination of a CoC be informed that its protection will not apply to them. Issuance of a CoC is not an endorsement of the research by DHHS.

Data Analysis, Dissemination and Retention

PIs shall consider taking additional safeguards that were not feasible while the research was ongoing, including, but not limited to:

- Removing identifiers (e.g., name, medical record number, student identification number) and coding the information;
- Limiting the number of individuals who have access to participant identifiable information;
- Using secure archival methods or ITS-approved long-term storage services; and/or
- Using ITS-approved encryption software in combination with password protection to database.

PIs are responsible for the secure store of signed consent documents for at least three (3) years after the completion of the research. PIs shall refer to the covered entit(ies)' policies where the research was conducted for retention length on HIPAA authorizations.

Health Information Portability and Accountability Act (HIPAA)

Any research to be conducted by one or more of the medical facilities where UH has a cooperative agreement (i.e., Queens Medical Center, Hawaii Pacific Health, Castle Medical Center) are reviewed under the HIPAA policies of those facilities.

Legal Requirement to Release Private Information

The IRB identifies research that might collect information that could be subject to legally mandated release of information, to the extent that this can be ascertained in advance. When such protocols are identified in advance, the IRB requires that the Investigator notify the participants through language in the consent and HIPAA authorization document(s), as appropriate, of the possibility of legally mandated disclosure. Examples of reportable information may include:

- Child abuse reporting⁶¹
- Sexual assault and rape reporting⁶²
- Reporting to law enforcement when an individual is deemed a danger to others⁶³
- Release under a search warrant or a subpoena (e.g., civil or criminal litigation)⁶⁴

Investigators may seek advice from the IRB or the UH General Counsel on additional questions concerning compliance with these laws.

208.3 Confidentiality Breach – Unauthorized Research of Information

The IRB requires that the Principal Investigator immediately reports to the IRB any possible or actual unauthorized release of information. Individuals outside of the research team, including participants themselves, may also file a complaint or allegation with the Human Studies Program staff if they feel that private identifiable information collected and maintained for research has been released without authority.

⁶¹ Chapter 350, Hawaii Revised Statutes

⁶² Chapters 707-730, Hawaii Revised Statutes

⁶³ Chapter 626-1, Hawaii Revised Statutes

⁶⁴ Chapter 803, Hawaii Revised Statutes

The HSP and its IRBs consider such release or allegations of release as possible non-compliance, and follows the policies and procedures set forth in [Section 203.6](#), **SOP 108: Determining and Reporting Non-Compliance and Protocol Violations**, and **GUIDE 614: Events and Information That Require Prompt Reporting to the IRB** to review and respond to the situation appropriately.

Informed Consent and Assent

GPM 209

Revised Date: December 18, 2015

Informed consent is an ongoing process that begins with the initial presentation of a research activity to a prospective human participant by the Investigator, or a member of the study team, and continues through the end of the research activity. The process of informed consent is fundamental to ensuring the continuous and adequate disclosure of research risks and benefits before agreement to participation.

209.1 Requirement for Informed Consent

Unless waived by the IRB, legally effective informed consent must be obtained from participants or their legally authorized representative(s) as a condition for their research participation. All pertinent requirements in the OHRP's 45 C.F.R. §§ 46.111 and 46.116, and the FDA regulations in 21 C.F.R. §§ 50.20, 50.25, 50.27 and 56.1111 that are applicable to the consent process and the consent document to be used for the research must be satisfied prior to approval of the protocol or proposal.

Assessing research compliance includes the evaluation of informed consent requirements. This is operationalized by:

1. The IRB review of the informed consent process information and document(s) provided by the Investigator.
2. Survey and comparison of signed and dated consents with the IRB-approved consent documents during review process by the Compliance Specialist.
3. Observation of the consent process, performed either as a periodic review function of the Compliance Specialist, or as request by the convened IRB.

209.2 Elements of Informed Consent

Legally effective informed consent includes the eight (8) basic required elements of disclosures and the six additional elements of disclosures specified in 45 C.F.R. 46.116 and 21 C.F.R. 50.25. See **GUIDE 608: Informed Consent Requirements Checklist** for the list of elements of disclosures.

Informed consent requirements for vulnerable and other special populations are addressed in [Section 209.6](#).

209.3 Additional Consent Requirement

New Findings: During the process of obtaining informed consent, the Investigator must provide participants with a statement that significant new findings developed during the course of the research

which may relate to the participants' willingness to continue participation. The Investigator must also provide that information to already enrolled participants.

The UH OGC provides assistance to investigators and the IRB in resolving any conflicts among applicable laws.

1. [Hawai'i Law](#)
2. [HIPAA](#)
3. [HIV Testing/ Research on AIDS](#)
4. [Biospecimen and Biorepositories](#)
5. [International Research](#)
6. [Other Federal Agencies](#)

1. Hawai'i Law

Under Hawai'i Law, there are specific requirements regarding the informed consent process under certain situations.

Hawai'i Law on Health-Care Decisions Act: Under the Hawai'i Uniform Health-Care Decision Act a guardian, an agent, or a surrogate may make health-care decisions on behalf of a patient.^{65,66} If a patient is determined to lack capacity by the primary physician and no guardian, agent, or surrogate has been appointed or reasonably available, the primary physician must make reasonable efforts to locate as many interested persons as practicable. If the interested persons present could not come to consensus, any of the interested persons may seek guardianship through guardianship proceedings.⁶⁷

A health-care decision by a guardian takes precedence over that of an agent.⁶⁸ A surrogate may make health-care decisions if the patient has been determined incapacitated and no guardian or agent has been appointed or reasonably available.⁶⁹

Legally Authorized Representative (LAR): The issue as to who can be an LAR is determined by the laws of the jurisdiction where the research is conducted. Hawai'i law does not specifically address the issue who can consent to participate in research on behalf of another individual. OHRP would consider an individual as an LAR under the Regulations if the law of the jurisdiction where the research is being conducted provides reasonable basis for authorizing an individual to consent on behalf of a prospective subject to participate in the research procedures.⁷⁰

Therefore, if research is conducted in Hawai'i, a guardian, an agent under a power of attorney, or a surrogate of a prospective subject may be the LAR to consent on behalf of the subject to participate in studies if the subject has been determined to lack capacity to consent. If research is conducted outside of Hawai'i, local law determines who may be an LAR.

Guardianship: Under Hawai'i law, "guardian" is defined as a person who has qualified as a guardian of a minor or incapacitated person pursuant to appointment by a parent, spouse, reciprocal beneficiary, or by the court. The term includes a limited, emergency, and temporary substitute guardian

⁶⁵ Haw. Rev. Stat. §§ 327E-2, -3(b), -5(b), -6.

⁶⁶ Haw. Rev. Stat. §§ 327E-1–327E-16.

⁶⁷ Haw. Rev. Stat. § 327E-5(b).

⁶⁸ Haw. Rev. Stat. § 327E-6(b).

⁶⁹ Haw. Rev. Stat. § 327E-5(b).

⁷⁰ Who Can Be a Legally Authorized Representative (LAR) for the Purpose of Providing Consent on Behalf of a Prospective Subject?, HHS, <http://answers.hhs.gov/ohrp/questions/7264> (Jan. 20, 2011).

but not a guardian ad litem.⁷¹ The guardian may consent to medical care for the minor.⁷² This power of the guardian fits the definition of "guardian" under the Regulations. The IRB adopts the policy that a duly appointed guardian under Hawai'i law is a guardian for the purpose of human participant research.

2. Health Insurance Portability and Accountability Act (HIPAA)

If the research involves protected health information (PHI) as defined by HIPAA, then HIPAA authorization may be included in the consent process. HIPAA authorization is an authorization to use or disclose PHI, and must be executed by a separate signature. The UH IRB accepts the HIPAA policies and language provided by the covered entities where the research will be conducted.

3. HIV Testing/ AIDS Research

Public Health System (PHS) Funded Research: If the research is supported financially by the DHHS and includes testing for HIV, the consent documentation must state that identifiable participants will be informed of their results and provided with the opportunity for counseling. The IRB requires this except in cases where it is not required by PHS policy.

4. Biospecimen and Biorepositories

The [NIH Guidance on Data and Tissue Repositories](#) provides pertinent information for investigators who collect data or tissues of participants for repositories, and HSP staff and IRB reviewers who review such protocols.

When such repositories collect individual identifiable health information from participants, the HIPAA privacy regulations in 45 C.F.R. parts 160 and 164 must also be met. This may require either a written HIPAA authorization from the participants or a waiver of authorization by the IRB.

5. International Research

When conducting research in certain communities or social contexts, whether domestically in the U.S. or abroad, it may be inappropriate to document consent by using the standard written and signed consent document. Other consent procedures may be more culturally or socially sensitive and may provide better protection to participants.

Investigators may request IRB to approve a waiver or alteration of some of the mandatory elements of consent (45 C.F.R. § 46.116(d)), or a waiver of documentation of consent (45 C.F.R. § 46.117(c); 21 C.F.R. § 56.109(c)) as appropriate for the research. Such waiver or alteration of consent or documentation of consent must be approved by the IRB before the Investigator utilizes such documentation or process for obtaining consent.

6. Other Federal Agencies

Additional requirement may apply, depending on the sources of support/ funding. See **GUIDE: 617 Other Federal Agencies: - Additional Requirements.**

⁷¹ § 560:5-102. HRS

⁷² § 560:5-208(b)(4), HRS.

209.4 Documentation of Informed Consent – Signature Requirements

Documentation of informed consent refers to a participant, or the participant’s LAR, signing and dating an IRB-approved, dated consent document, which includes the eight basic elements of informed consent and the six additional elements of informed consent, when appropriate (45 C.F.R. § 46.116; 21 C.F.R. § 50.25(a),(b)).

Documentation of Informed Consent – Signature Requirements

When a person agrees to be a participant in a research study, signing the consent document indicates that they have participated in the consent process, and understand the information provided to them. Documentation requirements for informed consent are specified in OHRP in 45 C.F.R § 46.117(a),(b) and FDA 21 C.F.R. § 50.27(a),(b).

In order to approve research, the IRB must determine that informed consent will be appropriately documented, unless the IRB waives documentation under OHRP or FDA regulations (see [Section 209.5](#) below.). If a participant lacks the capacity to consent, then consent for research must be obtained from the participant’s LAR (See [Section 209.6](#) below).

Consent is documented through the use of a written consent document signed and dated by the participant or the participant’s LAR that includes all the required elements of informed consent (see [Section 209.2](#)). Only the IRB-approved informed consent document and/or process may be used, and unless the requirement is waived by the IRB, the consent document must be signed by the participant (or the participant’s LAR), and a copy must be provided to the person who signed the form. FDA regulations required that the signature on the consent form also be dated.

Short Form Consent Process – Additional Signature Requirements

If a short form written consent document (see [Section 209.5](#) on Short Form Consent) with the requirements and process specified in OHRP 45 C.F.R. § 46.117(b)(2) and the FDA regulations in 21 C.F.R. § 50.27(b)(2) is approved for used by the IRB, the following signatures are required to obtain legally-effective consent to participate in the study:

On the short form consent document (translated):

- Participant or the participant’s LAR
- Witness (the interpreter may act as the witness)

On the summary form (English):

- Person obtaining consent
- Witness (the interpreter may act as the witness)

For more detailed information on using the short form consent process see **GUIDE 622: Informed Consent Process for Non-English Speakers and Persons with Limited Literacy**.

Documentation of Informed Consent and Assent for Research Involving Children as Participants

In general, research involving children as participants requires the consent of the parents, or the legally appointed guardian. If the IRB deems that the children participants in a particular research are capable of providing assent, the committee may determine whether and how assent must be documented. See the following for further guidance:

- Children as Participants under [Section 209.6](#)
- **GUIDE 623: Consent for Adults and Assent for Research Involving Children Requirements** (includes children)
- Templates on HSP website for parental consents and assent forms

209.5 Types of Informed Consent Process and Documentation

The IRB requires the use of a full written consent form on research involving human participants. However, federal regulations permit a waiver or alteration of some of the mandatory elements of consent, or a waiver of documentation of consent with prior approval from the IRB.

The following are permitted variations of informed consent processes and documentation requirement:

1. [Written informed consent](#) by the subject or the subject's LAR;
2. [Short form](#) of consent documentation;
3. Waiver or alteration of the consent process; and
 - (a) [Waiver or alteration of informed consent in non-emergency situations](#); or
 - i. [Research involving deception](#),
 - ii. [Research involving children: waiving parental permission](#),
 - (b) [Waiver of informed consent for emergency research](#); or
 - i. [Planned Emergency Research](#),
 - ii. [Emergency Use of a Test Article](#),
4. [Waiver of consent documentation](#) requirements.

Written Informed Consent

In most circumstances, a written consent form, also called long form of consent documentation, is required, and only the current IRB-approved consent document may be used. If the long form of consent documentation is used, the Investigator must satisfy the following procedures⁷³:

1. The consent document must include the required and appropriate additional disclosures;
 - a. Research subject to FDA requirements need to include the additional following disclosures in the consent document:
 - i. Statement noting the possibility that the FDA may audit the records that will be provided to each participant; and
 - ii. Statement that a description of the clinical trial will be available on

⁷³ 45 C.F.R. § 46.117(b)(1).

ClinicalTrials.gov as required by U.S. law.

2. The participant or the participant's LAR signs the consent document;
3. The Investigator must give the participant or the participant's LAR adequate opportunity to read the consent document before he/she signs; and
4. The Investigator (or person obtaining informed consent) gives a copy of the consent document to the person signing the consent document.

If the majority of the potential participants to be enrolled do not speak English, the consent document shall be translated to the primary language of that majority and provided to those potential participants (see Short Form below for alternate option).

When necessary, the written consent form shall be read to the subject or the subject's LAR.⁷⁴ The original consent document shall be maintained by the Investigator.

Short Form of Consent Documentation

When only a small portion of potential participants will not be able to understand the consent document in English, short form consent documentation may be used for non-English speaking potential participants.

If the short form of consent documentation is used, the Investigator must satisfy the following procedures⁷⁵:

1. The short form of consent document states that the required and appropriate additional disclosures have been orally presented to the participant or the participant's LAR;
2. A written summary must embody the required and appropriate additional disclosures;
3. The Investigator orally presents the required and appropriate additional disclosures to the participant or the participant's LAR;
4. A witness must be present during the oral presentation;
5. If the participant or the participant's LAR does not speak English, the witness must be conversant in English and the language that the participant or the LAR speaks;
6. The participant or the participant's LAR signs the consent document;
7. The witness signs the consent document and a copy of the written summary;
8. The person obtaining the consent signs the copy of the written summary;

A copy of the signed consent document and the signed written summary is given to the participant or the participant's LAR.

Waiver or Alteration of Informed Consent Requirements

FDA regulations do not provide for a waiver or alteration of the informed consent process. The only exceptions to the informed consent requirement are for specified situations of emergency use of a test article (see [section here](#), and **SOP 121: Emergency Use of a Test Article**), and waiver granted for planned emergency research (see **SOP 122: Planned Emergency Research**, and **GUIDE 624: Planned Emergency Use Research**). Aside from emergency research, the remainder of this section's discussion below applies only to non-FDA-regulated research:

⁷⁴ 45 C.F.R. § 46.117(b)(1).

⁷⁵ 45 C.F.R. § 117(b)(2).

1. Waiver or Alteration of the Consent Process
 - a. [Non-Emergency Situation](#)
 - i. [Research Involving Deception](#)
 - ii. [Waiver of Parental Permission/ Guardian Consent](#)
 - b. [Emergency Research](#)
 - i. [Planned Emergency Research](#)
 - ii. [Emergency Use of a Test Article](#)
2. [Waiver of Consent Documentation](#) (“waiver of signature”)

Waiver or Alteration of Informed Consent in Non-Emergency Situations

Under OHRP 45 C.F.R. §§ 46.116(c) (d), and (e), IRBs have authority to alter or waive the requirement to obtain informed consent.

There are circumstances in which the IRB may approve research without meeting all of the required elements of informed consent. The IRB may approve the alteration or waiver of informed consent requirements if the Investigator demonstrates the following⁷⁶:

1. The research involves no more than minimal risk to the participant;
2. The waiver or alteration will not adversely affect the rights and welfare of the participants;
3. The research could not practicably be carried out without the waiver or alteration; and
4. Whenever appropriate, participants will be provided with additional pertinent information after participation.

Note: The criterion, "[t]he research could not practicably be carried out without the waiver or alteration," means that the circumstances make it impracticable to carry out the research if informed consent must be obtained.⁷⁷ It does not mean that the circumstances make it impracticable to obtain consent.

Approval for alteration or waiver of informed consent requirement may also be granted if the project meets the criteria under 45 C.F.R. § 46.116(c) for research on certain public benefit or service programs, but such situations are rarely applicable.

To request a waiver or alteration of the informed consent process, the Investigator must address each of the criteria under 45 C.F.R. § 46.116(c) or (d) for a given research protocol or proposal in the **APP 04: New Research for Initial Approval, Non-Exempt Application**.

The IRB must find and document that all regulatory criteria under 45 C.F.R. § 46.116(d) (OHRP) are met and that the research is not subject to FDA regulations for it to approve an alteration or waiver of informed consent process.

Special Considerations for Research Involving Deception

In research involving deception, the Investigator may, with protocol-specific justification, request an alteration of the consent process. The IRB may approve the research, including the request to alter the requirement for informed consent if the Investigator demonstrates that deception or incomplete disclosure is necessary and addresses concerns relating to participant protection.

⁷⁶ 45 C.F.R § 46.116(c), (d).

⁷⁷ Id.

Use of a debriefing form and specific debriefing procedures is required with the protocol or proposal submission for IRB review and approval before its use. Debriefing forms will be considered as informed consent documentation, and only participants whose signatures are obtained through the debriefing form are considered consented participants.

See guidance documents on informed consents and **TMP 465** for debriefing form template.

Research Involving Children: Waiver of Parental Permission/Guardian Consent

Research regulated by the FDA is not eligible for waiver of parental permission, except for the use of an FDA test article meeting the emergency exception (see below).

The IRB may consider a request for a waiver or partial waiver of parental permission for minimal risk research to be conducted in a classroom (exempt category 1) or in situations where the child is a truant (e.g., runaway, refugee).

The IRB may waive parental permission by determining that the criteria for waivers or alterations are met. However, research is ordinarily not suitable for a waiver of parental permission if it involves any of the following issues:

1. Parental political affiliations or beliefs
2. Mental or psychological problems
3. Sexual behavior or attitudes
4. Illegal, antisocial, or self-incriminating behavior
5. Appraisals of other individuals with whom the minor has a familial relationship
6. Relationships legally recognized as privileged (lawyers, doctors, clergy), and
7. Religious affiliations or beliefs.

If the IRB waives the requirement for parental permission, the committee may require an alternative mechanism to protect child participants (e.g., appoint a qualified child advocate).

Waiver of Informed Consent in Emergency Research

Planned Emergency Research

“Planned emergency research” refers to research planned for emergency settings, including the planned use of a test article. Such type of research requires an extensive approval process, including FDA approval, prospective IRB review, and approval and consultation with representatives of the communities where the research will be conducted and from where participants will be recruited.

Investigators must submit a protocol application including a description of the informed consent process or a request to waive informed consent; often in emergency settings it is not possible to obtain informed consent from a potential participant when there is insufficient time and an LAR is not available.

The IRB may waive the requirement for informed consent in accordance with an exception under 21 C.F.R. § 50.24 (FDA) or 45 C.F.R. § 46.101(i) or 45 C.F.R. § 46.116(f) (OHRP), depending on whether or not the research is subject to FDA regulation, given that all required IRB determinations under these provisions can be made. Under these regulations, the IRB may allow planned research in an emergency setting without the informed consent of the participants or their legally authorized representatives in a limited class of emergent situations where the participant is in need of an emergency experimental

intervention, but cannot provide informed consent due to a life-threatening medical condition and there is not sufficient time to obtain consent from the participant's legally authorized representative. This waiver does not apply to research involving fetuses, pregnant women, neonates (subpart B of 45 C.F.R. part 46), or prisoners (subpart C of 45 C.F.R. part 46).⁷⁸

In addition, advance notice of such planned emergency research protocols will be provided to the OHRP pursuant to 45 C.F.R. § 46.101(i).

See also:

- [Informed Consent Requirements in Emergency Research](#) [OHRP]
- [Exception from Informed Consent for Studies Conducted in Emergency Settings](#) [FDA]
- **SOP 122: Planned Emergency Research**

Emergency Use of a Test Article

Emergency Use of a Test Article refers to the use of a test article on a human patient in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval. Unlike planned emergency research, emergency use of a test article does not constitute research under the HHS regulations. Therefore, the patient may not be considered a research participant, and any data derived from the use may not be included in any report of research activities.⁷⁹

The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each participant, the participant's LAR if the participant remains incapacitated, or a family member if such an LAR is not reasonably available, of⁸⁰:

- The participant's inclusion in the study, the details of the research, and other information contained in the informed consent document; and
- The right to discontinue participation in the research at any time without penalty or loss of benefits to which the participant is otherwise entitled.

If an LAR or a family member is told about the research and the participant's condition improves and regains capacity for informed consent, the participant is to be informed as soon as possible. If a participant is entered into an emergency use situation with waived consent and dies before an LAR or a family member can be contacted, information about the usage is to be provided to the participant's LAR or family member, if feasible.

See **SOP 121: Emergency Use of a Test Article** for more details on and procedures to implement this type of procedure.

Waiver of Documentation of Consent – (“waiver of signature”)

In some situations, a written consent form is used, but the participant or the participant's LAR is not required to sign the consent form. Per OHRP and FDA regulations⁸¹, the IRB may waive the requirement to obtain written documentation of informed consent. A waiver of documentation of consent, however, does not preclude the requirements of the consent process.

⁷⁸ Waiver of Informed Consent Requirements in Certain Emergency Research, 61 Fed. Reg. 51,531 (Oct. 2, 1996).

⁷⁹ 45 C.F.R. § 46.103(b) (2014); [HHS on Emergency Care](#), *supra* note 198.

⁸⁰ 61 Fed. Reg. 51,532.

⁸¹ OHRP (45 C.F.R. § 46.117 (c)) and FDA regulations (21 C.F.R. § 56.109(c))

Even if a waiver of documentation is granted by the IRB, the Investigator must still provide the participant with all of the necessary information described in [Section 209.2](#). The Investigator is required to develop a complete and appropriate consent process, through an information sheet, or through an oral script in a language understandable to the participants. In all cases in which the requirement for documentation of consent is waived, the IRB may require the PI to provide participants with the written consent document with an option to sign the consent document, or with a written statement regarding the research.

Approval of a waiver of documentation is granted when the IRB finds that the protocol-specific justification for waiving documentation satisfies regulatory criteria. Specifically, the request for waiver must meet one of the following regulatory criteria:

- (a) Under OHRP (45 C.F.R. § 46.117(c)(1) only, the IRB must find and document either:
 - (1) the only record linking the participants and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality. Each participant will be asked whether he/she wants documentation linking the participant with the research, and the participant's wishes will govern; or
 - (2) the research presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context;

OR

- (b) For research subject to OHRP *and* FDA regulations, the IRB must find and document that:
 - (1) the research involves no more than minimal risk to participants; and
 - (2) involves no procedures for which written consent is normally required outside of the research context.(45 C.F.R. § 46.117(c)(2), 21 C.F.R. § 56.109(c)(1)).

IRB approval to waive consent documentation must be obtained prior to research implementation.

See **GUIDE 625: Findings for Waiver or Alterations of Consent Requirements** on the HSP website.

Waiver or Alteration of HIPAA Authorization

In order to waive or alter a HIPAA authorization, the PI must provide sufficient information on which the IRB can determine that it meets the following three (3) findings specified by the Privacy Rule (45 C.F.R. § 164.512(i)(2)(ii):

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

3. The research could not be practically conducted without access to and use of the protected health information.

209.6 Consenting Vulnerable and Other Special Populations

Special attention is given to protecting the welfare of vulnerable participants, such as children, prisoners, pregnant women, human fetuses and neonates, individuals with decisionally-impaired capacity, or economically or educationally disadvantaged individuals (45 C.F.R. § 46.111(b) and 21 C.F.R. § 56.111(b)). In fact, there are specific regulations governing research involving pregnant women, fetuses, and neonates (45 C.F.R. 46, Subpart B), prisoners (45 C.F.R. 46, Subpart C), and children (45 C.F.R. 46, Subpart D and 21 C.F.R. 50 Subpart D).

Children as Research Participants

Children, with regards to human participant research, are individuals who have not attained the legal age for consent to treatment or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. In Hawaii, one under 18 years of age is considered a “child,” and may not legally give consent, although there are certain exceptions for emancipated and self-sufficient minors.

Parental Consent: As such, parental permission must be provided by at least one parent or guardian in non-exempt research involving children. The documentation of parental permission is similar to that of informed consent for the general population. The IRB may waive the requirement of documentation if it finds the waiver is appropriate under 45 C.F.R. § 46.117. See **GUIDE 623: Consent and Assent for Research Involving Children**.

Assent: The IRB determines whether child assent is required for a study if the children are capable of providing assent.⁸² In assessing whether children are capable of assenting, the IRB takes into account the age, maturity, and psychological state of the children involved, and the complexity of the proposed study procedures.⁸³ The IRB also considers the degree of risk involved in the procedures. This judgment may be made for all children to be involved in a particular protocol, or for each child, as the IRB deems appropriate.

The IRB may waive the requirement of child assent in the following situations⁸⁴:

1. when the IRB finds that the capability of some or all of the children is so limited that they cannot reasonably be consulted;
2. the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, or
3. consent may be waived in accordance with 45 C.F.R. § 46.116.

Individuals with Diminished Decision-Making Capacity as Research Participants

All adults, regardless of their diagnosis or condition, will be presumed competent to consent to

⁸² 45 C.F.R. § 46.408(a).

⁸³ See *id.*

⁸⁴ 45 C.F.R. § 46.408(a); OHRP [Children FAQ](#), at Question 13.

participate in research unless there is evidence that their reasoning or judgment is impaired. Mental disability alone will not disqualify a person from consenting to participate in research; rather, specific evidence of the individual's incapacity to understand and make a decision will be required.

Assessing Capacity: For individuals whose capacity appears diminished, there must be an assessment of the participant's capacity to consent to participate before the enrollment of the participant in the study. The IRB may request that an assessment be undertaken by a qualified mental health professional whose training and credentials are suitable for the assessment, given the nature of the participant's illness and the study. The assessor must be independent from the study to avoid the appearance of conflicts of interest. The research plan must indicate how the capacity will be assessed. Factors to be considered in the assessment include:

- the ability of the prospective participants to understand the research, and its risks and benefits;
- the prospective participant's medical condition; and
- the voluntariness of the participant's consent in the light of the subject's ability to assess the provided information and to make informed decisions.

Consent: If the prospective participant lacks the capacity to consent to participate in a research study, consent can only be given by an individual who is the participant's legally authorized representative (LAR) under the jurisdiction where the research is to be conducted. Officials of the institution where the incapacitated patient resides are not generally considered as appropriate participant representatives because their supervisory duties may give rise to conflicting interests. In that case, use of a participant advocate is recommended.

If a participant's capacity may become impaired during the course of a study, the protocol and the consent form will detail the specific mechanisms for monitoring the participant to determine if there is a decrease in capacity.

Assent: The IRB may require the Investigator to obtain assent from the participant and, if so, will determine whether the plan for assent is adequate.

Non-English Speakers and Persons with Limited Literacy

The Regulations require that informed consent information must be presented in a language understandable to the subject and, in most situations, in writing.⁸⁵ When subjects do not speak or read English, the requirements on documentation of the consent process can be met in two ways⁸⁶:

1. Consent documents written in the subject's preferred language with all the necessary elements for legally effective informed consent; or
2. An oral presentation of informed consent information in conjunction with short form written consent.

See **GUIDE 622: Consent Process for Non-English Speakers and Persons with Limited Literacy.**

209.7 Consent Templates and Guidance

⁸⁵ 45 C.F.R. §§ 46.116, 46.117.

⁸⁶ OHRP, *Obtaining and Documenting Informed Consent of Subjects Who Do Not Speak English*, HHS (Nov. 9, 1995), <http://www.hhs.gov/ohrp/policy/ic-non-e.html> [hereinafter *OHRP Guidance on Non-English Speaker*].

The [Human Studies Program website](#) provides various consent form templates which address the required elements of informed consent, as well as providing language for various situations (e.g., genetic testing, curriculum studies) and settings (e.g., anonymous online surveys) in which certain additional information may need to be provided to participants. Assent templates are also provided on the website for research involving children.

Guidance on consent documentation and process, including discussion on appropriate reading level and length for the various types of consent or assent, are also available on the website.

209.8 IRB Review of the Consent Process and Documentation

PIs shall refer to the **GUIDE 601: Investigator's Handbook** for information regarding the development of an informed consent process and method of documentation appropriate to the type of research and study population.

PIs must submit for IRB review any consent document(s) and explanation of the circumstances under which informed consent will be sought for initial review, and whenever a modification to the consent process or documents is requested.

The New Research Application needs to include information necessary for the IRB to evaluate whether the informed consent process will be conducted appropriately given the research-specific situation (e.g., level of risk, inclusion of vulnerable population) and protects its participants adequately. Approval of informed consent process and documentation for non-exempt research is contingent upon the following four criteria:

1. Prospective participants or their LAR are given sufficient opportunity to discuss concerns and decide whether to participate in the research;
2. The possibility of coercion or undue influence are minimized;
3. The information provided about the research will be in a language that is understandable to the participant or the LAR; and
4. That no informed consent, whether oral or written, may include any exculpatory language, through which the participant or their LAR is made to waive, or appear to waive, any of the participant's legal rights, or which releases or appears to release the Investigator, sponsor, or institution from liability for negligence.

Any new information that could impact participants' risk (e.g., adverse event) or procedure changes shall be submitted as a modification request, along with the consent documents appropriately updated and submitted for IRB review.

The IRB needs to be aware of the relationship between the person(s) who will recruit potential participants and obtain consent and the potential participant, to determine whether that the relationship sets the participants at risk for coercion and undue influence. The IRB requires that the circumstances of the consent process be culturally and linguistically appropriate for the intended participants.

The IRB also reviews any direct advertising (e.g., newspaper, TV or radio ads, posters, flyers, letters or postcards, emails, postings on bulletin boards/ internet/ web), since it is considered by the FDA "to be the start of the informed consent and subject selection process." In order to approve advertisements, the IRB must determine that the direct advertising is not unduly coercive and does not promise a certainty of

cure or favorable outcome or other benefits beyond what is outlined in the consent and the protocol or proposal.

See

- [GPM Chapter 207](#)
- **GUIDE 620: Advertisements: Appropriate Language for Recruitment Material.**

Considerations during Full-Board Review

The IRB determines that all basic, and all additional elements of disclosure appropriate to the research, are included in the consent process. All the relevant requirements in OHRP in 45 C.F.R. §§ 46.109(b) and 46.116, and in the FDA regulations in 21 C.F.R. §§ 56.109(b), 50.20 and 50.25, that are applicable to the consent process and the consent document, must be satisfied for IRB approval.

Upon IRB approval, the consent form document must include the approval date and expiration date. If the consent form document was approved between review periods, the expiration date on that consent form shall reflect the expiration date provided in the previous continuing review (or initial review) approval letter.

209.9 Observation of the Consent Process

As part of the IRB oversight responsibilities, the IRB may require that an HSP staff member or an outside third party observe the consenting of research participants to determine:

- Whether the informed consent process has been appropriately completed and documented;
- Whether the participant has had sufficient time to consider study participation, that no coercion has been used by the consenting staff; and
- That the information presented to the participant reflects the content of the consent form and is conveyed in understandable language.

The IRB may require that one or more informed consent process situations be observed for selected protocols or proposals. IRB considerations used to choose such protocols include:

- High risk studies
- Studies that involve particularly complicated procedures or interventions
- Studies involving potentially vulnerable populations (e.g., ICU patients, children)
- Studies involving study staff with minimal experience in administering consent to potential study participants, or
- Situations when the IRB has concerns that the consent process is not proceeding well.

See:

- **SOP 110: Quality Improvement Activities**
- **WKSH 322: Consent Observation Checklist**
- **WKSH 353: Post Approval Monitoring Checklist for Biomedical, Clinical Research**
- **WKSH 354: Post Approval Monitoring Checklist for Social & Behavioral Sciences Research**

Knowledge of Human Research Protection

GPM 210
Revised Date: December 18, 2015

210.1 Education and Training of Individuals Responsible for Human Research

Education and training are provided to all individuals involved with the human research protection program. This policy manual details the education requirements for IRB members and HSP staff. Education requirements for Investigators and key personnel on the research team are specified in the **GUIDE 601: Investigator's Handbook** and the [Human Studies Program Learning Commons website](#). The HSP works with the UH campuses and departments, John A. Burns School of Medicine, and other institutions, to offer comprehensive education to the UH research community.

Education Unit (EU)

The HSP and the ORC has full- and part-time staff, responsible for developing and providing education for IRB members, HSP staff, and the research community regarding human research protections.

Evaluation of Qualifications

In addition to receiving training on human participant research protections, the IRB members and HSP staff are reviewed periodically to evaluate their understanding of the HRPP (i.e., ethical principles, policies and procedures, and regulations and requirements).

HSP staff qualifications are assessed at least annually or as needed to ensure a high level of commitment to the HRPP.

IRB member qualifications are reviewed by the HSP Director during the recruitment process, and IRB members are officially appointed by the IRB Chair and HSP Director. IRB members, including IRB Chairs, are evaluated annually to ensure that their service on the IRB contributes to the ethical and regulatory review of research at UH. Feedback from these evaluations is communicated to each IRB Member and each IRB Chair. Investigators at UH are evaluated according to individual institution, school, and department policies.

The Quality Improvement Unit (QIU) evaluates the effectiveness of the education provided. Results of the QIU assessments are used to revise the content of educational materials, improve delivery methods and identify appropriate audiences, and to communicate with the other components of the HRPP about updating their education and training.

See **SOP 110: Quality Improvement Activities** for the human research protection program.

Contributing to the Improvement of Expertise

New IRB members and HSP staff receive orientation to the UH HRPP, including written and electronic IRB reference material. All IRB members and HSP staff receive regular, continuous training and education. Opportunities for continuing education in human research protections are announced on an ongoing basis. IRB member and HSP staff attendance is encouraged at regulatory and professional meetings and conferences, and for web seminars at UH and in the greater community. The HSP also supports and encourages professional certification for qualified HSP staff.

Educational Materials and Resources

The UH research community, IRB members, HSP staff and other individuals involved in the protection of human research participants have access to a plethora of educational material, available online and in printed format, or offered as lectures or workshops.

They include, among others:

- The HSP website, with links to the UH Human Studies Program General Policy Manual, the Investigator's Handbook, instructional information, FAQs, educational material, document templates, forms and guidance.
- Access to required and elective training through the interactive online Collaborative Institutional Training Initiative (CITI) Course: Human Subjects Research, GCP, working with vulnerable populations, and Information Privacy and Security/ HIPAA.
- The ORC website
- The eProtocol electronic protocol submission system, providing instructional text and explanation within the application.
- eProtocol training
- Links to pertinent federal regulations, codes of ethics, policies and procedures of collaborating non-UH research institutions.
- Past presentations on human research protection.

Additional education and training are provided through seminars, workshops, classes and training courses offered by the HSP and other [HRPP components](#).

210.2 Required Training in Human Research Protections

Completion of human subject training by all staff working on a research protocol or proposal (all Investigators and other study personnel, including all individuals who are responsible for the design, conduct, data analysis or reporting) is one of the requirements for research approval by the IRB. Principal Investigators, as part of the protocol submission process, acknowledge their obligation to protect the rights and welfare of research participants. See **APP 04: New Research for Initial Approval, Non-Exempt Application** "Obligations" section.

UH provides access to the required training through an interactive online tutorial - CITI (Collaborative Institutional Training Initiative) Course. CITI offers a basic (initial) course and then a refresher course, which must be taken every three years. The required training has been customized for different learner groups (biomedical and social & behavioral sciences Investigators, Investigators conducting exempt research, IRB members, and HSP staff).

Once required courses are completed, a certificate of completions for each completed courses can be saved or printed from the CITI website. Individual Investigators must maintain their own records or training. It is the responsibility of the Principal Investigator to ensure the completion of the required training by all study personnel, including all persons who are responsible for the design, conduct, data analysis or reporting, and to have all certificates of completions available for audits.

The HSP Director maintains record on training of all staff and IRB members, including completion and expiration dates. CITI sends an email reminder to CITI subscribers of upcoming expiration on their training.

IRB Member and HSP Staff Required Training

CITI Training	Biomedical/ Cooperative IRB Members and Chairs	Social & Behavioral Sciences IRB Members and Chairs	HSP Reviewing Staff (HSP Director, IRB Coordinators, Compliance Specialist)
Human Subjects Research – basic/ refresher	<i>Cooperative and Biomedical IRB Members</i>	<i>Social and Behavioral IRB Members</i>	<i>IRB Administrators</i>
Supplemental Modules <ul style="list-style-type: none"> • Children (Biomed Focus) • Prisoners (Biomed Focus) • Pregnant Women, Fetuses, and Neonates (Biomed Focus) • Children (Social & Behavioral Focus) • Prisoners (Social & Behavioral Focus) • Working with Elementary & Secondary Schools 	<i>Optional, but encouraged:</i> <ul style="list-style-type: none"> • <i>Children (Biomed Focus)</i> • <i>Prisoners (Biomed Focus)</i> • <i>Pregnant Women, Fetuses, and Neonates (Biomed Focus)</i> 	<i>Optional, but encouraged:</i> <ul style="list-style-type: none"> • <i>Children (Social & Behavioral Focus)</i> • <i>Prisoners (Social & Behavioral Focus)</i> • <i>Working with Elementary & Secondary Schools</i> 	<ul style="list-style-type: none"> • <i>Children (Biomed Focus)</i> • <i>Prisoners (Biomed Focus)</i> • <i>Pregnant Women, Fetuses, and Neonates (Biomed Focus)</i> • <i>Children (Social & Behavioral Focus)</i> • <i>Prisoners (Social & Behavioral Focus)</i> • <i>Working with Elementary & Secondary Schools</i>
Information Privacy and Security (IPS)	<i>Cooperative and Biomedical IRB Members</i>	<i>Social and Behavioral IRB Members</i>	<i>IRB Administrators</i>
Good Clinical Practice (GCP)	<i>Good Clinical Practice Course, US FDA Focus</i>	<i>N/A</i>	<i>Good Clinical Practice Course, US FDA Focus</i>

Supplemental human research protection training sessions for the HSP staff are held during HSP staff meetings, and held during convened-IRB meetings for IRB members. These training sessions are not required, but are mainly conducted to enhance better understanding of regulations and policies on human research protection.

If an HSP staff or IRB member does not meet the CITI training requirements, the staff or member may not review any study.

Investigator Required Training

UH requires that Principal Investigators and other key personnel involved in the design or conduct of a project, including those projects that may be deemed exempt under 45 C.F.R. 46, provide evidence of training and qualifications by submitting relevant documentation as requested by the sponsor, IRB, or regulatory authorities.

Investigators must complete the required training before submitting an application for IRB review. The HSP staff checks the Investigator's training when prescreening the Investigator's application for review. If an Investigator does not meet the training requirements, the IRB will not approve the Investigator's application.

PIs must submit to the IRB the names of all key research personnel (i.e., individuals involved in the development of the research design, collection of participant consent, participant data, and analysis of identifiable research data) with their training completion information in the eProtocol system. PIs must submit a modification for new personnel acquired during active review period and secure IRB approval before the new personnel can be involved in the research.

See the HSP website for detail in [training requirements on Investigators and key personnel](#) involved in human participant research.

Education and Outreach

GPM 211
Revised Date

The UH has numerous vehicles for communication and education to increase public awareness and educate potential research participants on human subjects research, as well as mechanisms for receiving feedback from participants and communities.

211.1 Online Resources and Educational Materials

Along with the Human Studies Program website (<https://manoa.hawaii.edu/researchcompliance/human-studies>) as described in Section 210.1, there are a number of other UH resources on HRPP:

- [RCMI Multidisciplinary and Translational Research Infrastructure Expansion \(RMATRIX\)](#), hosted by the John A. Burns School of Medicine, provides research support for UH clinical Investigators conduct human participant research.
- The [Social Science Research Institute \(SSRI\)](#) serves as the sponsored research division of the College of Social Sciences. They provide administrative support for pre- and post-award activities related to extramural research and training grants and contacts in the College.
- **SONA** is the participant pool platform often utilized by faculty and student researchers conducting human participant research in the Department of Psychology and the Department of Communicology.
- As steward to the university's institutional data, the [UH Institutional Data Governance Program](#) provide training such as Information Security Awareness Training

211.2 Participant Research Inquiries

Using a database of studies, HSP staff may provide PI contact information to prospective and enrolled participants for active research being conducted at UH.

The Human Studies Program website also provides a list of resources regarding participant's rights and other information pertinent to participants, including contact information of appropriate individuals or entities.

211.3 Outreach

Community-Based Research

Increasingly research design involves members of the community. Community members, organizations, and researchers may work together in all aspects of the research process. Depending on the level of involvement, community-based research ranges from community-engaged research to community-based participatory research (CBPR).

Community-engaged research encourages the nonacademic researchers to participate in and influence research. It is done with communities, not on communities. This approach to research recognizes the strengths of the community and builds on those strengths.

CBPR actively involves the community in the research process. Research development can take years to reach most clinics, doctors' offices, or community health centers, not to mention disadvantaged communities. CBPR seeks to directly benefit the public in a process that

- includes community members, organizations, and researchers in all aspects of the research process;
- enhances the understanding of mutually-interested public health issues; and
- puts findings into action to improve the health and well-being of community members.

In CBPR, community members are also involved in informing others about the research and promoting the use of the research findings. This involvement can help improve the health and well-being of the community by putting new knowledge in the hands of those who need such information to make changes.

Community-based research presents challenges for both researchers and IRBs, such as whether the community partners are subjects, members of the research team, or both; what training is required; how to manage conflicts of interest; when it is appropriate to establish community advisory boards and how to solicit their input in ongoing involvement; whether and what kind of collaborative agreements are required; and how or when to disseminate results. In many cases it will not be necessary or appropriate to apply the same policies and requirements to community partners as those applied to UH Investigators. For example, it may be more appropriate for the Investigator to provide training tailored to the role of community partners (e.g., church members and community advocates) than through the completion of online CITI modules.

Because there is a continuum of involvement between researchers and communities, a single set of guidelines is not appropriate. One thing is common though: the fact that Investigators interact with the community that goes beyond interactions with individual potential research subjects. So Investigators shall consider the risks and benefits to the entire community, not just individual subjects. In addition to those principles for human subjects research, researchers conducting community-based research shall follow best practices for respectful and productive relationships. The following are guidelines for community-based research depending the level of involvement with the community.

1. In conducting community-engaged research, the Investigators shall
 - (a) be aware and respectful of community interests that go beyond those of individual potential research subjects;
 - (b) identify potential community stakeholders as well as individual research subjects;
 - (c) inform the community stakeholders and potential research subjects about the research; and

- (d) invite feedback regarding concerns about the research from community stakeholders and individual potential research subjects.
2. In addition to the above principles, the Investigators conducting basic community-partnership research shall
 - (a) respect the community partner's interest in the project and be open to ways that the community may want to use the information.
 - (b) disseminate research findings to both community stakeholders and individual research subjects.
 3. In addition to all above, the Investigator conducting CBPR shall
 - (a) have the research topic addressing a community-defined need, question, or problem, and strive to combine knowledge with action to achieve necessary changes;
 - (b) recognize the research as a partnership and be open to the guidance of community insight and experience;
 - (c) balance the decision-making power between the researchers and the community participants to a point that is mutually acceptable;
 - (d) strive to communicate with community partners openly and clearly so to understand each other's needs and interests;
 - (e) recognizes race, ethnicity, class, and other aspects of culture matter and talk openly about these issues;
 - (f) obtain feedback from all stakeholders in the partnership, with the goals of continuously improving the partnership; and
 - (g) realize that partnerships can dissolve and plan a closure process.

211.4 Evaluation

Evaluation is an ongoing process. The various departments within UH's HRPP evaluate their impact on an ongoing basis. The Human Studies Program website allows prospective and active participants, and their communities to provide feedback by submitting comments either through the website or by emailing the HSP office directly.

All HSP staff, IRB members and Chairs are requested to report both positive and negative feedback about all HRPP outreach activities to the Quality Improvement and Education Units, who tract this input in order to make changes to improve outreach activities.

Addressing Research Participants' Concerns

GPM 212

Revised Date: December 18, 2015

212.1 Written Materials

Participants or their representative can contact the Human Studies Program office⁸⁷ or the Principal Investigator if they want to discuss concerns, obtain information, or offer input regarding a study or human subjects research in general. Contact information for HSP and the PI are found on the IRB-approved informed consent document. They also can contact the IO or the OHRP about such matters. If a complaint about the HSP or the IRB is filed with the IO, the IO will investigate the complaint, with the help of the HSP Director and IRBs as appropriate.

Usually the HSP addresses the participants' rights in the research while the PI addresses the content of the study. The HSP consent templates and UH IRB-approved consent forms include that contact information. The HSP also post its contact information and information on being research participants on its website.

Consent Form Requirements

The IRB requires that all consent form documents include information on how to contact the Investigator(s) conducting the research study. Participants are instructed to call or email the Investigators if they have any questions about the research or if they believe they have suffered a research-related injury, and contact the Human Studies Program/UH IRB if they have questions about their rights as a research participant.

Each consent form must include the telephone number for the IRB. The IRB contact information affords current or past research participants or their designated representatives a means to contact an informed individual who is independent of the research team. The IRB also serves as a conduit for receiving information from any party who is not satisfied with the manner in which a study is (or was) being conducted, or if any party has any concerns, complaints or general questions about research the rights of research participants.

[Consent form templates](#), found on the Human Studies Program website, include instructional text and verbatim language for the inclusion of the Investigator's contact information and IRB telephone numbers under the consent form heading "Questions." The Human Studies Program/UH IRB's email address is included in the consent form template to also allow for written communication.

Recruitment Material Requirements

All recruitment materials must include the appropriate contact information for the Investigator(s) conducting the research. The IRB reviews all recruitment materials, and the addition of IRB contact information is required when appropriate.

⁸⁷ The HSP posts its contact information at its website <http://manoa.hawaii.edu/researchcompliance/human-studies>.

See **GUIDE 619: Recruitment Guidelines** for appropriate language and content to include in recruitment material.

Telephone (Screening) Scripts

Telephone scripts are often used to screen prospective participants. Like the consent forms, telephone scripts must include contact information for the IRB and the Investigator(s). This information provides prospective participants ways to ask the Investigators and the IRB questions, communicate concerns and complaints, provide input and acquire information.

As with recruitment materials, the IRB reviews all telephone or screening scripts and materials and must approve them before use.

212.2 Responding to Participant Concerns

Concerns from research participants, prospective and current, are followed up by the HSP Director who contacts the individual to gather more information. As appropriate, concerns may be forwarded to the Compliance Specialist. Minor concerns are generally resolved by any HSP staff member via phone call.

More complicated concerns are followed up by the HSP Director with the relevant IRB Chair and others in the ORC. If necessary, the Principal Investigator may be contacted for concerns regarding a particular Investigator, research staff, or the research itself.

See **SOP 118: Addressing Concerns of Research Participants** for procedures on how participant concerns and questions are handled.

212.3 Website Information for Participants

The HSP website includes participant outreach information addressing the general rights of research participants and provides links to various research resources. Additionally, the website has a local number listed for participants to ask questions, offer input, raise concerns or complaints about research, a research-related injury, or any question about the rights of research participants.

Investigational or Unlicensed Test Articles – Research with Drugs, Devices or Biologics

GPM 213
Revised Date: April 21, 2016

The FDA regulates clinical investigations (research) “that support applications for research or marketing permits for projects regulated by the Food and Drug Administration, including foods, dietary supplements that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, biological projects for human use, and electronic products.”⁸⁸

Therefore, such research must be conducted in accordance with FDA requirements for informed consent and IRB review, regardless of funding source or sponsor.

The following GPM focuses on:

- Research using investigational (unapproved) drugs, devices, or biologics
- Research with FDA-approved drugs, approved/ cleared devices, or licensed biologics (aka “commercially available”)
- Sponsor-Investigator research
- Handling of investigational drugs, devices or biologics
- Emergency, humanitarian, or compassionate use of investigational drugs, devices, or biologics

Registration Requirements

Clinicaltrials.gov: Applicable clinical trials, as defined in 42 U.S.C. § 282(j)(1)(A), must be registered on ClinicalTrials.gov; clinical trial information must be submitted for inclusion in the clinical trial registry databank (Public Health Service Act, section 402(j) and a corresponding statement added to the consent form (see **GUIDE 606: Consent Form Guidance**). The following are considered applicable clinical trials:

- Drug or biologic studies, with or without IND (except Phase 1, expanded access/ compassionate use, or drug being used as part of routine care and not under study)
- Device studies, with or without IDE (except small feasibility studies, expanded access/ compassionate use, or device being used as part of routine care and not under study)

⁸⁸ 21 C.F.R. § 56.101

213.1 Research with Test Articles

Research with FDA-regulated test articles may start only after the IRB has approved the protocol and:

- Received documentation that the research will be conducted under an applicable Investigational New Drug Application (IND) or Investigational Device Exemption (IDE); or
 - The IND goes into effect generally thirty (30) days after the FDA assigns the FDA, unless the sponsor receives earlier notice from the FDA
- Formally determines and documents that the proposed use of any investigational device satisfies the FDA criteria for non-significant risk devices; or
- Formally determines that satisfactory justification has been provided by the Investigator as to why an IND or IDE is not required.

The IRB collaborates with local research hospitals and regulatory offices such as The Queen's Medical Center, Hawaii Pacific Health Research Institute, and the UH Cancer Center Regulatory Office to support UH clinical Investigators who conduct FDA-regulated research.

213.2 Research Involving Drugs

Clinical investigations of drugs are subject to the Investigational New Drug Application (IND) regulations, 21 C.F.R. Part 312.

An investigational new drug application (IND) is synonymous with "Notice of Claimed Investigational Exemption for a New Drug." An investigational drug must have an IND before it can be transported, unless one of the exemptions listed in 21 C.F.R. § 312.2 is met.

Applications for research on the use of a drug, unless that research is exempt from the IND regulations, must be accompanied by documentation from the FDA that includes a valid IND number. The IND number must either match the number on the sponsor protocol with the same title as the proposed research, or be listed on communication from the sponsor specific to the proposed research, or on communication with the FDA. IND numbers may not be validated with an Investigator Brochure because it may cover multiple INDs.

Investigators who are planning ANY rigorous, carefully controlled clinical investigations of off-label uses of approved drugs or biologics shall contact the FDA regarding obtaining an IND before submitting a protocol to the IRB. For any FDA-regulated research involving an investigational drug where the FDA required, a valid IND must be obtained before the research can commence.

For FDA-regulated research involving an investigational drug conducted outside the U.S., an IND is not required provided the protocol is conducted in accordance with the Good Clinical Practice guidelines and FDA is able to validate the data from the protocol through an onsite inspection if FDA requires it.

Exempt Drug Research

Per 21 C.F.R. § 312.2(b), clinical investigation of a drug is exempt from the IND regulations if it meets any of the FDA exemptions from the requirement to have an IND:

Exemption 1: If the drug is lawfully marketed in the United States and all of the following are true:

1. The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug;
2. If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product;
3. The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug project;
4. The investigation is conducted in compliance with the requirements for institutional review set forth in part 56 and with the requirements for informed consent set forth in part 50; and
5. The investigation is conducted in compliance with the requirements of 21 C.F.R. § 312.7 (Promotion and charging for investigational drugs).

Exemption 2:

1. A clinical investigation is for an in vitro diagnostic procedure that involves one or more of the following:
 - a. Blood group serum
 - b. Reagent red blood cells
 - c. Anti-human globulin;
2. The diagnostic test is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic procedure or procedure; and
3. The diagnostic test is shipped in compliance with 21 CFR 312.160.

A clinical investigation involving the use of a placebo is also exempt from the requirements of 21 C.F.R. Part 312 if the investigation does not otherwise require submission of an IND. Clinical investigations that are exempt from IND regulations still require IRB review and approval.

213.3 Research with Devices

Clinical investigations of devices are subject to the IDE regulations, 21 C.F.R. Part 812.

An approved investigational device exemption (IDE) permits a device that is not approved (via premarket authorization (PMA)) or cleared to market (pursuant to § 510(k)) by the FDA to be shipped to conduct clinical investigations of that device. Significant risk investigational devices must have an IDE issued by FDA before they can be shipped. Non-significant risk devices are considered to have an approved IDE when the IRB concurs with the sponsor that the device meets the criteria for non-significant risk device.

Research with devices falls into three categories:

1. Investigations of significant risk devices to determine safety and effectiveness of the device
2. Investigations of non-significant risk devices to determine safety and effectiveness of the device
3. Investigations exempted from the IDE regulations

See:

- Significant Risk and Non-significant Risk Medical Device Studies [FDA]
- Frequently Asked Questions Medical Devices [FDA]

Studies that include medical device use in an incidental way, where the device or the use of the device is not the focus of the research, are generally not considered to be FDA-regulated research or subject to 21 C.F.R. Part 812, and in some instances are eligible for IRB review according to the expedited review categories 1 or 4.

Significant Risk Device Research

Applications for research on the use of a significant risk device must be accompanied by documentation from the FDA that includes a valid IDE number. The IDE number must either match the number on the sponsor protocol with the same protocol title as the proposed research, or be listed on communication from the sponsor specific to the proposed research, or on communication with the FDA. IDE numbers may not be validated with a device manual because it may cover multiple IDEs.

Non-Significant Risk Device Research

When research is conducted to determine the safety or effectiveness of a device, the organization confirms that the device fulfills the requirements for an abbreviated IDE (per 21 C.F.R. § 812.2(b)(1)):

- The device is not a banned device;
- The sponsor labels the device in accordance with 21 C.F.R. § 812.5;
- The sponsor obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval;
- The sponsor ensures that each Investigator participating in an investigation of the device obtains from each subject under the Investigator's care, consent under 21 C.F.R. 50 and documents it, unless documentation is waived;
- The sponsor complies with the requirements of 21 C.F.R. § 812.46 with respect to monitoring investigations;
- The sponsor maintains the records required under 21 C.F.R. §§ 812.140(b)(4) and (5) and makes the reports required under 21 C.F.R. §§ 812.150(b)(1) through (3) and (5) through (10);
- The sponsor ensures that participating Investigators maintain the records required by 21 C.F.R. § 812.140(a)(3)(i) and make the reports required under 21 C.F.R. 812.150(a)(1), (2), (5), and (7); and
- The sponsor complies with the prohibitions in 21 C.F.R. § 812.7 against promotion and other practices.

If the Investigator applies to the IRB for a non-significant risk determination for a device study, but the IRB determines that the device is significant risk, the IRB shall notify the Investigator and sponsor, if appropriate.

Exempt Device Research

Clinical investigations that are exempt from IDE regulations still require IRB review and approval. An investigation of a medical device in human participant research that is exempt from the IDE regulations must fall into one of the following categories (per criteria under 21 C.F.R. § 812.2(c)):

- A device legally marketed in the U.S. that is used or investigated in accordance with the indications in the FDA-approved labeling.
- A diagnostic device (i.e., an in vitro diagnostic device) if the testing:
 - Is noninvasive.
 - Does not require an invasive sampling procedure that presents significant risk.
 - Does not by design or intention introduce energy into a subject.
 - Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
- A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk.
- A custom device as defined in 21 C.F.R. § 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.
- A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time.
- A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence.

213.4 Research with Biologics

Clinical investigations of biologics are regulated in the same way as clinical investigations for drugs, and require an IND, unless the biologic is part of a combination product that the FDA has assigned for premarket approval to the Center for Device and Radiological Health (CDRH). In such cases, the biologic/ device combination product would require an IDE prior to research approved by the IRB.

Usually, protocols using biological agents or recombinant DNA vectors are reviewed by Biosafety Committee. The Biosafety Program provides more information about research with biohazardous agents and human participants.

213.5 Handling of Test Articles

The University does not have medical facilities (e.g., clinics, hospitals) that physically hold test articles. Research that requires the internal handling of test articles are kept in medical facilities stated in the protocol, and as such follow the policies and procedures of the involved facilities.

Most clinical investigations involve local hospitals such as The Queen’s Medical Center (QMC), Hawaii Pacific Health (HPH) facilities, and Castle Medical Center (Castle). The policies for QMC, HPH, and Castle outline the standards related to drugs and devices for pharmacy practices, inventory control and documentation.

213.6 Emergency Use of a Test Article

An **Emergency Use** is defined as the use of a test article on a human patient in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.⁸⁹

Under the HHS regulations, emergency use of a test article does not constitute research; the patient may not be considered as a research subject/ participant; and any data derived from the use may not be included in any report of research activities. This is because HHS regulations do not permit research activities to be initiated without prior IRB review and approval, even in emergency.⁹⁰

FDA regulations allow emergency use of a test article when the human subject have been in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval.⁹¹ A clinical investigation involving emergency use is still a clinical investigation under the FDA regulations. FDA may require data from emergency use to be included in marketing applications.⁹²

Emergency use involves four (4) major issues:

- (1) approval by or notification to FDA;
- (2) exemption from prospective IRB approval;
- (3) waiver or alteration of informed consent requirements in emergency research; and
- (4) emergency exception from informed consent requirements.

Specific additional requirements apply. See:

- **SOP 121: Emergency Use of a Test Article**
- [Section 209.5](#) for information on consent and approval for emergency use

213.7 Planned Emergency Research

Planned Emergency Research applies to a narrow exception to the FDA requirement to obtain and document informed consent; applies to a limited class of research activities involving human participants who are in need of emergency medical intervention, but cannot provide legally effective informed consent (See 21 C.F.R. § 50.24).

The research plan must be approved in advance by the FDA and IRB. The research plan must also be disclosed to the communities where the research will be conducted and from where participants will be

⁸⁹ 21 C.F.R. § 56.102(d).

⁹⁰ 45 C.F.R. § 46.103(b) (2014); [HHS on Emergency Care](#).

⁹¹ 21 C.F.R. § 56.102(d).

⁹² 21 C.F.R. §§ 314.50, 814.20(b)(2) (2014).

drawn, including presentation of the risks and expected benefits of the research. An independent data monitoring committee (DMC) must be established to provide oversight of the research. Advance notice of these protocols will be provided to the OHRP pursuant to federal regulations 45 C.F.R. § 46.101(i).

- PIs who wish to conduct planned emergency research shall consult with HSP staff prior to submission of the protocol to the IRB.
- Planned emergency research is usually not eligible for emergency use approvals.

See [Exception from Informed Consent Requirements for Emergency Research](#) [FDA].

Communication among IRBs in Multi-Site and Collaborative Research

GPM 214

Revised Date: December 18, 2015

214.1 Communication among IRBs in Multi-Site and Collaborative Research

The UH IRB is responsible for the review of all UH research that involves human research participants, whether the research is done at UH, a UH affiliate institution, or another site outside of UH.

When UH is conducting research at an external site (e.g., school, hospital) and is not the coordinating site or lead Investigator, and that site is engaged in research, the UH IRB requires contact information for the coordinating/lead site, whether the site has an IRB, and if so, confirmation of the IRB's permission to conduct the research.

UH's IRB relies on the IRBs of other sites and also agrees to have other sites rely on UH's IRB on occasion. Currently, the UH IRB relies on the Western IRBs (WIRB), Queens Medical Center IRB (QMC IRB), and the National Cancer Institute's IRBs (CIRB) on human participant research that meet certain criteria. Additionally, UH's IRB may rely on other external IRBs for single research projects.

If UH agrees to serve as the IRB of Record for an external site, that site obtains an FWA through OHRP which subsequently cites UH's IRBs registration number(s). OHRP notifies UH of this addition. An IRB Authorization Agreement is signed by the institutional officials of UH and the external site, authorizing UH to serve as IRB of Record for that site.

PI's Responsibilities for Research in which UH Serves as a Participating Institution

When UH is a participating institution (i.e., sending data or biospecimen samples out of UH), the PI is responsible for submitting data to the coordinating institution, reporting unanticipated problems (UPs), and other reportable events in a timely manner to the coordinating institution and the UH IRB. The PI is also responsible for ensuring that the PI's research team has the current approved version of the protocol, consent form and other pertinent study documents (e.g., recruitment material, data collection instruments).

214.2 Managing Information in Multi-Site Research

UH Serving as the Coordinating Institution

When UH is serving as the coordinating institution, the PI must include a protocol for communicating information relevant to the protection of participants among participating site and institutions as part of

the **APP 04: New Research for Initial Approval, Non-Exempt Application**, including communication of adverse outcomes, protocol modifications, and interim results.

When completing the eProtocol Application, PIs must indicate if UH is serving as the coordinating institution. The PI must list all other sites involved with the proposed research, the contact person at each site and contact information, such as phone number and email address. The PI must also indicate if each participating site has an IRB and if that IRB has reviewed and approved the research.

When UH is the coordinating institution receiving data or tissue sample from other sites the PI must submit the following documentation for each of the other participating sites along with the Protocol Application to the IRB before receiving any data or tissue sample from a site:

- IRB approval letter from each participating site that includes the type of review, the date of approval, and
- When appropriate, the IRB-approved consent forms from all participating sites.

The UH IRB will keep this information on file for all internal and external reviews.

By submitting the protocol application form, the PI documents his/her acceptance of the responsibility of ensuring that all participating sites have obtained IRB approval prior to initiation of the research at that site. The participating sites must have written procedures that define the scope of studies subject to review by their IRB. The HSP staff will review and confirm that each protocol application for a UH coordinating site project includes the appropriate documentation from all participating institutions.

If a participating site does not have an IRB, that site may request that the UH IRB serve as the IRB of Record. A written agreement (aka Memorandum of Agreement) must be reached between the participating site and the UH IRB that clearly outlines the review and approval procedures. This written agreement must be reviewed, approved and signed by the Institutional Official. See **SOP 120.2: Collaborative Research for information on establishing an IRB Authorization Agreement** and Memorandum of Agreement.

For a prospective clinical trial, the consent forms used at all sites must indicate that data or samples are being sent to UH. Data or tissue sample, even though they are anonymous, may not be received from an outside institution whose consent form prohibits data or tissue from going outside the institution.

There must be documentation of regular communication with the participating sites to update and inform all participating sites about progress of the study.

Reporting to the IRBs in Multi-Site Research

As the lead Investigator at the coordinating institution, the PI is responsible for receiving data and reports from the external sites in a timely manner and distributing this information to the UH IRB as required (see [Section 203.7](#)). UH IRBs give the same considerations to such reports in multi-site research as they do to internal reports.

Identifying Material Changes in Multi-Site Protocols

The PI must report any material changes in the protocol that take place at any of the participating research sites. The IRB may require independent verification to ensure that no material changes have occurred in multi-site research or cooperative study protocols since the previous IRB review.

Additional Requirements

Additional requirements might apply, (such as a formal agreement to specify the roles and responsibilities of each party), depending on the source of support/ funding. See **GUIDE 617: Other Federal Agencies - Additional Requirements**.

Human Participant Protection in Sponsored Research

GPM 215
Revised Date: December 18, 2015

215.1 Protection of Human Participants Agreement

“Sponsored research” is defined as research funded by external entities through a grant or contract that involves a specified statement of work (e.g., the research proposal) with a related transfer of value to the sponsor. Sponsored research includes, but is not limited to, clinical trials involving investigational drugs, devices or biologics and federally-funded studies (e.g., studies funded by NIH, NSF, DOE, etc.).

For sponsored research at UH, protection of research participants are addressed by the following:

1. Including in their standard contract a provision that the sponsor acknowledges and understands that the UH HRPP is applicable to all human participant research. See:
 - [myGRANT Institutional Questions](#) form
2. Requiring the inclusion of such a provision in any proposed contract that does not already include this language in their standard contract template
3. Including in the cover letter accepting and acknowledging the grant an equivalent statement regarding the human research protection program in grants to UH.
4. At proposal stage, the Principal Investigator (PI) is required to identify whether the proposed project involves human research via UH’s internal system, *myGRANT*. The proposal is routed via *myGRANT* from the PI to the unit’s Fiscal Administrator, Chair/ Director, then the Office of Research Services (ORS). ORS is responsible for institutional approval of sponsored research proposals.
5. Before acceptance of an externally-funded award, the PI is required to provide ORS with documentation of IRB approval.

Additionally, the IRB will review the proposed consent form and reject any provision that requires a participant to waive or appear to waive any legal rights (i.e., exculpatory language).

215.2 Provision Addressing Medical Care for Participants

University of Hawaii

For UH sponsored research, medical care for participants is addressed by:

- Including in its standard contract template a provision that the sponsor will *reimburse UH for reasonable and customary costs incurred for treatment of an injury to the subject if it is determined that an adverse event was reasonably related to the administration of the study drug/ device/ biologic.* (See ORS’ **CTA Guide SOPP 301.1**)
- Included in the cover letter accepting and acknowledging the grant an equivalent statement regarding the human research protection program in grants to UH.

- Including the language of any such provision in the consent form.
- Including a statement in the consent form that participants *do not* waive any liability rights for personal injury by signing the consent form.

Communication from Sponsors Affecting IRB Oversight

GPM 216
Revised Date: May 6, 2016

216.1 General

The University has included in their standard sponsored research contract templates, provisions that the sponsor will notify the site-PI or the IRB promptly (no longer than within 30 days) of:

- Findings that could affect the safety of participants or influence the conduct of the study;
- Non-compliance with the protocol or applicable laws, particularly those laws related to participants, that could impact the safety or welfare of the participants;
- Serious adverse events that have been reported to the FDA or other governmental agency in relation to the protocol at UH or any other site;
- Unanticipated problems in the protocol at UH or any other site that could relate to risks to participating participants; and
- Circumstances that could affect participants' willingness to continue to participate in the protocol or the IRB's continuing approval of the protocol.

When non-standard contract templates are used, the sponsor is asked to include equivalent language.

See ORS' CTA Guide SOPP 301.1

216.2 Data and Safety Monitoring (DSM) in Sponsor Agreements

For sponsored research, UH contracts and other funding agreements specify, as appropriate:

- That provisions are made for monitoring study data which could affect participants' safety;
- That the Sponsor is required to send data and safety monitoring plans and reports to the researcher (PI).
- A timeframe for providing routine and urgent data and safety monitoring reports to the PI, as indicated in the data and safety monitoring plan approved by the IRB, and
- That the results of this monitoring are reported to the researcher (PI) so that:
 - Routine monitoring reports will be submitted as part of Continuing Review applications to the IRB, and
 - Urgent reports are submitted according to the guidelines specified in **GUIDE 614: Events and Information which Require Prompt Reporting to the IRB.**

See:

- ORS' CTA Guide SOPP 301.1
- ORS' CTA Training Start Clauses

Dissemination and Communication of Research Findings

GPM 217
Revised Date: December 18, 2015

217.1 Publication of Research Results

UH requires that provisions for fair and reasonable ownership of data and research results be included in its sponsored research agreement and has a process that allows Investigators to place their inventions in the public domain if that would be in the best interest of technology transfer and if doing so is not in violation of the terms of any agreements that supported or governed the work.

In all sponsored research, UH requires the dissemination of research results in a manner consistent with the above referenced policy.

UH implements this policy in agreements concerning sponsored research by:

- Including in its standard contract a provision that provides the Investigator with a right to publish the research results. See ORS' **CTA SOPP 301.1**.
- Revising any provision in any proposed contract that limits an Investigator's right to publish research results in a manner that is inconsistent with the SOPP.

217.2 Communicating Research Results to Participants

When the IRB becomes aware of events that could affect participant welfare after a study has closed (e.g., a drug tested at UH is withdrawn by the FDA), the IRB seeks information, deliberates, and considers whether (and how) to contact participants who might be affected. Even when the study is not yet closed, but participants have completed participation, the IRB informs past participants when information is learned that could affect their welfare.

For sponsored research, UH addresses communication with sponsors regarding the impact of research results on participant health and safety by:

- Including in the contract a provision that the sponsor will develop a plan of communication with the Principal Investigator that is acceptable to the IRB when new findings or results of the protocol might impact the willingness of participants to continue their participation in the research or directly affect their current or future safety or medical care, or by asking for the inclusion of such a provision in any proposed contract that does not use their standard template.
- See ORS' **CTA Guide (SOP 301.1)** and ORS' **CTA Start Clauses**

Definitions

Revised Date: December 18, 2015

<p>Affiliation (IRB Membership)</p>	<p>This refers to UH faculty members, staff, students (currently taking more than 1 credit per semester), and administrators of the University, and their immediate family members (i.e., spouse, domestic partners, dependent children). Alumni are not considered affiliates if they have since graduated from the University for at least 6 months.</p>
<p>Benefit</p>	<p>A valued or desired outcome; an advantage. Benefits of research fall into two categories:</p> <ol style="list-style-type: none"> 1. Benefit to subjects: Research subjects may undergo treatment, diagnosis or examination for illness, abnormal conditions, or social circumstances. This type of research can involve evaluation of a procedure or social situation that may benefit the subject by ameliorating or providing a better understanding of their condition or situation. 2. Benefit to society: Patients and healthy individuals may also agree to participate in research that is either not related to any illness they may have or that is related to their conditions, but not designed to provide any diagnostic or therapeutic benefit. Such research is designed principally to increase our understanding and store of knowledge about human physiology and behavior. Research that has no immediate therapeutic intent may, nonetheless, benefit society as a whole. These benefits take the form of increased knowledge, improved safety, technological advances, and better health.
<p>Confidentiality</p>	<p>Respecting a potential or active participant’s right to be free from unauthorized release of information that the individual has disclosed in a relationship of trust and with the expectation that it will not be shared with others without permission of the participant in ways that violate the original agreement. This agreement, in human subjects research, is usually the informed consent.</p>
<p>Non-scientist (IRB Membership)</p>	<p>Members whose training, background, and occupation would incline them to view research activities from a point-of-view outside of any behavioral or biomedical research discipline. For example:</p> <ul style="list-style-type: none"> • Humanities (e.g., Art, Classics, Drama, English, Music, Philosophy, Religion, Literature) • Natural Scientist (e.g., Physics, Biology, Chemistry, Math, Statistics, Earth Science) • Other Nonscientist (e.g., Library, Education, Business, Government, Law)
<p>Privacy</p>	<p>Respecting an individual’s right to be free from unauthorized or unreasonable intrusion, including control over the extent, timing and</p>

	circumstances of obtaining personal information from or about them.
Private Information	<p>Individually identifiable information:</p> <ul style="list-style-type: none"> • About behavior that occurs in a context in which an individual can reasonable expect that no observation or recording is taking place; and/or • Which has been provided for specific purposes by an individual and which the individual can reasonable expect will not be made public (e.g., medical records).
Risk	The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study, as distinguished from the risks of everyday life and of therapies the subjects would receive even if not participating in the research. Both the probability and magnitude of possible harm may vary from minimal to significant.
Scientist (IRB Membership)	<p>Members whose training, background, and occupation would incline them to view scientific activities from the point-of-view of someone within a behavioral or biomedical research discipline.</p> <p>For example:</p> <ul style="list-style-type: none"> • Physician Scientist (e.g., Medicine, Dentistry, Psychiatry) • Social Scientist (e.g., Anthropology, Communication, Economics, Political Science, Psychology, Sociology) • Other Scientist (e.g., Nursing, Pharmacy, Physical Therapy, Nutrition)
Sensitive Information	<p>Private information relating, but not limited, to:</p> <ul style="list-style-type: none"> • Sexual attitudes, preferences or practices • Use or treatment for alcohol, drugs or other addictive products • Illegal conduct • Information which if released could reasonably cause stigmatization or discrimination, or result in damage to areas such as financial well-being, employability, or reputation. • Certain health information, including psychological or mental health.