# Palo Alto University
# Human Research Protection Program
# (HRPP)

# Standard Operating Procedures

November 2025

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# 1 Human Research Protection Program

Palo Alto University fosters a research environment that promotes respect for the rights and welfare of individuals recruited for, or participating in, research conducted by or under the jurisdiction of Palo Alto University (See Section 1.8). In the review and conduct of research, actions by Palo Alto University will be guided by the principles set forth in the ***Ethical Principles and Guidelines for the Protection of Human Subjects of Research*** (often referred to as the *Belmont Report*): respect for persons, beneficence, and justice. The actions of Palo Alto University will conform to all applicable federal, state, and local laws and regulations and Institutional policies. In order to fulfill this policy, the Organization has established a Human Research Protection Program (HRPP), overseen by its HRPP Office. The Palo Alto University HRPP, in partnership with its research community, is responsible for ensuring the ethical and equitable treatment of all human research participants in research conducted under its jurisdiction. The applies regardless of whether research is externally funded, funded by Palo Alto University sources, or conducted without direct funding.

## 1.1 Mission

The mission of the HRPP is to:

- Safeguard and promote the health and welfare of participants in human research by ensuring that their rights, safety, and well-being are protected;
- Provide guidance and support to the research community in the conduct of human research;
- Assist the research community in ensuring compliance with relevant laws and regulations;
- Provide timely and high quality education, review, and monitoring of human research projects; and
- Facilitate excellence in human research.

The HRPP includes mechanisms to:

- Monitor, evaluate, and continually improve the protection of human research participants;
- Dedicate resources sufficient to do so;
- Exercise oversight of human subject protection;
- Educate investigators and research staff about their ethical responsibility to protect research participants;
- When appropriate, intervene in research and respond directly to concerns of research participants.

## 1.2 Institutional Authority

Palo Alto University's HRPP operates under the authority of the Organization policy "Human Research Protection Program (HRPP)." As stated in that policy, the operating procedures in this document "…serve as the governing procedures for the conduct and review of all human research conducted under the jurisdiction of the Palo Alto University." The HRPP Policy and these operating procedures are made available to all Palo Alto University investigators and research staff and are posted on the HRPP Office website.

## 1.3 Definitions

**Common Rule**: The Common Rule refers to the "Federal Policy for the Protection of Human Subjects" adopted by a number of federal agencies. Although the Common Rule is codified by each agency separately, the text is identical to DHHS regulations in 45 CFR 46 Subpart A. For the purposes of this document, references to the Common Rule will cite the DHHS regulations.

**Human Subjects Research**: Human Subjects Research means any activity that meets the definition of "research" and involves "human subjects" as defined by either the 2018 revised Common Rule (provisions effective January 21, 2019) or FDA regulations. Note: The terms "subject" and "participant" are used interchangeably in this document.

**Research:** The Common Rule defines research as "a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research…whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities." [45 CFR 46.102(l)]

For the purposes of this policy, a "systematic investigation" is any study plan that incorporates data collection, either quantitative or qualitative, and/or data analysis to answer a study question. Investigations designed to develop or contribute to generalizable knowledge are those designed to draw general conclusions (i.e., knowledge gained from a study may be applied to populations outside of the specific study population), inform policy, or generalize findings, regardless of intent to publish the findings.

Under the revised Rule, "the following activities are deemed not to be research:

(i) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

(ii) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

(iii) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

(iv) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions." [45 CFR 46.102(l)]

**Human Subject/Human Research Participant**. A human subject as defined by the 2018 Revised Common Rule is "a living individual about whom an investigator (whether professional or student) conducting research:

(i) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or

(ii) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens." [45 CFR 46.102(e)]

- **Intervention** includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- **Interaction** includes communication or interpersonal contact between investigator and subject" [for the purposes of this policy, interaction includes online interactions.]
- **"Private information** includes 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 that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).
- **Identifiable private information** is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information. Video and audio recordings are always identifiable because the individual's likeness and/or voice are recorded.

- An **identifiable biospecimen** is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen." [45 CFR 46.102(e)]

**Institutional Review Board (IRB)** - The IRB is a board designated by Palo Alto University to review, approve the initiation of, and conduct periodic review of research involving human participants, as defined above. The primary purpose of such review is to assure the protection of the rights and welfare of the human participants. The IRB may be assigned other review functions as deemed appropriate by Palo Alto University.

**Benign Behavioral Intervention**: A "benign behavioral intervention" is defined as one that is brief in duration, harmless, not physically invasive, painless, not embarrassing or offensive, and not likely to have a lasting adverse impact, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

**Clinical Trial**: A research study "in which one or more human participants are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on biomedical or behavioral health-related outcomes" [45 CFR 46.102(b)].

**Limited IRB Review**: A level of IRB review required as part of the exemption determination process for certain categories of research studies.

**Written**, or in writing, "refers to writing on a tangible medium (e.g., paper) or in an electronic format" [45 CFR 46.102(m)].

## 1.4 Ethical Principles

Palo Alto University is committed to conducting research with the highest regard for the welfare of human research participants. With the exception of transnational research, where consideration of alternative ethical principles may apply (See Section 25), Palo Alto University upholds and adheres to the principles of *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects in Research* by the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research (1979). These principles are:

a) **Respect for Persons**, which is ensured by obtaining informed consent, considering privacy and confidentiality, and by providing additional protections for vulnerable populations.
b) **Beneficence**, which is ensured by maximizing possible benefits and minimizing possible risks to all human research participants.
c) **Justice**, which is ensured by the equitable selection of research participants.

Palo Alto University's HRPP is responsible for ensuring the ethical and equitable treatment of all human participants in research conducted under its jurisdiction, in partnership with its research community including researchers and research staff, IRB members and chairs, IRB staff, the institutional official, employees and students.

## 1.5 Regulatory Compliance

The HRPP is responsible for ensuring compliance with federal regulations, state law and institutional policies, (including tribal laws passed by the official governing body of an

American Indian or Alaska Native tribe). All human research under the jurisdiction of Palo Alto University is conducted in accordance with the policy and regulations found in the Common Rule (45 CFR 46) and 21 CFR 50 and 56. The actions of Palo Alto University will also conform to other applicable federal, state, and local laws and regulations, including but not limited to regulations promulgated by the National Institutes of Health (NIH), Substance Abuse and Mental Health Services Administration (SAMHSA), National Science Foundation (NSF), Department of Education (DoE), as well as the Family Educational Rights and Privacy Act at 34 CFR 99 (FERPA, for research involving the use of student educational records).

Federalwide Assurance (FWA)

The federal regulations require that institutions conducting federally-funded human subjects research be covered by a Federalwide Assurance (FWA) approved by the DHHS Office for Human Research Protections (OHRP). An FWA is an organization's assurance to the federal government that human subject research conducted under its auspices is in compliance with federal regulations pertaining to the protection of human subjects. The FWA designates the Institutional Review Board(s) that will review and oversee the research, specifies the ethical principles under which the research will be conducted, and names the individuals who will be responsible for ensuring the proper conduct of the research.

Palo Alto University has an OHRP-approved Federalwide Assurance [FWA 00010885; IORG0008571] and has designated 1 IRB (registered as IRB00010258) to review all human research plans.

For non-exempt research not supported by federal funds, Palo Alto University follows policies and procedures that are the same as those required under 45 CFR 46. Any deviations from this regulation are identified as such in these SOPs.

Research conducted or supported by the U.S. **Department of Education (ED)** is subject to the Common Rule with regulations published at 34 CFR 97. Research conducted or supported by ED is reviewed by the PAU IRB in accordance with the Common Rule as described throughout this manual with the following variations and additional requirements.

> ED has not adopted Subpart B (Pregnant Women, Fetuses, or Neonates) or Subpart C (Prisoners) of the Common Rule.
>
> ED requires reporting of **alleged** (1) unanticipated problems involving risks to subjects or others; and, (2) serious or continuing noncompliance with the Common Rule or Subpart D (protection of children in research). Other mandated reports, as described in Section 17, are submitted to ED instead of OHRP when the research is funded or sponsored by ED. When applicable, PAU will follow the directions for incident reporting provided on ED's Protection of Human Subjects in Research website.

In addition to the Common Rule, human subjects research involving education records conducted at institutions receiving ED funding must comply with additional requirements, including the Family Educational Rights and Privacy Act (FERPA) (34 CFR 99) and the Protection of Pupil Rights Amendment (PPRA) (34 CFR 98). Investigators should consult these regulations and resources provided by DOE when developing their research protocol. The IRB will evaluate the research in accordance with these regulations when applicable. See the Special Topics Section (Section 23.6) of this manual for more information.

### 1.6 Research under the Jurisdiction of Palo Alto University

Research under the jurisdiction of Palo Alto University includes research conducted at Palo Alto University, conducted by or under the direction of any employee or agent of Palo Alto University in connection with his or her institutional responsibilities, or conducted by or under the direction of any employee or agent of Palo Alto University using any Palo Alto University property or facility.

**Agent.** Agents include all individuals who (1) act on behalf of the institution; (2) exercise institutional authority or responsibility; or (3) perform institutionally designated activities. Agents can include staff, students, contractors, and volunteers, among others, regardless of whether the individual is receiving compensation. [OHRP Guidance on Engagement of Institutions in Human Subjects Research (2008)]

**Engagement.** The Department of Health and Human Services (HHS) regulations [45 CFR 46.103[a]] require that an institution "engaged" in human subjects research conducted or supported by a Federal Department or Agency provide the Office for Human Research Protections (OHRP) with a satisfactory assurance of compliance with the HHS regulations, unless the research is exempt under 45 CFR 46.104. *In general, an institution is considered engaged in a particular non-exempt human subjects research project* or exempt research for which limited IRB review is required *when its employees or agents for the purposes of the research project: (1) obtain information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (2) obtain, use, study, analyze or generate identifiable private or identifiable biospecimens; or (3) the informed consent of human subjects for the research.* In general, institutions that receive an award through a grant, contract, or cooperative agreement directly from HHS for non-exempt human subjects research (i.e. awardee institutions) (or exempt research for which limited IRB review takes place pursuant to § 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), (d)(7), or (d)(8)) are also considered engaged in research even where all activities involving human subjects are carried out by employees or agents of another institution.

The HRPP Administrator, with the assistance of the IRB Chair or Vice Chair and legal counsel as needed, will determine whether Palo Alto University is engaged in a particular research study. Investigators and other institutions may not independently determine Palo Alto University's engagement.

If an agent or employee of PAU is going to be involved in research at another institution that is completely separate from their role at PAU, they must submit an "**Attestation for non-PAU Research**" xForm. For example, if a PAU student is employed in a lab at another institution as a psychometrician, but is not receiving course credit or practicum credit and they will not use any research from that role to meet any requirements for graduation at PAU (e.g., won't use it to meet PAU's publication requirement for PhD students). The HRPP Administrator will review all Attestation for non-PAU Research xForms and will either verify that the research is completely separate from the person's PAU role or will inform the researcher that they must file either a Request for Human Subjects Research Determination xForm or an Initial Submission xForm or PAU must enter into a Reliance Agreement with the other institution. The researcher will receive an email through IRB Manager and the decision will be documented in that system.

When Palo Alto University is engaged in research, the Institutional Official may choose to enter into an agreement to cede review to an external IRB.

For additional information on determining engagement please refer to Guidance on Engagement on Institutions in Human Subjects Research, *http://www.hhs.gov/ohrp/policy/engage08.html*

## 1.7 Active research studies approved prior to January 21, 2019

Decisions about whether to transition previously approved studies to the new regulations will be made at the time of continuing review starting on January 21, 2019. The majority of research will be transitioned. Studies for which this would cause undue burden will not be transitioned (e.g., a study that is nearly done with data collection that would require substantial changes to the consent form to comply with the 2018 requirements). If a study is not transitioned to the new requirements, a standard continuing review will be required the following year if the study is to remain open. If a study is transitioned to the new rule, the study team will be informed regarding whether they must submit a continuing review form or an annual report form in 2020 in the approval letter. ALL studies that seek to remain open MUST submit the continuing review form with sufficient time for review prior to expiration. Investigators may want to begin this process earlier than usual, given that they may be required to make changes to comply with the new rule.

## 1.8 Written policies and procedures

Palo Alto University's Standard Operating Procedures for Human Research Protection ("SOPs") detail the policies and regulations governing research with human participants and the requirements for submitting research proposals for review by the Palo Alto University IRB. The SOPs are reviewed by the HRPP Administrator, IRB Chair, and IO at least annually and revised by the HRPP Administrator as needed. Substantive changes are reviewed by the IRB members, Institutional Official and other offices, as applicable, with policies and procedures revised as the need for changes are identified.

The HRPP Office keeps Palo Alto University's research community apprised of new information that may affect the human research protection program, including laws, regulations, policies, procedures, and emerging ethical and scientific issues on its website and through campus electronic mailing lists. The policies and procedures are available on Palo Alto University's HRPP Office website and copies are available upon request. Changes to the policies and procedures are communicated to investigators, research staff, and IRB members by way of electronic mail, newsletters, and/or in-person in-servicing.

## 1.9 HRPP/IRB Operations during an Emergency or Disaster

In the event of an emergency or disaster (e.g., public health or weather-related), the procedures in these SOPs may be modified as appropriate for the situation. Such modifications may include alternative meeting procedures, alternative procedures for the submission and review of modifications, alternative procedures for prompt reporting, and any other changes necessary to ensure appropriate ongoing oversight and conduct of research. Because procedural modifications may vary based on the nature of the event, these cannot be anticipated and described in these SOPs. Instead, such procedural modifications will be recorded in an addendum to the SOPs, note-to-file, or other appropriate means of documentation and communicated to the research community. This documentation will be maintained in accordance with applicable record retention requirements.

## 1.10 Palo Alto University's HRPP Structure

The HRPP consists of the following individuals and committees: the Institutional Official, the HRPP Administrator, the IRB, Division of Academic Affairs, Legal Counsel, investigators, and research staff. The objective of this system is to assist the institution in meeting ethical principles and regulatory requirements for the protection of human research participants.

The following officials, administrative units, and individuals have primary responsibilities for the protection of human research participants:

## 1.11 Institutional Official

The ultimate responsibility of the HRPP resides with the Institutional Official (IO) of the program. The IO is legally authorized to represent Palo Alto University. The IO is the signatory of the FWA and assumes the obligations of the FWA. At Palo Alto University the Assistant Provost of Research Assessment and Institutional Effectiveness (RAIE) is the IO. The IO is responsible for ensuring that the Palo Alto University HRPP and IRB have the resources and support necessary to comply with all institutional policies, laws, and regulations that govern human research. Such resources include, but are not limited to:

- Staffing commensurate with the size and complexity of the research program;
- Appropriate office space, meeting space, equipment, materials, and technology;
- Resources for the production, maintenance, and secure storage of HRPP and IRB records;
- Resources for auditing and other compliance activities and investigation of noncompliance;
- Access to legal counsel;

- Support for educational opportunities related to human research protections for IRB members, relevant administrative staff, and all members of the research team;
- Support for evaluation of Conflict of Interest; and
- Support for Community Outreach.

With the assistance of the HRPP Administrator and IRB Chair, the IO performs an annual review of the HRPP and makes adjustments as needed. In addition to the above, the review includes evaluation of:

- Whether IRB membership remains appropriate or whether changes are needed (e.g., for expertise, due to attendance or performance issues, etc.);
- Whether there are any institutional or IRB member conflicts of interest that require management;
- The adequacy of the education provided to the IRB, HRPP/IRB staff, and the research community;
- The outcomes of the HRPP Quality Improvement activities and the plan for the upcoming year; and
- The adequacy of community outreach activities.

The IO is also responsible for:

- Fostering, supporting and maintaining an institutional culture that supports the ethical conduct of all human subjects research and the adherence to regulations and institutional policies;
- Ensuring that the IRB functions independently by, among other mechanisms, being directly accessible to the IRB Chair(s) and members if they experience undue influence or if they have concerns about the function of the IRB;
- Oversight of the Institutional Review Board (IRB);
- Determining when reliance upon an external IRB is acceptable and appropriate;
- Oversight over the conduct of human subjects research conducted by all Palo Alto University investigators;
- Providing training and educational opportunities for IRB members and staff to support their ability to review research in accordance with ethical standards and applicable regulations;
- Providing training and educational opportunities for investigators and research staff to support their ability to conduct research in accordance with ethical standards and applicable regulations; and
- Taking action as necessary to ensure the protection of human subjects and compliance with regulatory and other requirements.

The IO has the authority to suspend research or take other actions, such as sanctions or restrictions of research privileges or uses of research data, as necessary, to ensure the proper conduct of research, the protection of human subjects, the autonomy and authority of the IRB, and to ensure compliance with regulatory and other requirements. However, the IO may not approve research that has been disapproved (or not yet approved) by the IRB.

The Palo Alto University IO must complete appropriate training on human research protections [CITI]. The HRPP Office will support the continuing education of the IO by providing information and updates on topics related to human research protections.

The IO is made known to employees of the organization and is accessible by phone, email, in person, or other methods of communication. The IRB Chair and HRPP Administrator have direct access to the IO for any concerns or issues related to the IRB or HRPP.

In the performance of these duties, the IO has the authority to delegate such activities as may be necessary in order to effectively administer the program. However, the IO is ultimately responsible and is expected to be knowledgeable about all human research protections responsibilities at the organization.

### 1.12 HRPP Administrator

The HRPP Administrator reports to the IO and is responsible for:

1. Processing of human subjects research protocols
    a. Conducts pre-reviews of submissions (initial, continuing review requests, amendments, unanticipated problems, deviations, etc.)
    b. Makes exempt and/or not human subjects determinations
    c. Forwards submissions to the appropriate IRB member for review
    d. Acts as liaison between the IRB and researchers, serving as a subject matter expert and primary point of contact
    e. Coordinates IRB meetings
    f. Creates IRB Meeting Agendas
    g. Attends IRB meetings and drafts meeting minutes
    h. Prepares correspondence to researchers in response to an IRB review
2. Conducting post-approval monitoring (for cause and not-for-cause) of IRB approved activities.
3. Interpreting current Federal, State, & University laws, regulations, policies and guidelines governing human subject research and applying them to Institutional policies and procedures as well as the electronic management system; and providing appropriate ongoing education and training.

4. Establishing and implementing goals and objectives for quality assessment and improvement (QA/QI) of the HRPP. Working closely with Institutional leadership, and ensure transparency with investigators, regarding these QA/QI efforts.
5. Serve as principal point of contact/liaison to both internal constituencies (e.g., investigators, legal counsel, Grants office, etc.) and external constituencies (e.g., study sponsors, federal [e.g., OHRP, FDA etc.] and state oversight agencies) on professional and operational matters pertaining to the HRPP.
6. Developing and maintaining positive relationships with collaborating organizations, ensure execution of appropriate reliance agreements.
7. Providing advice, guidance, and problem resolution to research investigators and support personnel in the application of relevant Federal, State, and University laws, regulations, and guidelines.
8. Assisting with IRB-related non-compliance issues, as requested.
9. Submitting, implementing, and maintaining an approved FWA through the IO and the U.S. Department of Health and Human Services Office for Human Research Protections (OHRP).

### 1.13 Institutional Review Board (IRB)

Palo Alto University has one on-site IRB, with members recommended by department chairs and appointed by the IO. The IRB prospectively reviews and makes decisions concerning all human research conducted at Palo Alto University facilities, by its employees or agents, or under its jurisdiction unless another IRB has been designated by Palo Alto University to do so. The IRB is responsible for the protection of rights and welfare of human research participants at Palo Alto University, through review and oversight of safe and ethical research. It discharges this duty by complying with the requirements of federal and state regulations, the FWA, and institutional policies. (See Section 4 for a detailed discussion of the IRB.)

The IRB functions independently of, but in coordination with, other institutional entities and officials. The IRB, however, makes an independent determination whether to approve or disapprove a research plan based upon whether or not human research participants are adequately protected.

Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of the institution. However, those officials may not approve human research that has not been approved or has been disapproved by the IRB.

The IO is responsible to determine if the university will or will not proceed to engage in research that is approved by the IRB. The IO may choose to first seek internal or external advice. A final decision may be reviewed by the President if the President determines that further review is appropriate.

Palo Alto University also relies on external IRBs. Such IRBs may be authorized to approve research conducted by Palo Alto University investigators, as part of multi-site studies. In such cases, appropriate authorization agreements or reliance agreements will indicate each institution's responsibilities.

### 1.14 Legal Counsel's Office

The Palo Alto University HRPP relies on its Legal Counsel for the interpretation and application of state law and the laws of any other jurisdiction where Palo Alto University research is conducted, as they apply to human research. Legal Counsel will also advise the IRB about other legal issues such as who is a child, and who can serve as a legally authorized representative (LAR) or guardian. When there are any conflicts between federal or national law and other applicable laws, the Legal Counsel will determine the appropriate resolution.

### 1.15 The Principal Investigator

The principal investigator is the person responsible for the research project (See Section 18.1). If the protocol is to be conducted by a team of individuals, the principal investigator is the responsible leader of the team. The principal investigator is ultimately responsible for the protection of human research participants. The principal investigator is expected to abide by the highest ethical standards and develop a research plan that incorporates the principles of the Belmont Report. They are expected to conduct research in accordance with the IRB-approved research plan and to oversee all aspects of the research by providing training and supervision of support staff, including oversight of the informed consent process. All participants must give informed consent unless the requirement has specifically been waived by the IRB. The principal investigator must establish and maintain an open line of communication with research participants. In addition to complying with all the policies and standards of the governing regulatory bodies, the principal investigator must comply with institutional and administrative requirements for conducting research. The principal investigator is responsible for ensuring that all research staff complete all institutional required training as well as training for their responsibilities in any given specific research study.

### 1.16 Other Related Units

#### 1.16.1 Grants Office

Grants Office staff administer all grants from all outside funding agencies. This institutional review ensures that all terms of the award are in compliance with institutional policies.

When the grant or contract agreement includes human research activities that will be conducted (in part or in whole) by investigators who are not employees or agents of Palo Alto University, a subcontract is executed between Palo Alto University and the collaborating institution. The subcontract includes the requirement for the collaborating institution to assure compliance with federal regulations for the protection of human research participants and to provide documentation of current and ongoing IRB approval. The collaborating institution must also ensure that key personnel involved in human research are in compliance with the NIH policy on education in the protection of human research participants and provide documentation of education of key personnel to Palo Alto University when NIH is funding the study.

The Grants Office ensures that an account for an award is not set up for expenditures unless the IRB has issued approval for the activity.

## 1.17 Specific Coordination

In addition to IRB approval, an Investigator must obtain and document the approval, support, or permission of other entities impacted by the research, as applicable, including, but not limited to:

- Permission to enter classrooms;
- Permission to distribute recruitment materials through an online resource, agency, or mailing list;
- Permission from external research locations (sites);
- Paper file access permissions; ● Database access permissions; and ● Conflict of Interest.

For any that are indicated, a letter of support, collaboration, permission, or approval from the designated authority, is included in the Initial Submission for Human Subjects Research Review Form completed in IRB Manager. The application is reviewed in the HRPP Office to ensure that all necessary letters are included. Final IRB approval will not be given until all necessary letters are received.

Other committees and officials may not authorize human research to commence that has not been approved by or that has been disapproved by the IRB.

## 1.18 Collaborative Research Projects/ Cooperative Research

**Cooperative research** projects are those projects covered by this policy that involve more than one institution.

Beginning in January 2020, the revised common Rule requires that any institution located in the United States that is engaged in collaborative/cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States. The limited exceptions to this requirement are (1) studies for which more than single IRB review is required by law or (2) studies for which any Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular context [45 CFR 46.114(b)(2)].

In the conduct of collaborative research projects, Palo Alto University acknowledges that each organization is responsible for safeguarding the rights and welfare of human research participants and for complying with applicable federal regulations.

For IRB review, Palo Alto University may choose to enter into a joint review arrangement, rely on the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort. A formal relationship must be established between Palo Alto University and the other institution through an Institutional Agreement, a Memorandum of Understanding, Reliance Agreement, or other such written agreement. This relationship must be formalized before Palo Alto University will accept any human research proposals from the other institution or rely on the review of the other institution. When proposing cooperative research for which PAU will not be the lead or coordinating facility, the Principal Investigator must complete the Request for Reliance Agreement with Another IRB xForm in IRB Manager. See Section 9 for additional details.

When the Palo Alto University IRB reviews research conducted in whole or in part at another institution, the particular characteristics of each institution's local research context must be considered, either (i) through member knowledge of local research context or (ii) through the use of consultants or other sources of information.

Before a collaborative study can begin, it must be approved by the IRB of record for the lead or coordinating facility. Before the study can begin at a participating facility, it must be approved by the IRB of record for the participating facility and, when required, the IRB of record for the lead or coordinating facility.

For collaborative research when the Palo Alto University investigator is the lead investigator, or when Palo Alto University is the coordinating facility for a research study, the investigator must identify all institutions participating in the research, the responsible IRB(s), and the procedures for dissemination of study information (IRB initial and continuing approvals, relevant reports of unanticipated problems, study modifications, and interim reports) among all participating institutions. The investigator is responsible for serving as the liaison with regulatory and funding agencies, with other participating facilities, and for all aspects of internal review and oversight procedures. The investigator is responsible for ensuring that all participating facilities obtain review and approval from their IRB of record initially, for all modifications to the research plan, and for continuing review. The investigator is responsible for ensuring that the research study is reviewed and approved by any other applicable committees or entities at the lead or coordinating facility and at the participating facilities prior to enrollment of study participants.

The investigator must follow these procedures when Palo Alto University is the lead or coordinating facility:

- During the initial IRB submission of the multi-site study, the investigator indicates in the Initial Submission for Human Subjects Research Review Form in IRB Manager that Palo Alto University is the lead or coordinating facility of a multi-site study.
- The investigator submits a "Request for PAU to serve as IRB of Record" xForm upon approval of the Initial Submission xForm. This xForm includes:
    - o Name of each participating facility;
    - o Confirmation that each participating facility engaged in research has an FWA (including FWA number and expiration date); o Contact name and information for investigator/s at each participating facility; o Contact name and information for IRB

of record at each participating facility; o Method for assuring all participating facilities have the most current version of the research plan;

  - o Method for confirming that all modifications to the research plan are communicated to participating sites;
  - o Method for communicating to participating facilities any serious adverse events and unanticipated problems involving risks to subjects or others;
  - o Method for communicating interim analyses, including data safety reviews, to participating facilities, as applicable;
  - o Method of communicating regularly with participating sites about the progress of the study; and
  - o When appropriate, the plan for monitoring the conduct of the research at participating facilities.

- Following approval from Palo Alto University and after each reliance agreement is fully executed, research activities may commence at each site unless Palo Alto University's IRB has determined otherwise.
- The investigator maintains documentation of all correspondence between participating sites and their IRB of record.

When Palo Alto University is engaged in only part of a collaborative research project, and Palo Alto University is not the lead or coordinating site, the Palo Alto University IRB may choose to review and approve only the part(s) of the research in which the Palo Alto University investigator is engaged. For example, if Palo Alto University is operating the statistical center for a multicenter trial that receives identifiable private information from multiple other institutions, the Palo Alto University IRB reviews and approves the research activities related to the receipt and processing of the identifiable private information by the statistical center. In these cases, depending on the terms of any Institutional Agreement, Memorandum of Understanding, or Reliance Agreement, the Palo Alto University IRB may or may not be considered the IRB of record for purposes of reporting to OHRP or federal authorities.

### 1.18.1 Guidelines for PAU Students Engaging in Research External to PAU

The purpose of these guidelines is to provide guidance to faculty and students regarding when student involvement in external research as a member of the research team engages PAU in the research and thus requires interaction with the PAU IRB office. These guidelines represent common scenarios that are presented to the IRB office, not all possible scenarios.

1. When the research is **student-driven** (e.g., designed by the student for the purposes of undergraduate research or a thesis or dissertation) but takes place at an external organization (e.g., Stanford University, UCSF), the student **is** acting as an agent of PAU.

   **What is needed for PAU IRB?** PAU IRB review, determination of exempt status, or IRB reliance will be needed.

2. When the research is being conducted at or by the external organization (e.g., Stanford University, UCSF), **and the research will be modified** (e.g., additional survey questions, additional experiments, new or modified objectives) **for the purposes of the student** (e.g., for the student’s thesis or dissertation), the student **is** acting as an agent of PAU.

   **What is needed for PAU IRB?** PAU IRB review, determination of exempt status, or IRB reliance will be needed. The modifications to the research **cannot be implemented** until the review or reliance process is complete.

3. When the research is **being conducted at or by the external organization**, and the PAU student is being added as research staff, **without the research being modified for the purposes of the student** (e.g., additional survey questions, additional experiments, new or modified objectives), the student **is not** acting as an agent of PAU. This is true even when the experience will result in course credit or otherwise count towards the student’s degree progression.

   **What is needed for PAU IRB?** Submission to the PAU IRB is not required. Rather, the student will need to submit a Attestation for non-PAU Research xForm from the IRB website. If documentation of this is needed for the external organization, please provide a copy of these guidelines. If additional documentation is required, please contact irb@paloaltou.edu. Graduate and Doctoral students should consult with their degree programs regarding any IRB documentation that will be required for graduation.

4. When PAU (Faculty/Student) is the **prime awardee** on a federal grant, contract or agreement, PAU is engaged in human subjects research even when all activities involving human subjects are carried out by employees or agents of another institution(s) unless an exception has been granted by OHRP or another appropriate agency.

   **What is needed for PAU IRB?** PAU IRB review, determination of exempt status, or IRB reliance will be needed.

### 1.18.2 Collaborative Research Not Eligible for Reliance Agreements

When a multi-site study has been found exempt from the regulations at another institution, the PAU investigator(s) must submit a "Register Exempt Determination from another IRB" xForm. The HRPP Administrator, IRB Chair, or designee will determine whether the study meets criteria for exemption and is compliant with all local laws and regulations as well as the principles of the Belmont Report. If the previous institution's exemption finding or protections for human subjects research is not consistent with PAU's typical interpretation of the exemption categories or is not consistent with the Belmont Report or local laws and regulations, the PAU investigator(s) will be directed to file an Initial Submission xForm.

# 2 Quality Assurance

Palo Alto University performs Quality Assurance and Improvement activities for the purposes of monitoring the safety of ongoing studies and measuring and improving human research protection effectiveness, quality, and compliance with organizational policies and procedures and applicable federal, state, and local laws.

## 2.1 External Monitoring, Audit, and Inspection Reports

All reports from external monitors, auditors, or inspectors are submitted by investigators to the IRB for review. The IRB Chair or designee reviews such reports to look for issues that could impact the rights or welfare of human research participants and for issues indicative of possible serious or continuing non-compliance. If such issues are identified, the report is forwarded to the convened IRB to determine what additional actions are necessary.

## 2.2 Investigator Compliance Reviews

The HRPP Administrator is responsible for conducting post-approval directed ("for cause") audits and periodic ("not for cause") compliance audits of investigator research plans. Additionally, the IRB may appoint a subcommittee for the purpose of conducting a for-cause or not for-cause compliance audit of one or more research plans under its jurisdiction.  The subcommittee may be composed of IRB members and staff from within, or individuals from and outside of the organization.

Compliance reviews are conducted to assess investigator compliance with federal, state, and local law, the IRB-approved protocol and Palo Alto University policies, and to identify areas for improvement, and to provide recommendations based on existing policies and procedures. The results of compliance reviews are reported to the IRB for review, and, in the case of noted deficiencies, for approval of corrective action plans proposed by the HRPP Administrator. Any uncovered non-compliance is handled according to the procedures in Section 16.

If it is identified that research participants have been exposed to unexpected serious harm, the HRPP Administrator will promptly report such findings to the IRB Chair for immediate action, which may include suspension of the study while an investigation is initiated.

If issues are identified that indicate possible misconduct in research, the procedures in the Palo Alto University research misconduct policy are initiated. If the potential research misconduct also involves potential noncompliance with the IRB-approved protocol, any investigations will be coordinated between the HRPP Administrator and the Research Integrity Officer.

Compliance reviews may include:

a) Requesting progress reports from investigators;
b) Post-Approval Monitoring Self-Assessment xForms;

c) Examining investigator-held research records;
d) Contacting research participants;
e) Observing sites where research involving human participants and/or the informed consent process is being conducted;
f) Reviewing advertisements and other recruiting materials;
g) Reviewing projects to verify from sources other than the investigator that no unapproved changes have occurred since previous review;
h) Assuring that the consent document(s) includes the appropriate information and disclosures about conflicts of interest;
i) Assuring that the consent document includes all required elements for HIPAA authorization; and
j) Conducting other monitoring or auditing activities as deemed appropriate by the HRPP or IRB.

### 2.3 IRB Compliance Reviews

The HRPP Administrator periodically reviews the activities of the IRB to assess compliance with regulatory requirements and to identify areas for improvement; this includes a review of IRB records at least annually. Review activities may include:

a) Review of the IRB minutes to determine that adequate documentation of the meeting discussion has occurred. This review includes assessing the documentation surrounding the discussion for protections of vulnerable populations as well as risk/benefit ratio and consent issues that are included in the criteria for approval;
b) Review of the IRB minutes to assure that quorum was met and maintained;
c) Review of IRB documentation, including IRB minutes, to assess whether privacy provisions, according to HIPAA, have been adequately reviewed, discussed and documented;
d) Evaluating the continuing review discussions to assure they are substantive and meaningful and that, in the event of a lapse, no study activities took place;
e) Reviewing IRB files to assure retention of appropriate documentation and consistent organization of the IRB file according to current policies and procedures;
f) Reviewing the IRB database to assure all required fields are completed accurately;
k) Verifying IRB approvals for collaborating institutions or external performance sites;
l) Reviewing the appropriate metrics (for example, time from submission to first review) to evaluate the quality, efficiency, and effectiveness of the IRB review process; and
m) Other monitoring or auditing activities deemed appropriate.

The HRPP Administrator will provide the IRB with reports on the results of IRB compliance reviews for review at their next scheduled meeting. If any deficiencies are noted in a particular review, a proposed corrective action plan, developed by the HRPP Administrator, will be included as well. Once reviewed and approved by the IRB, the HRPP Administrator will have the responsibility for implementing the corrective action plan.

### 2.4 HRPP Quality Assessment and Improvement

An annual meeting of the Institutional Official, the HRPP Administrator, and IRB Chair is held during which a quality improvement plan for the coming year is identified, to be carried out by the HRPP Administrator. Results from the prior year's plan and from compliance reviews from the prior year are reviewed for trends and potential problem areas. Based on this information, the plan for the coming year will identify one goal for HRPP compliance (e.g., 100% compliance in 6 months of IRB members to fully complete their reviewer worksheets), and one goal for HRPP quality/efficiency (e.g., improvement by 50% in one year in the turn-around times for exemptions), with defined time periods for assessments and improvements made to achieve the goals.

The HRPP Office tracks internal metrics through its electronic management system that are informative in considering IRB and Investigator efficiency, such as the amount of time from receipt of a submission through pre-review, assignment to the IRB, and final approval and the amount of time it takes investigators to develop and submit responses to pre-review and IRB requirements. Metrics reports are reported to the Institutional Official and IRBs annually.

## 3 Education & Training

### 3.1 Training / Ongoing Education of IRB Chairs, Members, and Staff

Recognizing that a vital component of a comprehensive human research protection program is an education program, Palo Alto University is committed to providing training and an on-going educational process for IRB members and the staff of the IRB and HRPP Office, related to ethical concerns and regulatory and organizational requirements for the protection of human research participants.

### 3.1.1 Orientation

New IRB members, including alternate members, meet with the HRPP Administrator and/or IRB Chair for an orientation session. At the session, the federal regulations are reviewed and an orientation to IRB processes given. Each new member receives a copy of the following documents, and are expected to be familiar with:

- The Belmont Report;
- The Standard Operating Procedures; and ● Federal regulations relevant to the IRB.

### 3.1.2 Initial Education

IRB members must complete the following required CITI modules:

- Basic Course in the Protection of Human Research Subjects (Social Behavioral Educational track)
- IRB Member Module - "What Every New IRB Member Needs to Know”
- “I Have Agreed to be an IRB Community Member. Now What?” (Community members only)
- HRPP Policies and Procedures Module in the IRB Administration Basic Course
- Basic Course on Conflicts of Interest
- Responsible Conduct in Research (social behavioral track)
- Disaster Planning for the Research Enterprise (DPRE)
- Good Clinical Practice - Social and Behavioral Research Best Practices for Clinical Research

### 3.1.3 Continuing Education

To ensure that oversight of human research is ethically grounded and the decisions made by the IRB are consistent with current regulatory and policy requirements, training is continuous for IRB members throughout their service on the IRB.

IRB members must satisfy formal continuing education requirements via refresher coursework through CITI every 3 years (with the exception of the DPRE course, which need only be completed once). Additionally, the HRPP Administrator uses the following activities as a means for offering continuing education to IRB members:

- In-service training at IRB meetings;
- Training workshops;
- Copies of appropriate publications; and
- Identification and dissemination of new information that might affect the human research protection program, including laws, regulations, policies, procedures, and emerging ethical and scientific issues to IRB members via email, mail, or during IRB meetings.

IRB members who have not fulfilled the mandatory continuing education requirements may not be assigned as primary or secondary reviewer until they are fulfilled. Continuing non-compliance of these education requirements may result in the individual being removed or not renewed as an IRB member.

Each year, the Institutional Official (IO) provides support for as many members of the IRB as possible and the HRPP Administrator to attend the PRIM&R AER conference or regional OHRP conferences on human research protections.

## 3.2 Training / Ongoing Education of Investigators and Research Team

Another vital component of a comprehensive human research protection program is an education program for all individuals involved with human research participants. Palo Alto University is committed to providing training and an on-going educational process for investigators and members of their research team related to ethical concerns and regulatory and organizational requirements for the protection of human research participants.

### 3.2.1 Initial Education

Investigators and all other members of the research team must complete the following CITI courses:

- Basic Course in the Protection of Human Research Subjects (Social Behavioral Educational track)
- Responsible Conduct of Research (Social Behavioral track)
- Conflict of Interest (if the investigator conducts PHS funded research)
- Disaster Planning for the Research Enterprise
- Good Clinical Practice - Social and Behavioral Research Best Practices for Clinical Research (if the investigator is involved in any clinical trials)

Each member of the research team must complete the IRB Manager form entitled “Verification of CITI Training” each time they update their training.

New studies, amendments, and continuing reviews will not receive IRB approval unless all training requirements are current for all study team members.

#### 3.2.1.1 Waiver of Initial Education

If individuals can provide documentation verifying that they have successfully completed human subject research training equivalent to that required by Palo Alto University or, for non-PAUaffiliated researchers that they have completed the training required at their primary institution (e.g., Palo Alto VA Health Care System ), they may request a waiver of the requirement for Palo Alto University’s Initial Education with the exception of the requirement to review PAU’s HRPP Human Research Website, including these SOPs. The HRPP Administrator will review the documentation and determine if it satisfies organizational standards. However, all investigators and members of their research team must complete the requirements for Continuing Education as described below.

### 3.2.2 Continuing Education and Recertification

Investigators, key personnel, and other members of the research team must meet Palo Alto

University’s continuing education requirement for the SBR Basic Course and Responsible Conduct of Research Course every three (3) years after certification of Initial Education for as long as they are involved in research with human participants. There is no exception to this requirement. This requirement is met by completion of appropriate refresher modules at the CITI web-based training site.

Investigators who receive Public Health Service funding must complete refresher training for the Conflict of Interest course every three years.

Investigators who are involved in clinical trials must complete refresher training for the GCP course every three years.

Evidence of CITI education status is validated through the IRB Manager Verification of CITI Training form. New research plans and applications for continuing review, progress reports, and amendments will not be approved until all investigators listed in the study have current certification in human research protections through CITI.

Investigators who are also IRB Chairs, IRB members, or HRPP Office staff must satisfy the training requirements for IRB members and staff described in this policy under Section 3.1.

# 4 Institutional Review Board

Palo Alto University has established an Institutional Review Board (IRB) to ensure the protection of human research participants in studies conducted under the jurisdiction of Palo Alto University. All non-exempt human research conducted under the jurisdiction of Palo Alto University must be reviewed and approved by the Palo Alto University IRB, or another IRB with a signed reliance agreement with Palo Alto University and approval from the HRPP Office prior to the initiation of the research.

Palo Alto University may, for multicenter studies, enter into reliance agreements to be the IRB of record for external sites, or cede IRB review to external IRBs. External IRBs that serve as the IRB-of-record for Palo Alto University have the same authority as the on-site IRB. All determinations and findings of the authorized external IRB acting in its capacity as the IRB-ofrecord for a study conducted at Palo Alto University are equally binding on the specific study at Palo Alto University.

## 4.1 IRB Authority

The IRB derives its authority from Palo Alto University policy, as cited in Section 1.2. Under the federal regulations, IRBs have the authority:

1. To approve, require modifications to secure approval, or disapprove all human subjects research activities (including exempt research activities under 45 CFR 46.104 of the revised Common Rule for which limited IRB review is a condition of exemption) overseen and conducted under the jurisdiction of Palo Alto University;
2. To require that informed consent be obtained and documented in accordance with regulatory and policy requirements unless the IRB determines that the criteria for the

waiver or alteration of such requirements have been satisfied and approves the waiver or alteration. The IRB may require that information beyond that specifically mentioned in the regulations, be given to research participants when, in the IRB's judgment, the information would meaningfully add to the protection of the rights and welfare of participants;

3. Regarding Continuing Review:

   *For research subject to the 2018 Common Rule:*

   To conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk of the research, but not less than once per year, except as described in Section 7.2.1 and 7.8.2;

   To conducting continuing review of research approved through expedited review procedures when the reviewer indicated that continuing review was required;

   *For research is subject to other regulations (e.g., pre-2018 Common Rule, FDA, DOJ) or requirements (e.g., grant or contract terms):*

   To conduct continuing review of research at intervals appropriate to the degree of risk of the research, but not less than once per year

4. To suspend or terminate approval of research not being conducted in accordance with the IRB's requirements, or that has been associated with unexpected serious harm to participants;
5. To observe, or have a third party observe, the consent process; and
6. To observe, or have a third party observe, the conduct of the research.

The IRB functions independently. Attempts to coerce or otherwise unduly influence the actions of the IRB are forbidden by Palo Alto University policy, and are to be reported as described in Section 4.7. Likewise, the IRB must remain free from the influence of financial and other organizational interests. No individual with direct responsibility for the business and financial interests of the organization may serve as a voting member of the IRB. Individuals from these offices may provide information to the IRB and attend IRB meetings as invited guests or ex officio, non-voting members

Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of Palo Alto University. However, those officials may NOT approve human research if it has not been approved or has been disapproved by the IRB.  Reviewing officials may strengthen requirements and/or conditions, or add other modifications before approval, or may require additional institutional approval(s). Previously approved research proposals and/or consent forms must be re-approved by the IRB before initiating any changes or modifications that result from such additional reviews/approvals, except in circumstances where following the approved protocol may result in subject harm. In this case, the deviation from protocol taken to protect subjects must be immediately reported to the IRB for review.

When the IRB Chair or HRPP Administrator notes that a protocol may present concerns that are not relevant to human subjects protection but may be subject to administrative review by Palo Alto University (e.g., risks to researcher), the IRB Chair or HRPP Administrator will first consult with the IO. If there is agreement that the concern warrants notice to other administrative officials, the IRB Chair or HRPP Administrator will forward the concern to the Vice President of Academic Affairs (VPAA), along with any relevant documentation (e.g., Initial Submission xForm). The IRB Chair or HRPP Administrator will also notify the PI that the concern was forwarded to the VPAA.

## 4.2 Roles and Responsibilities

### 4.2.1 IRB Chair

Palo Alto University's Institutional Official (IO), in consultation with the HRPP Administrator, appoints the IRB Chair. The IRB Chair, in consultation with the IO and the HRPP Administrator, appoints the IRB Vice Chair.

With the exception noted below for interim Chairs, the IRB Chair should be a highly respected tenure-track individual, from within Palo Alto University, fully capable of managing the IRB and the matters brought before it, with fairness and impartiality. The task of making the IRB a respected part of the research community falls primarily on the shoulders of the Chair. The IRB must be perceived to be fair, impartial, and immune to pressure by administration, the investigators whose research plans are brought before it, and other committees and professional and nonprofessional offices/sources.

The IRB Chair is responsible for conducting the meetings and conducting expedited reviews, and may designate other experienced IRB members to perform duties such as expedited reviews and other IRB functions.

The IRB Chair is authorized to take immediate action to suspend a study or studies if information is presented regarding participant safety or for any other reason where such action would be deemed appropriate. Such action requires subsequent notice to and review by the convened IRB.

The IRB Chair advises the Institutional Official and the HRPP Administrator about IRB member performance and competence.

The performance of the IRB Chair is reviewed on an annual basis by the HRPP Administrator in consultation with the Institutional Official. Feedback of this review is provided to the Chair. If the Chair is not acting in accordance with the IRB's mission, fails to follow these policies and procedures, has an undue number of absences, or is otherwise not fulfilling the responsibilities of the Chair, he/she may be removed.

An interim IRB Chair who is not a member of the PAU community, can serve for up to a year when the Chair position cannot be filled by someone internal to PAU. The interim Chair must fill all the same qualifications and responsibilities described above.

### 4.2.2 IRB Vice Chair

The Vice Chair serves as the Chair of the IRB in the absence of the Chair and has the same qualifications, authority, and duties as the Chair.

The performance of the IRB Vice Chair is reviewed on an annual basis by the HRPP Administrator and the IRB Chair, in consultation with the Institutional Official. Feedback of this review is provided to the Vice Chair. If the Vice Chair is not acting in accordance with the IRB's mission, fails to follow these policies and procedures, has an undue number of absences, or is otherwise not fulfilling the responsibilities of the Chair, he/she may be removed.

### 4.2.3 IRB Members

The role of an IRB member is to ensure that human research activities comply with federal regulations, state and local laws, and organizational policies and procedures, by:

1. Completing member education and training, both initial and on-going (See Section 3.1).
2. Maintaining the confidentiality of IRB deliberations and research review by the IRB.
3. Conducting and documenting reviews of assigned research in a timely fashion.
4. Attending IRB meetings as scheduled.

   Members are expected to attend a minimum of 75% of all meetings. If a member is unable to attend a scheduled meeting, they inform the IRB administrative staff.

   If an IRB member is to be absent for an extended period of time, he/she is expected to notify the IRB administrative staff in advance. If the member has a designated alternate, the alternate can serve during the primary member's absence. If the member does not have a designated alternate and the member's area of expertise is needed and not represented by another member, an alternate for the absent member may be appointed by the Chair.

5. Recusing self from discussion and vote when he/she has a conflict of interest. The member may be asked to return during deliberations to answer questions or provide additional information.
6. Participating in subcommittees of the IRB if requested and available.
7. Conducting himself/herself in a professional and collegial manner.

Experienced members may be designated by the Chair to conduct expedited and exempt reviews.

The performance of IRB members is reviewed on an annual basis by the IRB Chair and the HRPP Administrator. Feedback of this review is provided to the member. Members who are not acting in accordance with the IRB's mission or not following policies and procedures or who have an undue number of absences may be removed.

### 4.2.4 Alternate IRB members

The appointment and function of alternate IRB members is the same as that for primary IRB members. An alternate's expertise and perspective should be comparable to those of the primary member. The role of the alternate member is to serve as a voting member of the IRB when the regular member is unavailable to attend a convened meeting. When an alternate member substitutes for a primary member, the alternate member receives and reviews the same materials prior to the IRB meeting that the primary member received.

The IRB roster identifies the primary member(s) or class of members (e.g., physician scientist) for whom each alternate member may substitute. The alternate member is not counted toward meeting quorum as a voting member unless the primary member is absent. The IRB minutes must document when an alternate member replaces a primary member.

Experienced alternate members may be designated by the Chair to conduct expedited and exempt reviews.

### 4.2.5 Subcommittees of the IRB

The IRB Chair, in consultation with the HRPP Administrator, may appoint IRB members to a subcommittee of the IRB to perform duties, as appropriate, and undertake other IRB functions, and to make recommendations to the IRB (e.g., to supplement the IRB's initial review, continuing review, review of modifications, and/or review of reports of unanticipated problems or of serious or continuing non-compliance). The number and composition of the IRB Subcommittee shall depend on the scope of duties delegated by the IRB Chair to such IRB Subcommittee (e.g., making recommendations, conducting an inquiry, etc.). Any such Subcommittee cannot approve research that requires approval at a convened IRB meeting.

## 4.3 IRB Membership

The structure and composition of the Palo Alto University IRB is appropriate to the amount and nature of the research that is reviewed. Every effort is made to have member representation with an understanding of the areas of specialty that encompasses most of the research performed at Palo Alto University.

The IRB includes members who are knowledgeable about and experienced working with vulnerable populations that typically participate in Palo Alto University research.

The IRB must promote respect for its advice and counsel in safeguarding the rights and welfare of human research participants; and possess the professional competence necessary to review specific research activities. Palo Alto University has procedures (See Section 7.2.2 and Section 7.4.3) that specifically outline the requirements for review of research plans by individuals with appropriate scientific or scholarly expertise.  A member of the IRB may fill multiple membership position requirements for the IRB.

## 4.4 Composition of the IRB

The requirements for the composition of the IRB under the revised Common Rule vary slightly from the pre-2018 rule. The composition of the PAU IRB complies with both rules. The following excerpt describes the requirements for the composition of the IRB under the revised Common Rule [45 CFR 46.107]:

1. The IRB has at least five members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the organization.
2. The IRB is sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.
3. In addition to possessing the professional competence necessary to review specific research activities, the IRB includes members able to ascertain the acceptability of proposed research in terms of institutional commitments (including policies and resources) and regulations, applicable law, and standards of professional conduct and practice.
4. If the IRB regularly reviews research that involves a category of subjects that is vulnerable to coercion or undue influence (e.g., children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons), consideration is given to the inclusion of one or more individuals on the IRB who are knowledgeable about and experienced in working with these populations.
5. Every effort is made to ensure that the IRB does not consist entirely of men or entirely of women, including the organization's consideration of qualified persons of both sexes, so long as no appointment is made to the IRB solely on the basis of gender. The IRB does not consist entirely of members of one profession.
6. The IRB includes at least one member whose primary concerns are in scientific areas.
7. The IRB includes at least one member whose primary concerns are in nonscientific areas (Community Member*) who is not otherwise affiliated with the organization and who is not part of the immediate family of a person who is affiliated with the organization.
8. No IRB may have a member participate in the IRB’s initial or continuing review of any project in which the member has conflicting interest, except to provide information requested by the IRB.
9. An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB. At PAU, a member may satisfy more than one membership category.
10. At PAU, the IRB Chair and Vice Chair are voting members of the IRB.
11. At PAU, the HRPP Administrator will serve as an alternate member of the IRB.

Given the social-behavioral science focus of PAU, the competence of the IRB to review research protocols outside of this focus, with or without the assistance of external consultation, will be made on a case-by-case basis. The HRPP Administrator and IRB Chair will address, in consultation with the IO as necessary, any concerns regarding whether the IRB has adequate expertise to review a protocol. If it is determined that the PAU IRB is not capable of conducting a review (even with an outside consultant's review), the investigator will be notified in writing and will be provided with recommended actions (e.g., PAU IRB entering into a reliance agreement with a collaborating institution that does have the necessary expertise on their Board, review by an independent IRB, etc.).

The IRB Chair and the HRPP Administrator shall review the membership and types of research being conducted at PAU to determine if the IRB continues to meet regulatory and organizational requirements, and if adjustments to membership are required.

### 4.4.1 Appointment of Members to the IRB

All PAU Tenure-track and Scholar-Educator track faculty are required to serve on the Institutional Review Board, according to the following guidelines:

Membership will rotate between all university Tenure-track and Scholar-Educator track faculty, starting from more senior ranked to more junior ranked faculty.

Primary responsibility for assigning the rotation of IRB service membership lay collaboratively with the Department Chairs.

Appointments are made for a three-years, renewable term of service, consisting of 2 years of active, voting membership followed by 1 year as an alternate member (with annual reviews that confirm continuation of the member). Any change in appointment or removal from the IRB requires written notification. Members may resign by written notification to the HRPP

Administrator.

The IRB Chair and HRPP Administrator shall review the membership and composition of the IRB annually to determine if they continue to meet regulatory and institutional requirements.

**Community Member(s)**: IRB members come from a variety of backgrounds, and it is important to have representation from the surrounding community. The mission of an IRB community member is to help to protect the rights and welfare of those individuals volunteering as research subjects. Community members are not required to have a scientific background. In fact, most have no scientific background but have the ability to review research materials. Each brings their individual knowledge and community experiences to the discussion to reflect the perspective of the volunteer research participants.

**Basic requirements:**

- **Non-affiliated status:** The member must not be affiliated with the research institution and is not part of the immediate family of a person who is affiliated with the institution: This includes a relative or someone related by marriage. Unaffiliated members bring diverse viewpoints to the IRB, reflecting the concerns of potential research subjects and the broader community.
- **No scientific background needed:** The role does not require a scientific background, focusing instead on community and nonscientific areas of concern.
- **Conflict of Interest Mitigation:** Their perspective is less affected by potential financial or nonfinancial conflicts of interest that may arise with institutional employees.
- **Protection of Human Subjects:** This member's role is vital in protecting the rights and welfare of research participants by offering insights from the perspective of the public.
- **Time commitment**: Community member(s) must commit to attending monthly IRB meeting. They are expected to review research proposals before IRB meetings (specifically recruitment materials and consent forms)..
- **Diversity:** The IRB's overall diversity is important, with considerations for race, gender, and cultural backgrounds, as stated in the regulations.
- **Good communication skills**: The members have good communication skills, are comfortable speaking to others in a meeting setting, like to read.
- **Computer savvy**: Comfortable working on a computer and a web-based system.
- **Complete Required Training: Community m**embers are required to complete training specific to IRB principles and the protection of human subjects.
- **Maintaining Confidentiality:** All information and discussions from IRB meetings must be kept confidential. (Sign Confidentiality Agreement?)

**Honorarium:**
Community members receive $100 honorarium to attend monthly meetings.

### 4.4.2 IRB Registration Updates

Changes in IRB Registration are reported to OHRP as follows:

1. A Palo Alto University decision to disband a registered IRB is reported in writing within 30 days after permanent cessation of the IRB's review of DHHS-conducted or supported research.
2. Changes regarding the contact person who provided the IRB registration information, or regarding the individual serving as IRB Chair, are reported within 90 days.
3. Additional IRBs to be added under the FWA will be reported and confirmed by OHRP before those IRBs review research conducted or supported by DHHS
4. Change in the membership roster of the IRB designated under the FWA is made within 90 days.

### 4.5 Use of Consultants

When necessary, the IRB Chair, IRB members, or the HRPP Administrator may solicit individuals from the organization or the research community with competence in special areas to assist in the review of issues or research plans that require scientific or scholarly expertise beyond or in addition to that available on the IRB. The HRPP Office ensures that all relevant materials are provided to the outside reviewer prior to the convened meeting.

Written statements from consultants are kept in the IRB study records. Key information provided by consultants at meetings is documented in the minutes.

Consultants are subject to Palo Alto University's Conflict of Interest Policy and must confirm that they do not have a conflict of interest prior to review. Individuals who have a conflict of interest or whose spouse or immediate family member(s) has a conflict of interest in the research, including any relationship to the sponsor, are not invited to provide consultation.

The consultant's findings are presented to the convened board for consideration either in person or in writing. If in attendance, the consultant may assist in the deliberation, but may not participate in the vote.

*Ad hoc* or informal consultations requested by individual members (rather than the convened board) are processed by the HRPP Office in a manner that protects the investigator's confidentiality and is in compliance with the IRB conflict of interest policy.

### 4.6 Liability Coverage for IRB Members

Palo Alto University defends and indemnifies its officers, faculty, and other employees for all acts and omissions that occur within the scope of employment or authorized activity including IRB matters. In addition, the University contracts with insurance companies that can provide additional protections for these matters.

### 4.7 Reporting and Investigation of Allegations of Undue Influence

If an IRB Chair or member feels that the IRB has been unduly influenced by any party, he/she shall make a confidential report to the HRPP Administrator or IO, depending on the circumstances. Undue influence means attempting to interfere with the normal functioning and decision making of the IRB or to influence an IRB member, staff, or any other member of the research team outside of the established processes or normal and accepted methods in order to obtain a particular result, decision or action by the IRB or one of its members or staff.

The HRPP Administrator or IO ensure that a thorough investigation is conducted, and if the allegation is determined valid, that corrective action is taken to prevent additional occurrences. In the event that the allegation is regarding the IO, the matter is referred to the President of Palo Alto University for investigation and any necessary action.

# 5 Human Subject Research Determination

Determinations concerning whether or not an activity constitutes human subject research may only be made by the HRPP Administrator or designee or the IRB Chair. To obtain such a determination, the investigator must submit the "Request for Human Subjects Research Determination" in IRB Manager. The HRPP Administrator or designee will render a decision, with input from the IRB Chair as necessary, and notify the investigator via IRB Manager of said determination.

# 6 Exempt Studies

Exempt human subjects studies are a subset of research involving human subjects that do not require comprehensive IRB review and approval because the **only** research activity involving the human subjects falls into one or more specific exemption categories as defined by the Common Rule.

Any activity that qualifies as Research (as defined above) and includes one or more Human Subjects (as defined above) **must be reviewed and approved or declared exempt by the PAU IRB** prior to the commencement of the study. At Palo Alto University, determination of exemption eligibility and need for Limited IRB Review (see Section 6.1 and Section 7.3) will be completed by the HRPP Administrator or designee, the IRB Chair or Vice Chair, or an experienced IRB member designated by the HRPP Administrator or IRB Chair. A decision to grant exemption will be made based on regulatory and institutional criteria, and the rationale for the exempt determination will be documented and communicated to the researcher. Study projects declared exempt will be exempt from annual IRB review. However, some of the new exempt categories will be subject to a "limited IRB review" as defined in Section 6.1 and Section 7.3.

For information on the process of registration of collaborative research previously found exempt at another institution, see Section 1.18.1.

Additionally, studies that receive official determination of exemption status are not exempt from ethical considerations. The following are among the ethical standards that still apply:

- Honoring the principles described in the Belmont Report.
- Except in the case of chart reviews or database research, potential subjects must be provided enough information (verbally or using an information sheet) to be able to choose whether or not to participate. The information should include the voluntariness of their participation, the purpose of the research, the nature of the subject's involvement, time commitments, and contact information for the investigator and the IRB Office.
- Research data must be handled and stored securely, in compliance with PAU IRB policy.
- Access to research data must be limited to study team members and other authorized personnel.

- All members of the research team must be current on human subjects training and must have a current conflict of interest disclosure.

The IRB Chair, HRPP Administrator, or designated IRB member making the determination of exemption will determine whether to require additional protections for research participants in keeping with ethical principles. The reviewer will also make a determination regarding any requested waivers or alterations of HIPAA authorization procedures.

Individuals involved in making the determination of an IRB exempt status of a proposed research project cannot be involved in the proposed research or have any apparent conflict of interest.

### 6.1 Limited IRB Review

*Limited IRB Review Process.* For exemption determination of certain categories of research studies, the PAU IRB will conduct *Limited IRB Review* via expedited review or by the convened IRB process, as appropriate. Limited IRB Review (excluding those requiring review by the convened IRB) will be completed by the HRPP Administrator, the IRB Chair or Vice Chair, or an experienced IRB member designated by the HRPP Administrator or IRB Chair.

When the research requires limited IRB review or a HIPAA determination (i.e., waivers or alterations of the requirement for HIPAA authorization), the review may be conducted using expedited review procedures by the IRB Chair or an experienced member of the IRB assigned by the HRPP Administrator. As with all other research subject to IRB review requirements, when conducting limited IRB review the IRB has the authority to approve, require modifications in (to secure approval), or disapprove all research activities; and to suspend or terminate IRB approval. Actions of disapproval may only be made by the convened IRB. [45 CFR 46.109(a), 45 CFR 46.110]

Proposed modifications to the aspects of research subject to limited IRB review must be submitted to and approved by the IRB prior to implementation, except when necessary to eliminate apparent immediate hazards to the subject(s), in which case the change must be promptly reported to the IRB (i.e., within 10 business days). [45 CFR 46.108(a)(3)(iii)]

*For exempt research subject to limited IRB review, the following criteria shall be applied:*

1. For exempt categories 2(iii) and 3(iii) (See Section 3.2), the IRB may approve the research when it determines that there are adequate provisions (1) to protect the privacy of subjects and (2) to maintain the confidentiality of data. The other findings listed in the criteria for approval outlined in Section 7.5 are not required.

### 6.2 Limitations on Exemptions

The categories of exemptions listed below in Section 6.3 apply to research involving pregnant women if the conditions of the exemption are met. The categories of exemption do **not** apply to research involving prisoners except research aimed at involving a broader subject population that only incidentally includes prisoners. Exemption categories 1, 4, 5, 6, 7, and 8 can be applied to research involving children if the conditions for exemption are met. Research involving children is eligible for Category 2 exemption only when it is related to educational tests or observations in which the investigators don't participate in the activities being observed. Additionally, research involving children is not eligible for this exemption if the project requires limited IRB review.

## 6.3 Categories of Exempt Research

Research activities in which the only involvement of human participants is determined to be in one or more of the following categories are exempt from the requirements of 45 CFR 46 if the research is <u>not regulated by the FDA</u> (with the exception of Category 6, which is the only exemption allowed for FDA-regulated research) and with the above-referenced limitations on the use of exemptions for specific types of vulnerable subjects:

1. **Category 1: Education Research Exemption:** Research, conducted in established or commonly accepted educational settings that specifically involves **normal educational practices** that are **not likely to adversely impact students' opportunity to learn** required educational content **or the assessment of educators who provide instruction.** This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
2. **Category 2: Surveys, Interviews, Educational tests, and Observation of public behavior:** Research that **only includes interactions** involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if ***at least one*** of the following criteria is met:

(i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

(ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(iii) The information obtained is recorded by the investigator in such a manner that the **identity of the human subjects** can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts **a *limited IRB review*** to make the determination required by 45 CFR 46.111(a)(7).*

** When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.*

3. ***Category 3*: Benign Behavioral Intervention (see definition in Section 1.3):** Research involving benign behavioral interventions in conjunction with the collection of information from an **adult subject** through verbal or written responses (including data entry) or audiovisual recording if the subject **prospectively agrees** to the intervention and information collection and at least one of the following criteria is met:
    i. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
    ii. Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or
    iii. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a *limited IRB review* to make the determination required by § 45 CFR 46.111(a)(7).*

    * *When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.*

If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

**Limitations on the use of Benign Intervention Exempt Category:**

- Participants must be adults who are able to prospectively agree to participate in the research. Subjects who require a LAR decision-maker may not be enrolled.
- The overall duration of the study must be brief. It should occur in a single day and not exceed more than a few hours.
- The research activities must be behavioral in nature; they cannot include medical interventions, even if those interventions are low risk.
- Data collection must only be through verbal and written responses by the subject, data entry by the subject or observation of the subject, which may include audiovisual recordings. Data from electronic sensors or devices would not be approvable in this exemption category.
- Changes to the subject's physical environment are allowed to the extent that they do not involve extremes of heat, cold, noise or light.

4. **Category 4: Secondary Research (identifiable private information/ biospecimens):** Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:
   (i) The identifiable private information or identifiable biospecimens are publicly available;

   (ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

   (iii)The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); or

   (iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with applicable federal privacy standards found in the E-Government Act of 2002 (44 USC 2501), Privacy Act of 1974 (5 USC 552a), and the Paperwork Reduction Act of 1995 (44 USC 3501 et seq.)

5. **Category 5: Public Benefit/Service Program Research (Federal demonstration projects):** Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.
   i. Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal website or

in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

6. **Category 6: Taste and food quality evaluation and consumer acceptance studies. Taste and food quality evaluation and consumer acceptance studies,**
   (i) If wholesome foods without additives are consumed; or
   (ii) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the FDA or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

   Note: This is the only exemption that is allowable for FDA-regulated research.

NOTE: PAU is not adopting Exemptions #7 and #8 at this time.

### 6.4 Procedures for Exemption Determination

Researchers are advised to contact IRB Office to discuss their project prior to submitting it through IRB Manager.

In order to obtain an exemption determination, investigators must submit all of the following:

1. A completed Initial Submission for Human Subjects Research Review xForm in IRB Manager;
2. Each research team member must have completed required CITI training and submitted the Verification of CITI Training form in IRB Manager. All required training must be complete before the exempt determination will be granted.
3. Each research team member must have a current Financial Disclosure xForm on file in IRB Manager. See the PAU’s Conflict of Interest Policy to details regarding when and how to file disclosures.

The following additional material must be submitted as part of the Initial Submission xForm prior to granting exempt status when applicable:

1. All recruitment materials (e.g., letter of invitation, recruitment script, flyer);
2. Consent form/disclosure/information sheet;
3. All surveys, questionnaires, instruments;
4. Data collection sheets;
5. Letter(s) of permission from each non-Palo Alto University site of performance;

6. If sponsored/funded, a pdf of the grant application(s) and/or contract.

The HRPP Administrator, IRB Chair, or designee reviews the Initial Submission xForm and determines whether the request meets the definition of research involving human participants and, if it does, determines whether the proposed research is eligible for exemption. The HRPP Administrator, IRB Chair, or designee also determines whether limited IRB review is required per the guidelines described above.

The reviewer indicates whether the request for exemption is approved or denied, and if approved, the rationale for the determination and category/s under which it is permitted. The reviewer determines whether to require additional protections for research participants, in keeping with the guidelines of the Belmont Report regardless of whether limited IRB review is required.

When limited IRB review is required, the reviewer determines whether there are adequate privacy and confidentiality protections in place. If the reviewer has concerns about these protections or feels that annual continuing review would be appropriate for the study, the reviewer will recommend the study undergo expedited or full board review procedures (see Sections 7.2 and 7.4).

If there are interactions (in-person or on-line) with participants, the reviewer should determine whether there should be a consent process that will disclose information such as: ● The activity involves research

- The participation is voluntary
- The purpose of the research
- Duration of the prospective subject participation
- The procedures and the nature of the subject’s involvement
- The reasonably foreseeable risks or discomforts to the prospective subject
- The benefits to the prospective subject or to others that may reasonably be expected from the research
- The name and contact information for the researcher
- The name and contact information of the office subjects can contact if they have research-related complains or with questions related to their rights.

The application, review, and determination letter are recorded and maintained in the same manner and for the same length of time as other IRB review documentation. Once the exemption review is completed, the investigator will receive a written determination indicating the exempt category, rationale for the exemption category, and whether the study required *limited IRB review*. The letter will also indicate if a continuing review application or an annual report is required.

**Investigator's Responsibilities:** While the study is active, despite exemption status, investigators will still be responsible and required to submit the following:

i. For studies that required limited IRB review: Annual reports: Investigators are responsible to provide an annual report or continuing review (as noted in their previous approval letter) to the IRB indicative of active study or submit study closure report;

ii. Any reportable events: Any reportable (see Section 13) event must be reviewed by the IRB. The IRB will determine if the reportable event is acceptable or the study requires modification.

iii. Any modifications to the research that may affect subjects or the exemption determination. Such proposed modifications must be reviewed and approved by the IRB Chair/HRPP Administrator or designee *prior* to implementing the modification.

# 7 IRB Review Process

The IRB reviews and ensures that Palo Alto University research involving human participants meets all required ethical and regulatory criteria for initial and any modifications of approved research. The IRB may conduct its review using the following review methods:

- Expedited Review
- Review by Convened IRB

The following describe the procedures required for the review of research by the on-site IRB. (See Section 9 for a description of the procedures for review of research by an External IRB.)

## 7.1 Definitions

**Minimal Risk:** 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 or during the performance of routine physical or psychological examinations or tests. [Note that the regulatory definition of "minimal risk" for research that involves prisoners is slightly different; see Section 12.6 for further discussion.]

**Minor Change**: For research reviewed by the convened IRB, a minor change is one that, in the judgment of the IRB reviewer, makes no substantial alteration in:

1. The acceptability of the risk-to-benefit analysis or increases the level of risks to participants;
2. The research design or methods (for example, adding procedures that are not eligible for expedited review [See Section 7.2.1] are considered more than a minor change);
3. The number of participants to be enrolled in the research locally if the study presents more than minimal risk;
4. The qualifications of the research team;

5. The facilities available to support safe conduct of the research; and
6. Any other factor that would warrant review of the proposed changes by the convened IRB.

**Quorum:** A quorum of the IRB consists of a majority (more than half) of the voting membership, including at least one member whose primary concern is in a non-scientific area.

**Suspension of IRB approval:** Suspension of IRB approval is a directive of the IRB to temporarily stop some or all previously approved research activities. Investigators must continue to provide reports on adverse events and unanticipated problems to both the IRB and sponsors just as if there had never been a suspension (i.e., all events that need to be reported during a study must continue to be reported during the suspension period). If a suspension is lifted after the current IRB approval period has expired, a continuing review is required before the study may resume.

**Termination of IRB approval**: Termination of IRB approval is a directive of the convened IRB to permanently stop all activities in an IRB approved research study. Terminated research studies are closed and no longer require continuing review.

## 7.2 Expedited Review

An IRB may use the expedited review procedure to review:

1. Some or all of the research appearing on the list of categories of research eligible for expedited review unless the reviewer determines that the research involves more than minimal risk. Please note additional requirements for eligibility under 7.2.1 (i.e., regarding potential harm if subjects and/or their responses were to be identified)
2. Minor changes in previously approved research by the convened IRB during the period (of one year or less) for which approval is authorized. Note: approval of minor changes does not alter the end-date of study approval.
3. Research for which limited IRB review is a condition of exemption under 45 CFR 46.104(d)(2)(iii) and (d)(3)(i)(C).

The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review--expedited or convened--used by the IRB.

### 7.2.1 Categories of Research Eligible for Expedited Review

Palo Alto University applies the categories of research eligible for expedited review, which were published in the Federal Register (https://www.hhs.gov/ohrp/regulations-andpolicy/guidance/categories-of-research-expedited-review-procedure-1998/index.html).

The activities listed below should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is *eligible* for review through the expedited review procedure *when the specific circumstances of the proposed research involve no more than minimal risk to human participants*.

The categories in this list apply regardless of the age of participants, except as noted in category 2.

*The expedited review procedure may not be used where identification of participants and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to a participant's financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections are implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.*

The expedited review procedure may not be used for classified research involving human participants.

**Expedited Research Categories one (1) through seven (7) may be used for both initial and continuing IRB review:**

***NOTE: Categories 5-7 are the most commonly applicable for behavioral science research***

(1) Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

  (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required.

    (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

  (b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

(2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

  (a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

  (b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

    (Note: Children are defined as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.")

(3) Prospective collection of biological specimens for research purposes by noninvasive means.

Examples: (a) hair and nail clippings in a non-disfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization; (k) vaginal swabs that do not go beyond the cervical os; rectal swabs that do not go beyond the rectum; and nasal swabs that do not go beyond the nares.

(4) Collection of data through noninvasive procedures, not involving general anesthesia or sedation, routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Note: Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject’s privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

(NOTE: Some research in this category may be exempt from the DHHS regulations for the protection of human subjects. See Exempt Categories and 45 CFR 46 101(b)(2) and b(3). This listing refers only to research that is not exempt.)

(6) Collection of data from voice, video, digital, or image recordings made for research purposes.

(7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior); or research employing survey, interview, oral

history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the DHHS regulations for the protection of human subjects. See Exempt Categories and 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

**Categories 8 and 9 apply only to continuing review.**

(8) Continuing review of research previously approved by the convened IRB as follows:

(a) Where

(i) the research at Palo Alto University is permanently closed to the 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

(Note: "Long-term follow-up" includes research *interactions* that involve no more than minimal risk to subjects (e.g., quality of life surveys); and collectio*n of follow-u*p data from procedures or interventions that would have been done as part of routine clinical practice to monitor a subject for disease progression or recurrence, regardless of whether the procedures or interventions are described in the research study, but not *interventions* that would not have been performed for clinical purposes, even if the research interventions involve no more than minimal risk.);

***or***

(b) Where no subjects have ever been enrolled at Palo Alto University and no additional risks have been identified

(Note: "no additional risks have been identified" means that neither the investigator nor the IRB has identified any additional risks from any institution engaged in the research project or from any other relevant source since the IRB's most recent prior review.); ***or***

(c) Where the remaining research activities at Palo Alto University are limited to data analysis.

(9) Continuing review of research previously approved by the IRB at a convened meeting that meets the following conditions:

- The research is not conducted under an investigational new drug application (IND) or an investigational device exemption (IDE);
- Expedited review categories (2) through (8) do not apply to the research;
- The IRB has determined and documented at a convened meeting that the research, or the remaining research activity involving human subjects, involves no greater than minimal risk to the subjects; and
- No additional risks of the research have been identified.

(Note: “no additional risks have been identified” means that neither the investigator nor the IRB has identified any additional risks from any institution engaged in the research project or from any other relevant source since the IRB’s most recent review.)

### 7.2.2 Expedited Review Procedures

Under an expedited review procedure, the review may be carried out by the IRB Chair or by one or more reviewers designated by the Chair or HRPP Administrator from among members of the IRB. Selection of IRB member(s) to conduct expedited reviews will take into account IRB members’ area(s) of expertise.

Under an expedited review procedure, IRB review is carried out by the IRB Chair or by one or more reviewers designated by the Chair or HRPP Administrator from among experienced members and alternate members of the IRB. Designated reviewers must be professionally competent (i.e., experienced with and having demonstrated the ability to apply IRB review requirements and with appropriate scientific or scholarly expertise) to conduct expedited reviews. The HRPP Administrator or IRB Chair will select expedited reviewers from that list. Selected reviewers will have the qualifications, experience and knowledge in type of research to be reviewed, as well as be knowledgeable of the requirements to approve research under expedited review. IRB members with a conflict of interest in the research (see Section 21.2) will not be selected.

When reviewing research under an expedited review procedure, the IRB Chair, or designated IRB member(s), receives and reviews all documentation submitted (the same documentation is submitted for all studies, whether expedited and convened review). This requirement applies to all categories of submissions including initial reviews, continuing reviews, and modifications. The reviewer determines and documents the regulatory criteria through the use of the expedited review procedure in IRB Manager. When a reviewer determines that research subject to the Common Rule falls within the expedited categories but involves more than minimal risk, the reviewer will document the rationale for that determination in the checklist and refer the research for review by the convened IRB. If the research otherwise does not meet the criteria for expedited review, the reviewer indicates that the research requires review by the convened IRB and the research study is placed on the next available IRB meeting agenda.

If the research meets the criteria allowing review using the expedited procedure, the reviewer(s) conducting initial or continuing review will complete the IRB Member Review Form in IRB Manager to determine whether the research meets the regulatory criteria for approval. The same criteria of approval apply to reviews conducted via expedited review as to those conducted by the convened board. The reviewer may require changes to the Initial Submission Form prior to approval. If the research does not meet the criteria for expedited review, then the reviewer will indicate that the research requires full review by the IRB and the research study will be placed on the next available agenda for an IRB meeting.

In the event that expedited review is carried out by more than one IRB member and the reviewers disagree, the IRB Chair may make a final determination, or the study may be referred to the convened IRB for review.

### 7.2.3 Informing the IRB

A list of all studies approved by expedited review (including Limited IRB Review process) is part of the IRB meeting agenda for review and acknowledgement by all members of the IRB.

## 7.3 Limited IRB Review

As noted in Section 6.1, the PAU IRB may conduct limited IRB review via expedited review or by the convened IRB process, as appropriate. Limited IRB review (excluding those requiring review by the convened IRB) will be completed by the HRPP Administrator, the IRB Chair or Vice Chair, or an experienced IRB member designated by the HRPP Administrator or IRB Chair.

## 7.4 Convened IRB Meetings

Except when an expedited review procedure is used, the IRB conducts initial and continuing review of all non-exempt research at convened meetings at which a quorum (see below) of the members is present.

### 7.4.1 IRB Meeting Schedule

The IRB maintains a monthly meeting schedule during the academic year, except during Summer Quarter, during which the IRB will have one meeting. The schedule for IRB meetings is posted on the IRB website. Special meetings may be called at any time by the IRB Chair or HRPP Administrator. The IRB will meet on the scheduled monthly dates as needed to address items that require convened Board review. When there are no items that require convened Board review (either Initial Submissions, Modifications, Continuing Reviews, and Reportable Events) and no planned educational activities, the IRB meeting will be cancelled. Board members will be notified one week (5 working days) in advance. The members are required to reserve the monthly meeting scheduled date and time, unless and until they receive word that the meeting is cancelled. When the monthly IRB meeting is cancelled, the IRB will be notified of expedited, exempt, or administrative review (including Initial Submissions, Modifications, Continuing Reviews, and Reportable Events) at the next convened meeting.

### 7.4.2 Pre-Review

The HRPP Administrator or designee (e.g., student assistant) conducts a pre-review of all submissions for determination of completeness and accuracy. Only complete submissions are placed on the IRB meeting agenda for review or distributed to reviewers for expedited or exempt review. Depending upon timing of the submission, and if feasible, the investigator is informed by e-mail, phone or in person of missing materials and the necessary date of receipt for inclusion on the agenda. If an investigator is submitting for the first time, or is not be well-versed in the submission procedures, the HRPP Administrator is available for guidance.

### 7.4.3 Reviewers

After it has been determined that the submission is complete, the HRPP Administrator, and/or the IRB Chair assign submissions for review, paying close attention to the subject matter of the research, the potential reviewer's area/s of expertise, and representation for any vulnerable populations involved in the research. A primary reviewer is assigned to each Initial Submission, Modification Request, and Continuing Review. Where possible, the reviewer for each Continuing Review and Amendment include the original primary reviewer for the study. A reviewer may be assigned several submissions or other items for review. When the IRB is presented with a research study that may be outside of the knowledge base or representative capacity of the IRB members, an outside consultant will be sought (See Section 4.5). Research studies for which appropriate expertise cannot be obtained for a given meeting are deferred to another meeting when appropriate expertise is available.

Primary reviewers are responsible for:

1. Having a thorough knowledge of all of the details of the proposed research;
2. Performing an in-depth review of the proposed research, including review of any relevant grant applications;
3. Completing the Reviewer Checklist at least one week prior to the convened meeting, which will be provided to the Chair for distribution to the full committee;
4. Beginning the discussion of the proposed research at the convened meeting, by summarizing the proposed research and leading the IRB through the regulatory criteria for approval (See Section 7.5); and
5. Making suggestions for changes to the proposed research, where applicable.

All IRB members receive and are expected to review **all** studies, not just those to which they are assigned as a reviewer.

When there is sufficient advance notice that a reviewer will be absent from the meeting, a new reviewer is assigned, provided that the new reviewer will have sufficient time to review the materials in advance of the meeting. An absent reviewer can submit written comments for presentation at the convened meeting, but such comments or recommendations do not count as a vote.

### 7.4.4 Materials received by the IRB

For inclusion on an IRB meeting agenda, all required materials must be submitted with the Initial Submission form by the first Thursday of the month for inclusion in the meeting the following month (e.g., submit by the first Thursday of September to be addressed in the meeting held on the first Monday of October).

The HRPP Administrator and/or IRB Chair will conduct a pre-review and return the xForm for any additional information required. If the xForm is returned to the study team, revisions must be received at least 10 business days before the scheduled meeting. The HRPP Administrator and/or IRB Chair will check the revised xForm for completeness within 24 hours. If the submission is ready for review, it will be sent to the IRB for review prior to the meeting. If the submission is not ready for review, it will be returned to the study team and the study will not be reviewed until the next IRB meeting.

The meeting agenda is prepared by the HRPP Administrator and/or IRB Chair. All IRB members receive the meeting agenda, which includes a list of research approved under expedited review procedures since the last meeting, applicable administrative items, continuing education materials, and research submission materials, no later than 10 business days before the scheduled meeting, to allow sufficient time for review. A review worksheet is completed by the primary reviewer. The worksheet(s) are projected during IRB meetings to guide discussion and determinations. While the worksheet(s) help prepare for and guide discussion. The IRB minutes serve as the official record of the convened IRB's deliberations, determinations, and actions.

All IRB members have access to all materials submitted for all studies on the agenda, which include the following, as applicable:

- The Initial Submission Form;
- All data collection measures/methods (e.g., surveys, interview questions);
- Proposed Consent / Parental Permission / Assent Form(s);
- Proposed recruitment materials, including advertisements intended to be seen or heard by potential study participants; and ● Grant application(s).

Additionally, for DHHS-supported multicenter clinical trials, the primary reviewer should receive and review a copy of the DHHS-approved sample informed consent document(s) (when one exists) and the complete DHHS-approved protocol/research plan (when one exists).

If an IRB member requires additional information to complete the review, he/she may contact the investigator directly or may contact the HRPP Office to make the request of the investigator.

### 7.4.5 Quorum

A quorum of the IRB consists of a majority (more than half) of the voting membership, including at least one member whose primary concern is in a non-scientific area. At IRB meetings, a quorum must be established and maintained for the deliberation and vote on all matters requiring a vote.

The IRB Chair, with the assistance of the HRPP Administrator, confirms that quorum is present before calling the meeting to order. These individuals also are responsible for ensuring that the IRB meeting remains appropriately convened. If quorum is not maintained, either by losing a majority of the members, losing all non-scientific members, losing another required member, or due to recusal of one or more members, the IRB will not take further action or vote on regulatory determinations until quorum is restored even if half of the members are still present.

It is expected that at least one unaffiliated member and at least one member who represents the general perspective of participants (one individual can serve in both capacities) is present at all

IRB meetings. The IRB may, on occasion, meet without this representation; however, this should be the exception. No more than 1/3 of the IRB meetings may take place without an unaffiliated member present.

If the IRB regularly reviews research that involves subjects vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, one or more individuals (e.g., IRB members, alternate members, or consultants) who are knowledgeable about and experienced with that population should be present during the review of the research.

When the IRB is presented with a research study that may be outside of the knowledge base or representative capacity of the IRB members, outside consultation will be sought. Research studies for which appropriate expertise cannot be obtained for a given meeting will be deferred to another meeting when appropriate expertise is available.

IRB members are considered present and participating at a convened IRB meeting when either physically present or participating through electronic means (e.g., teleconferencing or video conferencing) that permits them to listen to and speak during IRB deliberations and voting. Whether or not physically present, the IRB member must have received all pertinent materials prior to the meeting and must be able to participate actively and equally in all discussions.

Opinions of absent members that are transmitted by mail, telephone, facsimile, or e-mail may be considered by the attending IRB members but may not be counted as votes or to satisfy the quorum for convened meetings.

### 7.4.6 Meeting Procedures

Once it has been determined that a quorum is in place, the IRB Chair calls the meeting to order. At that time, the Chair reminds IRB members to recuse themselves from any discussion and vote when they have a conflict (and the member leaves the room prior to the start of the discussion).

The IRB reviews all submissions for initial and continuing review, amendments requiring full committee review, and other items requiring full committee review (e.g., incidents of noncompliance, potential UPs etc.). The reviewers present an overview of the research and assist the Chair in leading the IRB through a discussion of the regulatory criteria for approval, which are available during the meeting, either projected onto a screen or in hard copy, to help guide the discussion. In order for the research to be approved, it must receive the approval of a majority of those voting members present at the meeting.

The HRPP Administrator or designee take notes of the proceedings and is responsible for preparing the meeting minutes.

### 7.4.7 Guests

Investigators and research staff may be invited to the IRB meeting, at the discretion of the IRB, to make a brief presentation or to answer questions about the proposed or ongoing research. The investigator/research staff may not be present for the deliberations or vote on the research.

Other guests may be permitted to attend IRB meetings at the discretion of the IRB Chair and the HRPP Administrator. Such guests may be asked to sign a confidentiality agreement, do not participate in discussion unless requested by the IRB, and under no circumstances are they allowed to vote.

### 7.4.8 Alternate Members

The HRPP Administrator will serve as an alternate and thus will not vote unless they are substituting for an absent IRB member. The HRPP Administrator can only serve as an alternative for members of the same category. Thus, when the Administrator is a scientist, they can only serve as an alternate for scientist members of the IRB. When the Administrator is a non-scientist, they can only serve as an alternate for non-scientist members of the IRB. If the absent board member has specific expertise needed to adequately review a protocol, the HRPP Administrator will not vote for the member and a consultant will be relied upon to assist the board members present in conducting the review. The HRPP Administrator will review all materials for all submissions on the agenda regardless of serving as an alternate.

## 7.5 Criteria for IRB Approval of Research

In order for the IRB to approve human subjects research, either through expedited review or by the convened IRB, it must determine that the following requirements, as indicated at 45 CFR 46.111, are satisfied. These criteria apply to initial reviews, continuing reviews, and amendments of previously approved research. Not all criteria apply to limited IRB review (see Section 6.1).

(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 should 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 should 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 should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving subjects vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative (LAR), in accordance with, and to the extent required by the Federal Regulations [45 CFR 46.116].

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by the Federal Regulations [45 CFR 46.117].

(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, mentally disabled persons, or economically or educationally disadvantaged persons, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

While pregnant women are no longer described as vulnerable within the above criteria, the IRB shall continue to apply Subpart B “Additional Protections for Pregnant Women, Human Fetuses and Neonates” as described in Appendix A. The revised Common Rule does not eliminate or modify Subpart B.

### 7.5.1 Risk/Benefit Assessment

The goal of the assessment is to ensure that the risks to research participants posed by participation in the research are justified by the anticipated benefits to participants or society. The IRB must:

- Judge whether the anticipated benefit, either of new knowledge or of improved health or other direct benefit for the research participant, justifies asking any person to undertake the risks; and
- Disapprove research in which the risks are judged unreasonable in relation to the anticipated benefits.

The assessment of the risks and benefits of proposed research involves a series of steps:

1. **Identify the risks** associated with the research, as distinguished from the risks of activities, diagnostic tests, treatments, or therapies participants would receive even if not participating in research;

2. **Determine whether the risks are minimized** to the extent possible by evaluating the necessity of procedures that impart risk and whether the data could be gained by procedures that are already being performed for other purposes or by alternative procedures that impart less risk;

3. **Identify the anticipated benefits** to be derived from the research, both direct benefits to participants and possible benefits to society, science and others; and
4. **Determine whether the risks are reasonable in relation to the benefits**, if any, and assess the importance of the knowledge to be gained.

In addition to evaluation of the risks in the research, the IRB determines, based on the materials submitted by the investigator, that research studies have the resources necessary to protect participants, such as adequate time for the researchers to conduct and complete the research, adequate number of qualified staff, adequate facilities, access to a population that will allow recruitment of the necessary number of participants, availability of medical or psychosocial resources that participants might need as a consequence of the research.

The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks and benefits that fall within the purview of its responsibility.

#### 7.5.1.1 Scientific or Scholarly Review

In order to assess the risks and benefits of the proposed research, the IRB must determine that:

- The research uses procedures consistent with sound research design; and
- The research design is sound enough to reasonably expect the research to answer its proposed question.
- The knowledge expected to result from the research is sufficiently important to justify the risk

In making this determination, the IRB will draw on its own knowledge and expertise, with the following exceptions:

(1) If the proposed study has undergone scientific peer review (e.g., through grant review process), there is no need for scientific review by the IRB. The external review will be noted in the meeting minutes and/or expedited reviewer stage of the Initial Submission form.

(2) If the proposed research is a dissertation, scientific review by the IRB is not required if the student provides verification from the student's full dissertation committee that they approve of the study design in its current format. The committee approval will be noted in the meeting minutes and/or expedited reviewer stage of the Initial Submission form.

(3) Departmental scientific review committees could be relied upon to conduct the scientific review. The Department Chair determines the composition of the departmental scientific review committee. The departmental scientific review committee findings will be noted in the meeting minutes and/or expedited reviewer stage of the Initial Submission form.

### 7.5.2 Equitable Selection of Participants

The IRB determines by reviewing the application, protocol/research plan, and other materials that the selection of subjects is equitable with respect to gender, age, class, etc. The IRB will not approve a study that does not provide adequately for the equitable selection of research participants or does not provide an appropriate scientific and ethical justification for excluding classes of persons who might benefit from the research. In making this determination, the IRB evaluates:

- The purposes of the research;
- The setting in which the research occurs;
- Scientific and ethical justification for including subjects vulnerable to coercion or undue influence such as children, prisoners, individuals with impaired decisionmaking capacity, or economically or educationally disadvantaged persons;
- The scientific and ethical justification for excluding classes of persons who might benefit from the research; and
- The inclusion/exclusion criteria, and the procedures/materials intended for use for the identification and recruitment of potential participants.

At the time of continuing review the IRB verifies that there have been no changes in the participant selection criteria that were originally set forth at the time of the initial IRB review and approval.

#### 7.5.2.1 Recruitment of Participants

The investigator provides the IRB with a plan for recruitment of all potential participants. All recruitment materials are submitted to the IRB, including advertisements, flyers, scripts, information sheets, and brochures. The IRB ensures, as part of its review, that the recruitment plan and materials appropriately protect the rights and welfare of prospective participants (e.g., do not present undue influence). See Section 7.5.10 for a discussion of IRB review of advertisements and Section 7.5.11 for a discussion of IRB review of payments.

#### 7.5.2.2 Number of Participants to be Enrolled

The investigator is required to provide the total number of subjects they plan to enroll. A subject is considered “enrolled” when they consent to participate in the study. When providing the total number, the investigator should consider the expected proportion of individuals who may consent but do not complete the study (either due to drop out or because their participation is discontinued by the research team). For example, if the investigator expects (based on similar projects) that 25% of subjects will not complete the study, the investigator should incorporate this information into their calculation of the total subjects the investigator plan to enroll and into their justification for their sample size in the Initial Submission form. If the investigator requires additional subjects due to missing data, file a modification with the IRB prior to surpassing their approved enrollment number.

### 7.5.3 Informed Consent

The IRB ensures that informed consent will be sought from each prospective participant or the participant's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116 and 21 CFR 50.20. In addition, the IRB ensures that informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117 and 21 CFR 50.27. The IRB ensures, as part of its review, that the information in the consent document and process is consistent with the research plan, and, when applicable, the HIPAA authorization. See Section 11 for detailed policies on informed consent.

### 7.5.4 Data and Safety Monitoring (for more than minimal risk research)

For research that is more than minimal risk, the investigator should submit a data and safety monitoring plan. The initial plan submitted to the IRB should describe the procedures for safety monitoring, reporting of unanticipated problems involving risks to participants or others, descriptions of interim safety reviews and the procedures planned for transmitting the monitoring results to the IRB.

The IRB reviews the data and safety monitoring plan and determines if it makes adequate provision for monitoring the reactions of participants and the collection of data to ensure the safety of participants and address problems that may arise over the course of the study. If a plan is not submitted, the IRB determines whether or not a plan is required, and, depending on the circumstances, what the plan should include. The overall elements of the monitoring plan may vary depending on the potential risks, complexity, and nature of the research study.

The factors the IRB considers in determining whether the data and safety monitoring plan is adequate for the research include:

1. Monitoring is commensurate with the nature, complexity, size and risk involved;
2. Monitoring is timely; frequency commensurate with risk; and conclusions reported to the IRB;
3. For low risk studies, close monitoring by the study investigator or an independent individual may be adequate and appropriate, with prompt reporting of problems to the IRB, sponsor, and regulatory bodies, as applicable;
4. The Data and Safety Monitoring plan should specify:
    - The entity or person(s) who will perform the monitoring, and the independence or affiliation that the entity or person(s) has with the sponsor or investigator;
    - The safety information that will be collected and monitored, including serious adverse events and unanticipated problems;
    - The frequency of review of safety data;
    - The procedure for analysis and interpretation of the data;
    - The procedure for review of scientific literature and data from other sources that may inform the safety or conduct of the study;

- The conditions that will trigger a suspension or termination of the research (i.e., stopping rules), if applicable;
- The procedure for reporting to the IRB, including a summary description of what information, or type of information, will be provided.

Under certain circumstances, the IRB may require, as a condition of approval, the establishment of an actual data safety monitoring board, or committee to ensure the safe conduct of the research. Details will be provided regarding steps to be taken, if this is required.

### 7.5.5 Privacy and Confidentiality

The IRB determines if adequate procedures are in place to protect the privacy of participants and to maintain the confidentiality of the data.

#### 7.5.5.1 Definitions

**Privacy**: Control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others. It is the state or condition of being free from unauthorized intrusion, being observed, or being disturbed by other people.

**Confidentiality:** Methods used to ensure that information obtained by investigators about participants is not improperly divulged.

**Private information**: Information that 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).

**Sensitive Information:** Data or information, on any storage media or in any form or format, which requires protection due to the risk of harm that could result from inadvertent or deliberate disclosure, unauthorized access, misuse, alteration, or loss or destruction of the information (e.g., could reasonably place the participant at risk of criminal or civil liability or be damaging to the participant's financial standing, employability, or reputation).

**Identifiable information**: Information where the identity of the participant is available to, or may readily be ascertained by, the investigator.

**Protected Health Information (PHI):** The Health Insurance Portability and Accountability Act (HIPAA) defines PHI as individually identifiable health information held or transmitted by a covered entity or its business association.

Individually identifiable health information is information, including demographic data that relates to:

(1) the individual's past, present or future physical or mental health or condition,

(2) the provision of health care to the individual, or

(3) the past, present, or future payment for the provision of health care to the individual, **and** that identifies the individual or for which there is a reasonable basis to believe it can be used to identify the individual.

*Note that PAU is not a covered entity. Therefore, usually researchers at PAU will not be creating PHI even if they are gathering individually identifiable health information. If an investigator is collaborating with another Institution that is subject to HIPAA regulations, the investigator should contact the HRPP Office to discuss how to ensure compliance.*

#### 7.5.5.2 Privacy

The IRB must determine whether the activities in the research appropriately protect the privacy of potential and actual participants. In order to make that determination, the IRB must obtain information regarding how the investigators plan to access participants and/or participants' private, identifiable information, and the participants' expectations of privacy in the situation. Investigators must have appropriate authorization to access participants or the participants' information.

In developing strategies for the protection of participants' privacy, consideration is given to:

1. Methods used to identify and contact potential participants;
2. Settings in which a participant will be interacting with an investigator;
3. Appropriateness of all personnel present for research activities or having access to identifiable research data;
4. Methods used to obtain information about participants, and the nature of the requested information including minimizing the information obtained to achieve the aims of the research;
5. Information that is obtained about individuals other than the "target subjects," (e.g., a participant provides information about a family member for a survey) and whether such individuals meet the regulatory definition of "human subject".

#### 7.5.5.3 Confidentiality

The IRB must determine if appropriate protections are in place to minimize the likelihood that information about participants will be inappropriately divulged. Safeguards designed to protect confidentiality should be commensurate with the potential of harm from unauthorized, inappropriate or unintentional disclosure.

At the time of initial review, continuing review, and with any requests for revisions, the IRB assesses whether there are adequate provisions to protect data confidentiality. The IRB does this through the evaluation of the methods used to obtain, record, share, and store information about individuals who may be recruited to participate in studies and about individuals who agree to participate. The investigator provides the IRB with the plan to protect the confidentiality of research data and sensitive information, including information security procedures (use, maintenance, storage, and transmission) and the protection of paper documents and other physical media (e.g., audio or videotapes). The IRB reviews all information received and determines whether or not the confidentiality of research data is sufficiently protected. In some cases, the IRB may also require that a Certificate of Confidentiality be obtained to additionally protect research data (See Section 23.4).

In reviewing confidentiality protections, the IRB considers whether or not the data or other information accessed or gathered for research purposes is sensitive and the nature, probability, and magnitude of harms that would be likely to result from a disclosure of collected information outside the research. The IRB considers regulations and organizational policies and evaluates the effectiveness of proposed de-identification techniques, coding systems, encryption methods, methods of transmission, storage facilities, access limitations, and other relevant factors in determining the adequacy of confidentiality protections.

Research regulated by the FDA that involves the use of electronic data collection/storage systems must also comply with the requirements of 21 CFR Part 11.

### 7.5.6 Vulnerable Populations

Certain individuals, by nature of age or mental, physical, economic, educational, or other situation, may be more vulnerable to coercion or undue influence than others. At the time of initial review the IRB considers the scientific and ethical reasons for including vulnerable participants in research. The IRB may determine and require that, when appropriate, additional safeguards be put into place for vulnerable participants, such as those without decision-making capacity, or those in whom decision-making capacity is impaired.

For an extensive discussion about the IRB's review and approval process for individual populations of vulnerable participants, see Section 12.

## 7.6 Additional Considerations

### 7.6.1 Determination of Risk

At the time of initial and continuing review, the IRB makes a determination regarding the risks associated with the research. Risks associated with the research are classified as either “minimal” or “greater than minimal”. Risk determinations may fluctuate over the life of a research plan, depending on the procedures and risks to which the participants are exposed as the research progresses. The level of risk associated with the research influences eligibility for expedited review. The meeting minutes will reflect the convened IRB's determination regarding risk levels; expedited reviewers will document the determination of risk level on the IRB Manager Reviewer Form stage of the Initial Submission Form.

### 7.6.2 Period of Approval

At the time of initial review and at continuing review, the IRB makes a determination regarding the frequency of review of the study. All studies are reviewed by the IRB at intervals appropriate to the degree of risk. Annual Reports are required for studies requiring Limited IRB Review or expedited review but that do not require Continuing Review (see Section 7.8.2). For research subject to the Common Rule, the IRB will conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk of the research, but not less than once per year, except as described elsewhere in these SOPs (e.g., Seciton. 7.2.1);

In some circumstances, a shorter review interval (e.g., semi-annually, quarterly, or after accrual of a specific number of participants) may be required (see below). The meeting minutes will reflect the convened IRB's determination regarding review frequency; expedited reviewers will document the determination of review frequency on the Reviewer Form Stage of the Initial Submission Form.

### 7.6.3 Review More Often Than Annually

The following factors are considered when determining which studies require review more frequently than once per year:

1. The probability and magnitude of anticipated risks to participants;
2. The likely medical/psychological/social/legal/educational condition of the proposed participants;
3. The qualifications of the investigator and other members of the research team;
4. The specific experience of the investigator and other members of the research team in conducting similar research;
5. The nature and frequency of adverse events observed in similar research;
6. The novelty of the research, which may make unanticipated events/problems more likely;
7. The involvement of vulnerable populations likely to be subject to undue influence or coercion (e.g., undocumented individuals, terminally ill patients);
8. A history of serious or continuing non-compliance on the part of the investigator; and
9. Any other factors that the IRB deems relevant.

In specifying that continuing review is required, the IRB may define the period with either a time interval or a maximum number of participants either studied or enrolled. If a maximum number of participants studied or enrolled is used to define the approval period, the number of participants studied or enrolled determines the approval period only when that number of participants is studied or enrolled in less than one year (i.e., the approval period may not exceed one year even if the maximum number of participants has not yet been reached). If an approval period of less than one year is specified by the IRB for research that is subject to continuing review, the reason for more frequent review must be documented in the minutes or the IRB Member Review Form.

### 7.6.4 Independent Verification That No Material Changes Have Occurred

The IRB recognizes that protecting the rights and welfare of study participants sometimes requires that the IRB use sources other than the investigator to independently verify that no material changes occurred since previous IRB review.

The IRB determines the need for verification from outside sources on a case-by-case basis. When determining which studies require verification from outside sources, the IRB considers all factors, including, but not limited to:

1. The probability and magnitude of anticipated risks to participants;
2. The likely medical/psychological/social/legal/educational condition of the proposed participants;
3. The probable nature and frequency of changes that may ordinarily be expected in the type of research proposed;
4. Concern about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports or from other sources;
5. Investigators who have previously failed to comply with federal regulations and/or the requirements or determinations of the IRB; and
6. Research without a routine monitoring plan.

In making a determination about independent verification, the IRB may prospectively require that such verification take place at predetermined intervals during the approval period, or may require such verification at the time of continuing review, review of amendment requests, and/or report of an unanticipated problem.

If the IRB finds that any material changes have occurred without IRB review and approval, the IRB decides the corrective action to be taken (See Section 15 on Non-compliance).

### 7.6.5 Consent Monitoring

In reviewing the adequacy of informed consent procedures for proposed research, the IRB may determine that monitoring of the consent process by an impartial observer (e.g., consent monitor) is required in order to reduce the possibility of coercion and undue influence, ensure that the approved consent process is being followed, and/or ensure that participants are truly giving informed consent.

Such monitoring may be particularly warranted for:

1. High risk studies;
2. Studies that involve particularly complicated procedures or interventions;
3. Studies involving highly vulnerable populations (e.g., ICU patients, children who are wards);
4. Studies involving study staff with minimal experience in obtaining consent; or

5. Other situations when the IRB has concerns that the consent process may not be/is not being conducted appropriately (e.g., prior investigator non-compliance, etc.).

Monitoring may also be appropriate as a corrective action where the IRB has identified problems associated with a particular investigator or a research project.

If the IRB determines that consent monitoring is required, the IRB Chair and the HRPP Administrator develop a proposed monitoring plan and submit it to the IRB for approval. The consent monitoring may be conducted by IRB staff, IRB members, or another party, either affiliated or not with Palo Alto University. The investigator is notified of the IRB's determination and the reasons for the determination. Arrangements are made with the investigator for the monitoring of the consent process, typically for a specified number of participants. When observing the consent process, the monitor determines:

- Whether the informed consent process was appropriately conducted and documented;
- Whether the participant had sufficient time to consider study participation;
- Whether the consent process involved coercion or undue influence;
- Whether the information was accurate and conveyed in understandable language; and
- Whether the participant appeared to understand the information and gave voluntary consent.

Following the monitoring, a report of the findings is submitted to the IRB, which determines the appropriate action, if any, to be taken.

### 7.6.6 Investigator Qualifications

The IRB relies upon other PAU processes to verify the status and qualifications of faculty to conduct human subjects research and to oversee such research conducted by students.

### 7.6.7 Investigator Conflicts of Interest (COI)

The IRB Manager Initial Submission Form asks specific questions to identify potential COI of the investigator and research team and any COI management plan in place. As part of its review process, the IRB makes a final determination as to whether any COI is adequately addressed and protects the human participants in the research. The IRB has final authority to determine whether the declared COI and the management plan, if any, allow the study to be approved. (See Section 20 for a more detailed discussion of COI.)

### 7.6.8 Institutional Conflicts of Interest

The IRB has final authority to determine whether the Institutional Conflict, the Financial Interest, and the management plan, if any, allow the study to be approved. See Section 20.3 for a more detailed discussion of Institutional COI.

### 7.6.9 Significant New Findings

During the course of research, significant new knowledge or findings about the research and/or the condition under study may develop. The investigator must report any significant new findings to the IRB and the IRB reviews them with regard to the impact on the participants' rights and welfare. Because the new knowledge or findings may affect the risks or benefits to participants or participants' willingness to continue in the research, the IRB may require, during the ongoing review process, that the investigator contact the currently enrolled participants to inform them of the new information. The IRB communicates this requirement to the investigator. If the study is still enrolling participants, the consent document should be updated. The IRB may require that the currently enrolled participants be re-consented or otherwise provided with the new information. The IRB may also require that former participants be provided with the new information (e.g., if it affects their rights or welfare).

### 7.6.10 Advertisements and Recruitment Materials

The IRB must review and approve any and all recruitment materials prior to posting and/or distribution for studies that are conducted under the purview of Palo Alto University. The material the IRB reviews includes, but is not limited to:

1. The information contained in the advertisement;
2. The mode/method of its communication;
3. The final copy of printed advertisements or screenshots of web-based advertisements; and
4. The proposed script for in-person recruitment and/or final audio/video taped advertisements.

This information is submitted to the IRB with the initial application or, if recruitment is proposed after study approval, as an amendment.

The IRB reviews the material to assure that the material is accurate and is not coercive or unduly optimistic, creating undue influence on the participant. For example, the material must not include statements implying a certainty of favorable outcome or other benefits beyond what was outlined in the consent document and the research plan.

As with consent processes and documents, the IRB does not allow exculpatory language to be present in ads or recruitment material.

Recruitment materials should be limited to the information prospective participants need to determine possible eligibility and interest. When appropriately worded, the following items may be included:

1. The name and contact information for the investigator and/or research facility;
2. The condition being studied and/or the purpose of the research;
3. The location of the research and the person or office to contact for further information;

4. A clear statement that that study involves research and not treatment;
5. In summary form, the criteria used to determine eligibility for the study;
6. The time or other commitment required; and
7. A brief list of potential benefits.

Once approved by the IRB, an advertisement may not be altered or manipulated in any way without prior IRB approval.

For recruitment materials, the first contact prospective study participants make is often with a person who follows a script to determine basic eligibility for the specific study. This script and any screening questions for eligibility must be submitted with the initial IRB application (or submitted as an amendment request if developed after the study is approved), including a plan for the storage and protection of potential participants' contact information and any data from the screening questions that will be maintained. The IRB reviews the procedures to be followed and verifies that they adequately protect the rights and welfare of prospective participants.

The IRB recognizes that recruitment through external agencies (e.g., Qualtrics Panels) sometimes involves very brief messages from the agency with minimal content. Please provide as much information as possible regarding what subjects will receive.

### 7.6.10.1 Social Media Accounts and Research Recruitment

All of the above apply to the use of social media accounts for recruitment. In addition, the IRB must review:

1. The profile names and pictures that are associated with the account(s) that will post the materials.
2. A list of platforms that will be used (e.g., Facebook, X, Instagram, Tiktok, YouTube).
3. Either one of the following:

(a) a list of all sites the investigator will use or

(b) criteria the investigator will apply to choose sites that are appropriate to their subject population as described in the xForm and provide examples. Their criteria must match their desired sample as described in this xForm.

4. Their plan for responding to or otherwise managing public comments from subjects or others on social media.
5. Their plan for responding to private messages from subjects or others on social media.

Lab-based or study-based social media accounts are preferred to the use of personal social media accounts. The use of personal networks may undermine the generalizability of the sample, thus undermining the study's ability to reasonably expect the research to answer its proposed question (see Scientific or Scholarly Review, Section 7.5.1.1). Additionally, personal contacts may feel social pressure to participate even if the research team communicates the voluntariness of the study. Study teams may sometimes use personal accounts but must explain their appropriateness in the xForm. For example, a professional X (Twitter) account or LinkedIn account is less likely to result in a biased sample than a Facebook account that includes friends and family. Reasons for using personal accounts will be examined on a case-by-case basis.

If the investigator will approach closed groups to ask to post recruitment materials, they must provide the text of the message then will send to request permission.

### 7.6.11 Compensation provided to Research Participants

Compensation provided to research participants may be an incentive for participation or to reimburse a participant for travel and other out-of-pocket expenses incurred due to participation. However, compensation for participation is **not** considered a research benefit. Regardless of the form of remuneration, investigators must take care to avoid unduly influencing participants. The amount of compensation or reimbursement must be proportional to the time and inconveniences posed by participation in the study.

Investigators who wish to compensate research participants must submit to the IRB the amount and schedule of all payments. Investigators must indicate in the IRB application the justification for such payment. Such justification should substantiate that proposed payments are <u>reasonable and commensurate</u> with the expected contributions of the participant and do not constitute (or appear to constitute) undue pressure on the potential participant to volunteer for the research study.

The IRB must review both the amount of payment and the proposed method and timing of disbursement to assure that neither entails problems of coercion or undue influence.

In studies that require the participant to complete procedures over a series of visits, compensation must be prorated and not be contingent upon the participant completing the entire study. The IRB does not allow payment to be contingent upon completion of the study. Any amount paid as bonus for completion of the entire study may not be so great that it could unduly induce a participant to remain in the study when he/she otherwise would have withdrawn.

The consent form must describe the terms of payment including the amount and schedule of payments and any conditions under which participants will receive partial payment (e.g., if they withdraw from the study before participation is complete) or no payment.

The plan for compensation, including who actually receives said compensation, when vulnerable subjects are involved (e.g., minors, cognitively impaired adults, etc.) will be assessed according to such factors as (a) amount of compensation, (b) means of compensation (e.g., money, gift cards etc.), and (c) other factors as deemed necessary by the IRB.

Investigators are responsible for coordinating with the Grants Office to ensure compliance with policies for gift cards and other compensation.

When research panels are compensated by an external agency (e.g., Qualtrics Panels) with a range of options (e.g., airline miles, hotel points, etc.), the study team should report the maximum value of the compensation even though it won’t be provided as dollars (e.g., airline miles worth no more than 10 dollars). Subjects must be informed in the consent that their compensation will be consistent with the information provided to them by the agency (in addition to notice regarding circumstances under which they will not be compensated).

There are tax implications for individuals who earn more than $600 per year as research participants. As such, the HRPP Administrator will consult with legal counsel and the PAU Accounts Office to ensure that appropriate language is provided in consent documents explaining the extent to which identifying information from the participant will be needed to track such information.

When appropriate, the following language must be included in the investigator's consent form:

> Please check one of the following:
>
> __ You are a U.S. Citizen or Resident Alien. If you are paid $600 or more a year from PAU, your social security number and amount paid will be reported to those in charge of taxes (IRS) and you may have to pay taxes on this money.
>
> __ You are a Nonresident Alien. For tax purposes, all payments made to you, including those for your participation in this study, are subject to a 30% tax withholding. All withholdings and payments will be reported to those in charge of taxes (IRS) by PAU.
>
> If you do not wish to be paid for your participation in this study, please initial here: ____

#### 7.6.11.1 Drawings as Compensation

When proposing to offer a research-related drawing as a form of compensation, investigators must follow these guidelines to minimize the likelihood of triggering legal issues.

a. Researchers should use the term "drawing" rather than "lottery" or "raffle," since the latter terms imply purchase of tickets by participants.

b. To further avoid the possibility that a drawing would be perceived as a lottery, the Initial Submission xForm should describe procedures for ensuring that all individuals who are contacted concerning the research will be allowed to enter the drawing. This would encompass individuals who are invited to participate but decline, prospective subjects who are ineligible, and subjects who enroll but do not complete the study. Additionally, the Initial Submission xForm should explicitly state that the drawing may be entered by any individual who asks to be included and provide procedures to enable such entries into the raffle.

c. The protocol and consent document(s) should also include the following information:

(1) Description of the prizes, including estimated value, and the total number of prizes to be awarded.
(2) The odds of winning a prize, if known, or explanatory language similar to this: “For any drawing, the odds of winning a prize depend on how many people are entered in the drawing. As we do not know how many people will participate in this study related drawing, we cannot predict what will be the odds of winning a prize.” (3) The approximate timing of the drawing (e.g., month/year).
(4) How drawing winners will be notified.

### 7.6.12 Non-Monetary Gifts and Incentives

Similar to financial incentives, non-monetary gifts or incentives can also present problems of undue influence or coercion that affect a potential participant’s ability to fully and freely consider participation in research.

If participants are provided with non-monetary gifts or tokens of appreciation, such as tote bags, books, toys, or other such materials, the approximate retail value must be described to the IRB, along with a description, photo, or sample product to review.

The IRB reviews all gifts and incentives, being particularly sensitive to the influence of power or authority, whether perceived or actual, over free decision-making. Overt coercion (e.g., threatening loss of credit, or access to services or programs, to which potential participants are otherwise entitled) is never allowed. Regardless of an individual’s choice of participation, it will have no adverse effect on his/her relationship with the organization, its staff or the provision of services in any way (e.g., access to medical care).

Investigators should carefully structure incentives and methods of disbursement so that the incentive may serve as a factor in the decision to participate, but not serve to unduly influence or coerce participation.

See Sections 7.5.6 and for discussion of special considerations for vulnerable populations, which apply here to non-monetary gifts and incentives as well.

### 7.6.13 State and Local Laws

The IRB considers and adheres to all applicable state and local laws in the jurisdictions where the research is taking place. The HRPP and IRB rely on Palo Alto University Counsel for the interpretation and application of California law and the laws of any other jurisdiction where the research is being conducted as they apply to participants in human research. The IRB ensures that consent forms are consistent with applicable state and local laws.

## 7.7 Possible IRB Actions

**Approve**: The research, proposed modification to previously approved research, or other item is approved. The IRB has made all of the determinations required for approval (i.e., approval criteria and any applicable special determinations (e.g., waivers, alterations, vulnerable population determinations, etc.). No further action is needed.

**Modifications Required in Order to Secure Approval**: The research, proposed modification to previously approved research, or other item undergoing review requires additional information or conditions that must be met before the research may be approved. The additional information or conditions must be prescriptive in nature, e.g., having the investigator confirm the IRB's understanding of an issue, or providing exact language of changes that are required to the submission. Use of this action means that the IRB is able, based on the assumption that the conditions are satisfied, to make all of the determinations required for approval (i.e., approval criteria and any applicable special determinations such as waivers, alterations, vulnerable population determinations, etc.).

The required modifications are documented in the IRB minutes for research reviewed at a convened meeting or in the IRB Manager Reviewer Form Stage for research reviewed under an expedited review procedure.

When the convened IRB requires additional information or conditions prior to approval, the IRB designates the IRB Chair, reviewer(s), other qualified individual(s) or staff to review the investigator's response and determine that the conditions have been satisfied. If the conditions have not been satisfied, or are only partially satisfied, the response is referred to the convened IRB for review. When an expedited reviewer requires additional information or conditions prior to approval the original expedited reviewer and/or other qualified individual(s) receives the response.

The date of approval is the date the conditions were determined to be met. For continuing reviews: If the research expires before the conditions are reviewed and approved, all research activities must stop until approval is obtained.

After verification, the following is documented in IRB records and written communication to the investigator:

- The date when verification was made that all IRB conditions have been satisfied (i.e., the "effective date of approval"); and
- The date by which continuing review must occur or by which the study team must submit an Annual Report (as applicable).

The IRB is informed of the outcome of the review of the investigator's response in the next available meeting agenda.

**Deferred:** This action is taken by the convened IRB when substantive revisions are required in order to determine that one or more criteria for approval are satisfied (e.g., the risks and benefits cannot be assessed with the information provided).

The decision and the basis for it are documented in the IRB minutes (for convened review) or IRB Manager Reviewer Form Stage (for expedited review) and are communicated to the investigator in writing.

When the convened IRB defers a study, the response from the investigator is provided to the convened IRB for review at a subsequent meeting.

**Disapprove:** The IRB may determine that the proposed research cannot be conducted at Palo Alto University, by employees or agents of Palo Alto University or otherwise under the jurisdiction of Palo Alto University. Disapproval can only be decided at the convened IRB meeting. An expedited reviewer cannot disapprove a study or revisions to a study already approved.

**Tabled:** The IRB does not take an action on the agenda item, e.g., quorum is lost, reviewers are absent, submission items are missing etc.

## 7.8 Continuing Review

The IRB conducts a continuing review of certain ongoing research at intervals that are appropriate to the level of risk for each research plan, but not less than once per year, except as noted in Section 7.8.2 below. The date by which continuing review must occur is recorded in the IRB minutes or other IRB records and communicated in writing to the investigator.

### 7.8.1 Approval Period

At the time of initial review and at continuing review, the IRB makes a determination regarding the frequency of review of the research study. Studies that require continuing review are reviewed by the IRB at intervals appropriate to the degree of risk but no less than once per year. Studies that do require continuing review are addressed in Section 7.8.2. See Section 7.6.3 for a detailed discussion of Review More Often than Annually. For a new investigator or an investigator who has recently had a study suspended by the IRB due to regulatory concerns, an on-site review by a subcommittee or designee of the IRB might occur or approval might be subject to an audit of study performance after a few months of enrollment, or after enrollment of the first several participants. The review frequency is documented in IRB Manager and meeting minutes reflect the approval start and end date.

For a new study reviewed by the IRB, approval commences on the date that the IRB conducts its final review of the study; that is, the date that the convened IRB or expedited reviewer approves the research **or** the date ("effective date") that it is verified that the requirements of the IRB have been satisfied following an action of "Modifications Required in Order to Secure Approval." The expiration date of the initial approval period, which is the date by which the first continuing review must occur, may be as late as one year after the effective date of initial IRB approval. IRB approval ends at midnight on the expiration date of the approval (i.e., the expiration date is the last day research can be conducted).

The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of research must occur by midnight of the date when IRB approval expires. If the IRB performs continuing review within 30 days before the IRB approval period expires, the IRB may retain the anniversary date as the date by which the continuing review must occur.

The use of the effective date of IRB approval to determine the latest permissible date for continuing review *only applies to the first continuing review*. For all subsequent continuing reviews of a research study, the date the convened IRB or the expedited reviewer conducts continuing review and approves the study determines the latest permissible date of the next continuing review.

The approval date and approval expiration date are clearly noted on IRB determination letters and must be strictly adhered to. Investigators should allow sufficient time for development and review of continuing review submissions.

IRB review of a proposed modification to research does not alter the date by which continuing review must occur. This is because continuing review is review of the full research project, not simply a change to it.

### 7.8.2 Studies that do not Require Continuing Review

Under the revised Rule, continuing review of research is not required for the following types of research:

(1) Research eligible for expedited review in accordance with 45 CFR 46.110

(2) Research reviewed by the IRB in accordance with the limited IRB review described in 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(c), or (d)(7) or (8)

(3) Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB approved study:

(a) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or

(b) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

(4) Exempt research.

For research that fits into these categories, the PAU IRB still may determine continuing review ***is*** required when:

(1) Required by other applicable regulations (e.g., FDA)

(2) Required by the terms of a grant, contract, or other agreement

(3) The research involves topics, procedures, or data that may be considered sensitive or controversial;

(4) The research involves particularly vulnerable subjects or circumstances that increase subjects' vulnerability;

(5) An investigator has minimal experience in research or the research type, topic, or procedures; and/or

(6) An investigator has a history of noncompliance.

When the PAU IRB determines that continuing review is required for such research, it will document the rationale in the IRB record and communicate the requirement to the investigator in the IRB determination letter.

### 7.8.2.1 Responsibilities of Investigators when Continuing Review is Not Required:

Even though continuing review by the IRB may not be required for the above referenced categories the following requirements still apply:

(1) **Investigators must comply with reporting requirements**, including:

(A) submitting a modification request prior to making any changes to their procedures or study staffing

(B) notifying the IRB of any protocol deviations, complaints, non-compliance, unanticipated problems, or new potential conflicts of interest

(C) notifying the IRB if any information becomes available that suggests a change to the potential risks or benefits of the research.

(2) **Investigators must submit an annual progress report** (the Annual Report xForm in IRB Manager) to the IRB indicating whether the study is active (allowing for post-approval monitoring), and allowing for the assessment of institutional requirements (e.g., training and COI status of current research team). The only studies that do not require an annual progress report are those that were granted exemption status without the need for limited IRB review.

The Annual Report form will also include a question regarding whether subjects are still being enrolled. Investigators will be asked to verify current study staff list, whose required CITI training must be up-to-date and documented in IRB Manager. A reminder to complete the Annual Report form will be sent to the Principal Investigator 90 days, 60 days, and 30 days prior to the one-year anniversary of approval.

### 7.8.3 Continuing Review Process

As a courtesy to investigators, the HRPP Office sends 3 renewal reminders, 90, 60 and 30 days prior to expiration for expedited studies and 90, 60, and 45 days prior to expiration for studies that require full board review; however, it is the investigator's responsibility to ensure that the continuing review of ongoing research is approved prior to the expiration date. By federal regulation, no extension to that date can be granted. No changes may be made with the continuing review submission.

Investigators must submit the following for continuing review:

1. The continuing review form in IRB Manager, which will include information about the number and type of subjects enrolled to date, any available preliminary analyses, and a list of all protocol deviations and anticipated adverse events (see Section 13). Protocol exceptions and unanticipated problems involving risk to participants or others should have already been reported to the IRB during the review period;

2. A copy of the consent document of the last subject enrolled in the study, with subject name redacted, if applicable;
3. The most recent multi-center progress and /or safety report, if applicable; and
4. Clean copies of consent documents and recruitment materials for updated approval stamp

All information is submitted electronically and IRB members have access to the complete study file at all times.

### 7.8.4 Approval Considerations

In order to re-approve research at the time of continuing review, the IRB must determine that the regulatory criteria for approval continue to be satisfied. Because the research was previously found to satisfy the criteria for approval, the IRB focuses its considerations at the time of continuing review on whether any new information is available that would affect the IRB's prior determination that the criteria for approval are satisfied. The IRB pays particular attention to four aspects of the research:

1. Risk assessment and monitoring;
2. Adequacy of the informed consent process; 3. Local investigator and organizational issues; and

4. Research progress.

### 7.8.5 Convened Board Review

In conducting continuing review of research not eligible for expedited review, all IRB members are provided with access to all of the materials listed in Section 7.8.3 and are responsible for reviewing the project summary, the current consent document, the progress report, and, if applicable, the data and safety monitoring report, and multi-center study progress reports. The primary reviewer is responsible for reviewing the complete materials submitted for continuing review including the complete research plan and is given access to, and should review, the complete IRB file. At the meeting, the primary reviewer assists the Chair in leading the IRB through the discussion of the submission and the regulatory criteria for approval.

Review of currently approved consent documents occurs during the continuing review of research by the IRB. If the Continuing Review contains information that might alter the protocol, study procedures or consent document, for example the identification of new risks, the IRB considers whether changes are needed to the consent document, protocol or study procedures. If a change is needed to the consent document(s), consideration should be made regarding notification to currently enrolled subjects via a consent addendum.

### 7.8.6 Expedited Review

In conducting continuing review under expedited procedures, the reviewer receives all of the previously noted materials. The reviewer determines whether the research meets the criteria for continuing review using the expedited procedure, and if so, whether the research continues to meet the regulatory criteria for approval. If the research subject to the 2018 Requirements (the revised Common Rule) no longer requires continuing review (See Section 7.8.2) and the IRB reviewer determines that continuing review is required, the reviewer shall document the rationale in the xForm.

If research did not qualify for expedited review at the time of initial review, it does not qualify for expedited review at the time of continuing review, unless it has progressed to the point that it involves only one or both of the following:

- i) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
- ii) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care;

Expedited review is also available at the time of continuing review in limited circumstances described by expedited review categories (8) and (9) (see Expedited Review Categories in Section 7.2.1). It is also possible that research activities that previously qualified for expedited review have changed or will change such that expedited IRB review is no longer permitted for continuing review.

### 7.8.7 Possible IRB Actions after Continuing Review

At the time of Continuing Review, the Convened IRB or IRB Member(s) conducting expedited review may take any of the following actions (see Section 7.7 for a detailed description of these actions):

1. Approve
2. Modifications Required
3. Deferred
4. Tabled

Additionally, the convened IRB may vote to disapprove the study. If an IRB member conducting expedited review believes that the study should be disapproved, it is referred to the convened IRB for review. If the IRB has significant concerns, the IRB may vote to suspend or terminate the research (See Section 8 for a detailed discussion of suspensions and terminations).

### 7.8.8 Lapse in Approval

The regulations permit no grace period or approval extension after approval expires. Research that continues after the approval period has expired is research conducted without IRB approval. If re-approval does not occur before the stated expiration date, all research activities must stop, including recruitment (media advertisements must be withdrawn), enrollment, consent, interventions, interactions, data collection, and analysis of identifiable data, except as noted below. This must occur even if the investigator has submitted the Continuing Review form through IRB Manager before the expiration date. Expiration Notices are sent to Investigators the day following approval expiration. This occurs even if the investigator has submitted a Continuing Review form. The notice reminds investigators that all research activities must stop.

All submissions of studies for continuing review where approval has lapsed, or lapses during the period of IRB review but prior to IRB approval, will require inclusion of a statement from the investigator regarding a) research activities that occurred during the period of lapsed approval b) reason for lapse c) corrective actions taken to prevent recurrence of lapsed approval in the future.

The lapse of IRB approval due to a failure to complete continuing review and obtain re-approval prior to expiration of the prior approval does not ordinarily constitute a suspension or termination of IRB approval, for federal reporting purposes; however, the failure to meet continuing review obligations may be grounds for suspension or termination of the research. If the IRB notes a pattern of non-compliance with the requirements for continuing review (e.g., an investigator repeatedly or deliberately neglects to submit materials for continuing review in a timely fashion or the IRB itself is not meeting the continuing review dates), the IRB should determine the reasons for the non-compliance and take appropriate corrective actions. The IRB must report to OHRP any instance of serious or continuing non-compliance with federal regulations or IRB requirements or determinations.

If approval expires, enrollment of new participants cannot occur. Temporarily continuing participation of already enrolled participants may be necessary or appropriate, for example, when the research interventions hold out the prospect of direct benefit to the participants, or when withholding those interventions or safety monitoring procedures might pose a harm to participants. In these instances, the investigator must notify the IRB, at the earliest opportunity, and submit a request to continue those research activities that are in the best interests of participants. Such a request should specifically list the research activities that should continue, and provide justification, and indicate whether the request applies to all or only certain participants. The IRB Chair or designee reviews the request and provides a determination regarding what activities, if any, may continue during the lapse. Such a determination may include a time limit or other conditions or restrictions. If the IRB decides that already enrolled participants should continue to receive the interventions that were being administered to participants under the research project, data collection (especially safety information) should also continue for such participants.

When Continuing Review is not required, but the research was subject to Limited IRB Review, Expedited Review, or Full Board Review, the investigator must submit an annual progress report in the form of the Annual Report in IRB Manager (see Section 7.8). If an investigator fails to either submit the progress report or submit a study closure form by the due date listed in their notification letter and in the reminder emails automatically generated in IRB Manager, the IRB will not review any forms submitted by the PI (new Initial Submission forms, Continuing Review forms for other studies, Modification forms, or Reliance Agreement Request forms) until either a Study Closure form or Annual Report form has been submitted.

#### 7.8.8.1 Time Limit to Seek Continuing Review after Lapse in Approval

When a study expires, if the investigator has not yet submitted a continuing review form in IRB Manager, they must submit such a form within 5 business days.

Whether the investigator files the Continuing Review form prior to or within 5 days of expiration, they will be given 30 days to secure IRB approval of the Continuing Review. Therefore, if the committee requests any changes or additional information in response to the Continuing Review form, the investigator must respond promptly. Upon approval of the continuing review, study activities may resume.

If the investigator either (1) fails to submit a continuing review form within 5 business days of expiration or (2) fails to secure final approval of the continuing review within 30 calendar days of expiration, the study will be administratively closed. The status of the study in IRB Manager will be changed to closed. No study activities may resume. The IRB Office will send out a study closure letter to the principal investigator, IRB Chair, HRPP Administrator, and the IO indicating the reason for the study closure.

If the investigator wants to resume study activities after this point, a new Initial Submission form must be submitted to the IRB.

If the IRB notes a pattern of non-compliance with the requirements for continuing review (e.g., an investigator repeatedly or deliberately neglects to submit materials for continuing review in a timely fashion), the IRB should determine the reasons for the non-compliance and take appropriate corrective actions.

## 7.9 Amendment of an Approved Protocol

Investigators may wish to modify or amend their approved applications. **Investigators must seek IRB approval before making any changes, no matter how minor, in approved research subject to limited IRB review, expedited review, or full board review**. Specific exceptions for exempt research are outlined in Section 7.9.2.

The only exception to this requirement is if the change is necessary to eliminate an immediate hazard to the participant (and if this occurs, the IRB must then be notified at once). Changes in approved research that are initiated without IRB approval to eliminate apparent immediate hazards to the participant are reviewed by the IRB to determine whether each change was consistent with ensuring the participants' continued welfare.

Amendments may make changes to the protocol for all remaining participants or circumstances in which the specific procedures called for in a protocol are not applicable or in the best interests of a specific participant or group of participants (for example: one participant is just slightly outside the eligibility window on his or her score on the Beck Depression Inventory, but meets all other inclusion/exclusion criteria). In the latter case, this is considered a protocol exception and is a change that is planned and has prior agreement from IRB and sponsor (if applicable). See Section 13 for details on Protocol Exceptions. Note: Protocol Deviations are unplanned and are reported to the IRB after the fact.

Investigators should contact the HRPP Office regarding proposed changes to the research that might alter the original scope, purpose, or intent of the research, as such changes will likely require a new study application rather than allow such changes to be made through an amendment to the existing research plan.

### 7.9.1 Procedures

Investigators must submit documentation to inform the IRB about the proposed changes to the study, including, but not limited to:

- Completed Modification form in IRB Manager;
- If the amendment involves changes to the protocol a detailed summary of changes;
- If the amendment involves changes to the consent/permission/assent documents, revised consent/parental permission/assent documents must be provided with a detailed description of the requested changes including the location of the changes in the form (i.e., which sections/paragraphs);
- If the amendment involves changes to other study materials, the revised materials must be provided with a detailed description of the requested changes including the location of the changes in the revised materials (e.g., page numbers, paragraphs);
- Other documentation proposed to be provided to participants when the proposed change(s) to the research might relate to their willingness to continue to participate in the study; and
- Any other relevant documentation provided by the sponsor or coordinating center.

The Modification form requires investigators to select each type of change being proposed, with follow-up questions required for each type of change (e.g., for adding study personnel, for changing consent form or process).  The HRPP Administrator and/or IRB Chair reviews the submission and makes an initial determination whether the proposed change(s) may be administratively acknowledged, approved through an exempt review process for exempt research, expedited review process for minor changes, or whether the modification warrants convened board review. The reviewer(s) using the expedited procedure has the ultimate responsibility to determine whether the proposed change(s) may be approved through the expedited review procedure and, if not, must refer the research study for convened board review.

### 7.9.2 Amending Exempt Research Not Subject to Limited IRB Review

If significant changes are to be made in studies previously determined to be "Exempt" by the IRB, the investigators must request permission to make the changes to the study following all procedures in Section 7.9.1.

For research that was found to be **EXEMPT** that did **not** require Limited IRB Review, minor modifications/changes may be made by the principal investigator without seeking IRB approval in advance. *Minor changes do not alter the level of risks to subjects nor do they add new study procedures.* The following changes to the protocol do not require IRB review and approval before implementation.

Investigators making changes to their consent and recruitment documents that fit the minor changes definition should submit a Modification xForm, which will receive administrative acknowledgment for the purpose of providing updated, stamped versions of these documents.

Administrative acknowledgment is completed by the IRB Chair or HRPP Administrator. The Modification xForm will not be sent to an IRB member for review; the change will be acknowledged and the newly stamped documents will be provided. If the Chair or Administrator notices a change that does not fit the minor change definition, the Modification xForm will undergo further review under exempt, expedited, or full board review procedures as applicable.

**Examples of minor changes to EXEMPT protocols that did NOT require Limited IRB review**:

- Editorial changes, correction of typographical errors, formatting change (without changing content) or administrative revisions (e.g., updating phone numbers) to consent documents or other study documents
- Adding non-sensitive questions. Non-sensitive questions are those whose answers, if disclosed outside the research, would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation. *Any questions about mental health symptoms or diagnoses, substance use, sexual activity, abuse (perpetration or victimization), illegal activities, or stigmatized identities are considered sensitive*.

| Example Non-Sensitive Question | Example Sensitive Question |
|---|---|
| Have you ever served in the US Armed Forces? | What was the reason for your discharge from the armed services? |
| What is your household income? | Have you ever been diagnosed with a mental health condition? |

- Re-ordering of questions in a survey or interview or minor changes to wording of approved questions (i.e., for improved clarity).
- Increasing or decreasing the number of subjects approved by the IRB by no more than 10%

A modification to the Exempt study intended to eliminate an apparent, immediate hazard to a subject does not require prior approval from the IRB; however, this change and the hazard to subjects must be reported to the IRB as soon as possible.

The following are examples of that **must** be approved by the IRB **prior to implementation**. This is not an exhaustive list. Any change that impacts the level of risks to subjects (whether listed below or not) must be approved in advance by the IRB. Please consult with the IRB if you are uncertain whether the changes you wish to make require approval prior to implementation.

**Examples of significant changes to EXEMPT protocols that must be approved prior to implementation**

- Adding/removing Principal Investigator (PI), other investigators or research personnel who are directly involved in conducting research with study participants or who are directly involved in using study participants' identifiable private information during the course of the research.
- Changes to the subject population being recruited (e.g., addition of children, wards of the state, or prisoner participants, or any vulnerable population)
- Changes in recruitment procedures or addition of a new recruitment strategy
- Changes in the location of the study (e.g. from online to in-person, from on campus to community locations)
- Adding new study procedures (e.g., adding a survey when the exempt protocol included only a focus group; adding an interview when the exempt protocol included only record review).
- Changes to the survey or interview questions that address sensitive topics as noted above
- Changes to the survey or interview questions that include questions reasonably expected to provoke psychological anxiety or distress
- Changes to the funding source(s)
- Changes to collaborators
- Changes to research sites (e.g., addition of a community agency as a recruitment source)
- Changes related to financial (or other) conflicts of interest
- Collecting additional identifying information
- Changes in the planned compensation to participants

### 7.9.3 Convened IRB Review of Amendments

When a proposed change in a research study is not minor, the convened IRB must review and approve the proposed change at a convened meeting before the change can be implemented. The only exception is a change necessary to eliminate apparent immediate hazards to the research participants. In such a case, the IRB should be promptly informed of the change following its implementation and should review the change to determine that it is consistent with ensuring the participants' continued welfare.

All IRB members are provided and review all documents provided by the investigator.

At the meeting, the Reviewer presents an overview of the proposed changes and assists the IRB Chair in leading the IRB through the completion of the regulatory criteria for approval. The IRB also determines whether the research with the proposed changes continues to meet the regulatory criteria for approval. The IRB considers whether information about the changes might relate to participants' willingness to continue to take part in the research and if so, whether to provide that information to past/current/future participants.

### 7.9.4 Expedited Review of Amendments

An IRB may use expedited review procedures to review minor changes in ongoing previouslyapproved research during the period for which approval is authorized. An expedited review may be carried out by the IRB Chair and/or experienced designee(s) among the IRB members.

The reviewer(s) determines whether the amendment meets the criteria allowing review using the expedited procedure, and if so, whether the research with the proposed modifications continues to meet the regulatory criteria for approval. The reviewer also considers whether information about the changes might relate to participants' willingness to continue to take part in the research and if so, whether to provide that information to past/current/future participants.

### 7.9.5 Administrative Acknowledgement of Amendments

In addition to the circumstances described in Section 7.9.2, certain very minor modifications to studies approved via expedited or full board review can be administratively acknowledged. Administrative acknowledgment will be completed by the IRB Chair or HRPP Administrator for certain minor modifications to ensure all necessary documentation is provided and no changes that require expedited or full board review are being made. The following minor modifications can receive administrative acknowledgment.

(1) *Change/rewording Study Title*: The IRB Chair or HRPP Administrator may approve title changes, provided that the wording change does not reflect a change in objectives or modification of methods or procedures.

ii) *Correction of Typos*: The IRB Chair or HRPP Administrator may approve correction of typos or grammar problems that do not change the previously approved intended meaning in any documentation (consent, recruitment, or data collection materials).

iii) *Format change*: The IRB Chair or HRPP Administrator may approve a layout change or rearrangement of the approved content for consent, recruitment, or data collection documents if the approved content itself is unchanged.

### 7.9.6 Possible IRB Actions after Amendment Review

The Convened IRB or IRB Member(s) conducting expedited review may take any of the following actions (See Section 7.7 for a detailed description of these actions):

1. Approve
2. Modifications Required
3. Defer
4. Disapprove*

*Only the convened IRB may vote to disapprove the proposed change(s). If an IRB member conducting expedited review believes that the proposed change should be disapproved, the amendment is referred to the convened IRB for review.

If the proposed change(s) raise significant concerns on the part of the IRB, the IRB may vote to suspend or terminate the research (See Section 8 for a detailed discussion of suspensions and terminations).

### 7.10 Closing a Research Study

The completion of the study, or early closure of the study, are changes in activity and must be reported to the IRB. A final report to the IRB allows it to close its files as well as providing information that may be used by the IRB in the evaluation and approval of related studies.

Studies may be closed when the involvement of human participants ceases (interventions, interactions, observations, and the gathering, use, study, and analysis of identifiable private information, including specimens, are all complete). Studies may also be closed when the only remaining research activity involves the analysis of unidentifiable individual level data, or aggregate data sets.

For multi-center research, the study may be closed once all research activities (as above) are complete at Palo Alto University or any site for which the Palo Alto University IRB is the "IRB of record." If the investigator is serving as the lead investigator or Palo Alto University is the coordinating center the study must remain open as long as the coordinating center is still receiving, studying, using, or analyzing identifiable private information from other sites (even if local interventions, interactions, observations, and data gathering are complete).

Investigators submit a Study Closure xForm to the IRB, providing a summary of the research activity and any findings available at that time.

Investigators may maintain the data that they collected, including identifiable private data, if this is consistent with the IRB-approved research plan. However, investigators may not conduct any additional analysis of identified data without re-applying for IRB approval. Investigators must continue to protect the confidentiality of the data as described to the IRB and honor any other commitments that were agreed to as part of the approved research including, for example, future use of data or specimens, provision of research results to participants, and provision of any outstanding payments or compensation.

The HRPP Administrator reviews final reports and either closes the study, or requests additional information or confirmation of facts from the investigator.

### 7.11 Reporting IRB Actions

All IRB actions are communicated to the investigator, and designated research staff as applicable. The investigator receives electronic notification of approval. All approved documents are available electronically to the investigator, HRPP Administrator, HRPP Staff, and the IRB Chair and Vice Chair at all times. If applicable, a copy of the approved consent/permission/assent form(s) containing the IRB stamp with the approval and expiration dates. For revisions required, the notification identifies all conditions that must be satisfied and additional information requested. When a submission had been deferred, the notification includes the basis for the decision and all modifications and/or clarifications required. When a study is disapproved, terminated or suspended, the notification includes the basis for the decision. The investigator may respond in person or in writing.

All letters, notices and reminders to investigators are maintained in IRB Manager.

The IRB reports its findings and actions to the organization in the form of its minutes, which are distributed by HRPP Administrator to the Palo Alto University IO.

### 7.12 Failure to Respond

Failure to submit a response to IRB requirements within 30 days of the IRB date of determination results in a Failure to Respond Notice. Additional notices are sent every 30 days. When research has IRB approval, and the investigator fails to respond to requirements related to a subsequent submission (e.g., a request for modification), the HRPP Administrator or Chair reviews the circumstances, including any potential impact on human participants, and contacts the investigator to try to secure a response. If the investigator continues to be unresponsive, the failure of the investigator may be considered non-compliance and be reviewed in accordance with the procedures in Section 16. The investigator receives notification of non-compliance, including an explanation. An extension beyond 90 days may be granted by the IRB if sufficient cause is provided by the investigator.

### 7.13 Appeal of IRB Decisions

When the IRB disapproves a study, the IRB notifies the investigator in writing of the reason(s) for the decision. When research is suspended in part or in full, or terminated, the IRB notifies the investigator in writing of the suspension or termination and the reason(s) for the decision. The investigator may ask that the decision be reconsidered by submitting a request in writing to the IRB Chair. The request must contain the basis for the appeal, including any substantive new information that the Board did not have the opportunity to consider previously. The request is scheduled for review at a convened IRB meeting and the Investigator may be invited to attend the meeting.

Where there is disagreement between the IRB and the investigator regarding the nature and extent of the requested changes or the necessity of or basis for a suspension or termination, and these disagreements cannot be resolved, the investigator and/or the IRB may make an appeal to the IO for a resolution of the matter. The IO may organize a meeting to help facilitate discussion between the IRB and the investigator. While the IO may provide input and make recommendations to the investigator and IRB for expeditious resolution of the matter, final determinations for approval/disapproval remain under the purview of the IRB.

Because the IO is responsible for policies and procedures followed by the IRB, the IO may review IRB decisions to ensure that the decision-making process is appropriate. If the IO has concerns regarding the process that the IRB followed in making a decision, the IO may ask the IRB to reconsider the decision. However, the IO cannot overrule an IRB decision.

### 7.14 Research Previously Approved by Another IRB

When an investigator transfers research to Palo Alto University that was previously approved by another IRB, the investigator must submit the research for review under the procedures covered by this section. No research activity may take place under the jurisdiction of Palo Alto University without the appropriate review and approval.

Research determined to be exempt at the previous institution is reviewed according to the procedures in Section 6. All other research must be submitted as if it were undergoing initial review and is reviewed by expedited review or by the convened IRB. Research that solely involves the analysis of existing identifiable data may be considered under Expedited Review Category 5.

For research transfers where stopping research interventions might harm participants, the investigator may request permission from the IRB to continue research interventions under the oversight of the prior organization's IRB until final Palo Alto University approval is obtained.

## 8 Study Suspensions, Terminations

### 8.1 Suspension/Termination

IRB approval may be suspended or terminated if research is not being conducted in accordance with IRB or regulatory requirements (in California or the jurisdiction of data collection) or has been associated with unexpected problems or serious harm to subjects. (See Section 14 for a discussion of unanticipated problems and Section 15 for a discussion of non-compliance.) The IRB's authority to suspend or terminate research applies to all research subject to IRB approval, including exempt research with limited IRB review and research for which continuing review is no longer required.

**Suspension** of IRB approval is a directive of the convened IRB, IRB Chair, or IO to temporarily stop some or all previously approved research activities. Suspensions made by the IRB Chair or IO are reported to a meeting of the convened IRB. If IRB approval of a suspended research study expires and the suspension is lifted, a continuing review is required before the study may resume. Investigators must continue to provide reports on adverse events and unanticipated problems to both the IRB and sponsors just as if there had never been a suspension (i.e., all events that need to be reported during a study need to continue to be reported during the suspension period).

When approval of some or all research activities is suspended by the IRB, the IRB considers whether notification of study participants is required, as well as any other actions necessary to ensure that the rights, safety, and welfare of participants are appropriately protected.

The IRB shall notify the investigator in writing of a suspension and shall include a statement of the reasons for the IRB’s actions and any requirements or conditions associated with the suspension (e.g., notification of participants). The investigator shall be provided with an opportunity to respond in person or in writing.

Suspensions of IRB approval are reported promptly to the Palo Alto University IO, Department Chair, Grants Office and study sponsor(s), including federal department or agency heads (if the study is funded, and federal oversight agencies according to applicable federal and organizational requirements. See Section 17 for a detailed discussion of reporting requirements.

**Termination** of IRB approval is a directive of the convened IRB to permanently stop all activities in a previously approved research study. Terminated research studies are closed. When study approval is terminated by the IRB, in addition to stopping all research activities, the IRB considers whether notification of participants is required, as well as any other actions necessary to ensure that the rights, safety, and welfare of research participants are appropriately protected.

The IRB shall notify the investigator in writing of a study termination and shall include a statement of the reasons for the IRB's actions and any requirements associated with the termination (e.g., notification of participants). The investigator shall be provided with an opportunity to respond in person or in writing.

Terminations of IRB approval are reported promptly to the Palo Alto University IO, Department Chair, Grants Office and study sponsor(s), including federal department or agency heads (if the study is funded, and federal oversight agencies according to applicable federal and organizational requirements. See Section 17 for a detailed discussion of reporting requirements.

Note: Suspension or termination of research studies approved by the IRB can also be issued by Organization officials (e.g., Department Chairs) acting outside of and unrelated to the interests of the IRB (i.e., not necessarily related to protecting the rights and welfare of study participants, e.g., loss of departmental funding for a particular study). The investigator must report any suspension or termination of the conduct of research to the IRB.

## 8.2 Protection of Currently Enrolled and Former Participants

Before a study suspension or termination is put into effect the IRB Chair or IRB considers whether any additional procedures need to be followed to protect the rights and welfare of current and/or former participants. Such procedures might include:

- Transferring participants to another investigator/site
- Making arrangements for clinical care outside the research
- Allowing continuation of some research activities under the supervision of an independent monitor
- Requiring or permitting follow-up of participants for safety reasons

- Requiring adverse events or outcomes to be reported to the IRB and the sponsor
- Notification of current participants
- Notification of former participants

# 9 Reliance on External IRB Review

## 9.1 External IRB review

Palo Alto University investigators who collaborate with investigators at one or more institutions may wish to enter into reliance agreements to have a collaborating institutions' IRB review the activity on behalf of all sites. Such a decision should be made in consultation with the HRPP Office. It should be noted that effective January 2018, all NIH-funded multicenter studies are required to be reviewed by a single IRB, so discussions with the HRPP Office should commence as soon as the investigator knows that such a study is being proposed.

### 9.1.1 PAU Investigator Responsibilities for External IRB Review

1. Submit all paperwork to the external IRB per their requirements.
2. Submit the following to HRPP Office so that ceding to the external IRB can be documented, and institutional requirements can be reviewed and confirmed (submission can be submitted concurrently with #1 above, but will not be finalized and formally acknowledged until external IRB approval has been obtained):
   a. Palo Alto University IRB Reliance Agreement form in IRB Manager: this form is necessary for record-keeping, and to document the members of the study team who will be conducting the study locally at PAU;
   b. Protocol/research plan and consent documents;
   c. External IRB approval letter (when available); and
   d. External IRB's IRB Authorization Agreement (IAA) for review and signature by IO

### 9.1.2 Palo Alto University Responsibilities Prior to Accepting External Oversight for a Study

When the submission packet is received, the HRPP Administrator reviews the submission materials and verifies:

- Acceptability of external IRB review (given type of study, populations etc.)
- Investigator and study staff documentation (confirmation of training/credentialing, COI reporting, assessment of prior non-compliance or other issues)
- Ancillary approvals and organizational processes for financial disclosure/ COI management requirements, Finance Office review, and contract negotiation, and other required committee or ancillary reviews are either in process or completed.

Once the external IRB has approved the study, and PAU has acknowledged the local submission, the IAA will be signed and provided to the PAU investigator for their records and to supply to the external IRB. Additional reminders of local policies concerning special topics (e.g., reporting responsibilities to PAU, etc.) and Investigator Responsibilities may also be included in the notification to the investigator.

### 9.1.3 Palo Alto University Responsibilities Post Approval

Palo Alto University retains certain on-site responsibilities for all studies where Palo Alto University relied upon external IRB review. Reports of site monitoring activities that have any findings that potentially impact human subject protections must be shared between the external IRB and Palo Alto University.

Investigators approved through an external IRB review must still report changes to the study, including changes in study personnel (prior to the personnel assuming any study responsibilities), local unanticipated problems, complaints, non-compliance, Annual Report xForm(s), and and a Study Closure xForm to Palo Alto University's HRPP Office in compliance with Palo Alto University policy, in addition to any external IRB reporting requirements.

# 10 Documentation and Records

Palo Alto University's HRPP Office maintains adequate documentation of the IRB's activities. All records are accessible for inspection and copying by authorized representatives of OHRP, sponsors, and other authorized entities at reasonable times and in a reasonable manner.

## 10.1 IRB Records

IRB records include, but are not limited to:

1. Written operating procedures;
2. IRB membership rosters;
3. Training records documenting that investigators, IRB members, and IRB staff have fulfilled Palo Alto University's human research training requirements;
4. IRB correspondence including reports to regulatory agencies;
5. IRB Study Records (Study Files) including correspondence with investigator and research team;
6. Documentation of exemptions granted and documentation of when limited IRB review is a condition of exemption;
7. Convened IRB meeting minutes;
8. Reports to the IRB of expedited approvals (in the form of the meeting minutes);
9. Documentation of review by another institution's IRB, when appropriate, as well as associated IRB reliance and cooperative review agreements;

For nonexempt research involving human subjects covered by the Common Rule (or exempt research for which limited IRB review takes place as described in Section 6.1) that takes place at an institution in which IRB oversight is conducted by an IRB that is not operated by the institution, the institution and the organization operating the IRB shall document the institution's reliance on the IRB for oversight of the research and the responsibilities that each entity will undertake to ensure compliance with the requirements of this policy (e.g., in a written agreement between the institution and the IRB, by implementation of an institution-wide policy directive providing the allocation of responsibilities between the institution and an IRB that is not affiliated with the institution, or as set forth in a research protocol)

10. Documentation of independent or external investigator agreements ;
11. Palo Alto University's Federalwide Assurance;
12. Materials submitted to external review or accrediting organizations;
13. IRB Registrations; and
14. Documentation of complaints and any related findings and/or resolution.

### 10.2 IRB Study Files

The IRB maintains a separate IRB study file for each research application (study) that it receives for review. Research studies are submitted through the IRB electronic system and assigned a unique identification number by the system.

Accurate records are maintained of all communications to and from the IRB and are a part of the electronic study file. As of January 2018, all records for all active studies are stored in the IRB Manager system. The records available for each research study include, but are not limited to:

1. The initial application and all associated documents and materials;
2. Modification requests and all associated documents and materials;
3. Continuing review/progress reports and all associated documents and materials, including the rationale for conducting continuing review of research that otherwise would not require continuing review as described in Section 7.8.2;
4. Closure reports and all associated documents and materials;
5. Reports submitted after study or HUD approval including reports of significant new findings, data and safety monitoring reports, protocol violation reports, complaints, noncompliance, and reports of injuries to subjects including reports of potential unanticipated adverse device events and unanticipated problems involving risks to subjects or others;
6. IRB-approved consent, parental permission, and assent forms;
7. DHHS-approved sample consent form and protocol;
8. IRB reviewer forms and checklists (when expedited review procedures are used);

9. Documentation of scientific or scholarly review (if available);
10. Documentation of the type of IRB review. For exempt determinations and expedited review, this will include the category under which the review is allowed;
11. For expedited review, documentation of any findings and determinations required by the regulations and study-specific findings supporting those determinations, including, but not limited to, waiver or alteration of consent, waiver of documentation of consent, research involving pregnant women, fetuses, and neonates, research involving prisoners, and research involving children. For research reviewed by the convened board these findings and determinations are recorded in the minutes;
12. For expedited review, documentation of the risk determination and period of approval (when continuing review is required). For research reviewed by the convened board these determinations are recorded in the minutes;
13. For expedited review, the rationale for an expedited reviewer's determination under 45 CFR 46.110(b)(1)(i) that research appearing on the expedited review list described in 45 CFR 46.110(a) is more than minimal risk.
14. Documentation of all IRB review actions;
15. Notification of expiration of IRB approval to the investigator;
16. Notification of suspension or termination of research;
17. Letters to investigator informing them of IRB review outcomes;
18. IRB correspondence to and from investigators related to the protocol;
19. All other IRB correspondence related to the research;
20. For studies evaluating the safety or effectiveness of medical devices, documentation of the device determination (exempt, non-significant risk, significant risk); 21. Reports of unanticipated problems involving risk to subjects or others; and
22. Any statements of significant new findings provided to subjects.

### 10.3 The IRB Minutes

Draft minutes of the IRB meeting proceedings are written and available for review by the IRB Chair and members. Committee members are given one week after distribution of the draft to offer feedback regarding the minutes. After considering this feedback, the Chair makes the final determination that the minutes are accepted. Changes may not be made to finalized minutes without re-review by the IRB to verify accuracy.

A copy of IRB minutes for each IRB meeting is sent to the IO.

Minutes of IRB meetings contain sufficient detail to show:

1. Attendance

   a. Each member’s (or alternate’s) full name
   b. Each member’s (or alternate’s) representative capacity (e.g., scientist, non-scientist, unaffiliated, member who represents the general perspective of research subjects)
   c. Names of members and alternate members who are participating through videoconference or teleconference and documentation that those attending remotely received all pertinent material prior to the meeting and were able to actively and equally participate in all discussions
   d. Names of alternate(s) attending in lieu of specified (named) absent members (Alternates may substitute for specific absent members or categories of members only as designated on the official IRB membership roster)
   e. Names of any consultants present, a brief explanation of their expertise, and documentation to support that the consultant(s) did not vote
   f. Names of investigators present
   g. Names of other non-members and guests present, such as IRB staff and study coordinators

   **Note:** The minutes will indicate, by name, those members who enter or leave the meeting. The vote on each action will reflect the numbers of members present for the vote on that item.

2. The presence of a quorum throughout the meeting, including the presence of one member whose primary concern is in a non-scientific area.
3. When both a member and an alternate are present, the minutes will reflect if and when the alternate substituted for the member. Generally, the member votes, but an alternate may substitute when appropriate (e.g., the member has a conflict of interest, the alternate has needed expertise, etc.);
4. Business Items discussed, and any education provided
5. Actions taken, including separate deliberations, actions, and votes for each submission undergoing review by the convened IRB
6. Vote counts on these actions (Total Number Voting; Number voting for; Number voting against; Number abstaining; Number of those recused). When a member is recused due to conflict of interest, the name of the member and reason for the recusal will be noted
7. Basis or justification for actions disapproving or requiring changes in research
8. Summary of controverted issues and their resolution
9. Approval period for initial and continuing reviews, including the basis for a determination that continuing review is required for a study otherwise fitting the criteria in Section 7.8.2 and the basis for a determination that continuing review more often than annually is warranted

10. **For research subject to the revised Common Rule (2018 requirements)**: The rationale for requiring continuing review of research that otherwise would not require continuing review as described in Section 7.8.2
11. Risk determination for initial and continuing reviews, and modifications when the modification alters the prior risk determination
12. Justification for deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document
13. Study-specific findings supporting that the research meets each of the required criteria when approving a consent procedure that does not include or that alters some or all of the required elements of informed consent, or when waiving the requirement to obtain informed consent altogether
14. Study-specific findings supporting that that the research meets each of the required criteria when the requirements for documentation of consent are waived
15. Study-specific findings supporting that the research meets each of the criteria for approval for vulnerable populations under any applicable Subparts
16. Exempt/significant risk/non-significant risk device determinations and the basis for those determinations
17. Determinations of conflict of interest and acceptance or modification of conflict management plans
18. Identification of any research for which there is need for verification from sources other than the investigator that no material changes are made in the research.
19. Review and determinations related to interim reports (e.g., unanticipated problems or safety reports; modification requests; report of violation/deviations; serious or continuing noncompliance; suspensions/terminations, or subject complaints etc.)
20. A list of research approved under expedited review procedures, including limited IRB reviews conducted using expedited procedures, since the time of the last such report
21. When an IRB member or alternate has a conflict of interest (see Section 21.2) with the research under review, an indication that the IRB member or alternate was not present during the final deliberation or vote
22. Key information provided by consultants, either in person or in a report 23. Basis or justification for actions disapproving or requiring changes in research
24. Times that meeting convened and adjourned.

### 10.4 IRB Membership Roster

A membership list of IRB members is maintained and submitted to OHRP as required. The list contains the following information about members:

1. Name
2. Earned degree(s)
3. Employment or other relationship between each member and the organization (i.e., affiliated or non-affiliated). To be categorized as non-affiliated, neither the member nor an immediate family member of the member may be affiliated with Palo Alto University
4. Status as scientist or non-scientist. Members whose training, background, and occupation would incline them to view scientific activities from the standpoint of someone within a behavioral or biomedical research discipline are considered a scientist for the purposes of the roster, while members whose training, background, and occupation would incline them to view research activities from a standpoint outside of any biomedical or behavioral scientific discipline are considered a nonscientist.
5. Indications of experience, such as board certifications, licenses, and areas of practice sufficient to describe each member's chief anticipated contributions to IRB deliberations.
6. Representative capacities of each IRB member; including which IRB member(s) is a prisoner representative, and which IRB members are knowledgeable about or experienced in working with children, pregnant women, cognitively impaired individuals, and other subjects vulnerable to coercion or undue influence commonly involved in Palo Alto University research.
7. Role on the IRB (Chair, Vice-Chair, Member, Alternate Member)
8. Voting status
9. For alternate members, the primary member or class of members for whom the member could substitute

The HRPP Office must keep the IRB membership list current. The HRPP Office reports changes in IRB membership to OHRP within 90 days of the change.

### 10.5 Documentation of Exemptions

Documentation of verified exemptions consists of the reviewer's citation of a specific exemption category and written determination that the activity described in the investigator's proposed study meets the conditions of the cited exemption category, as detailed in Section 6. When an exemption includes limited IRB review, the documentation will include this fact and the IRB action taken on those aspects of the research subject to limited IRB review in accordance with the procedures described for the review procedures used (expedited or convened board) elsewhere in this manual.

### 10.6 Documentation of Expedited Reviews

IRB records for initial and continuing review by the expedited procedure include: the specific permissible category(ies) or status as exempt but requiring limited IRB review; that the activity described by the investigator satisfies all of the criteria for approval; the approval period (when applicable); and any determinations required by the regulations including study-specific findings justifying the following determinations:

1. Approving a procedure that waives or alters the informed consent process;
2. Approving a request for waiver or alteration of the requirement for documentation of consent;
3. Approving research involving pregnant women, human fetuses, or neonates;
4. Approving research involving children;
5. Approving research involving participants with diminished capacity; and
6. Approving research involving prisoners.

### 10.7 Access to IRB Records

The IRB has policies and procedures to protect the confidentiality of research information:

1. All paper IRB records are kept in locked filing cabinets or locked storage rooms. Archival paper records for studies that were closed by January 2018 are maintained in secure storage off-site. No paper records will be generated starting in January 2018. Doors to the HRPP Offices are closed and locked when the rooms are unattended. Appropriate access controls are maintained for electronic records.
2. Ordinarily, access to all IRB records is limited to the HRPP Administrator, IRB Chair, IRB members, authorized organizational officials, and officials of federal and state regulatory agencies. Research investigators are provided reasonable access to files related to their research. Appropriate accreditation bodies are provided access. All other access to IRB records is limited to those who have legitimate need for them, as determined by the IO and HRPP Administrator.
3. Records are accessible for inspection and copying by authorized representatives of federal regulatory agencies during regular business hours.
4. Records may not be removed from the HRPP Office; however, the HRPP Administrator provides copies of records for authorized personnel if requested.
5. All other access to IRB study files is prohibited.

### 10.8 Record Retention

In order to comply with the requirements of OHRP policy IRB records are maintained for at least three (3) years after completion of the research.

# 11 Obtaining Informed Consent from Research Participants

No investigator conducting research under the jurisdiction of Palo Alto University may involve a human being as a research participant without obtaining the legally effective informed consent of the participant or the participant's legally authorized representative, unless a waiver of consent has been approved by the IRB in accordance with Section 11.9. Except as provided in Section 11.10, informed consent must be documented by the use of a written consent form approved by the IRB.

The IRB evaluates both the consent process and the procedures for documenting informed consent to ensure that adequate informed consent is obtained from participants.

The following procedures describe the requirements for obtaining consent from participants in research conducted under the auspices of Palo Alto University.

## 11.1 Definitions

**Legally Authorized Representative**:
A legally authorized representative (LAR) is an individual or body authorized under applicable law to provide permission on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. If there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the nonresearch context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research. Under California law, the order of authority to provide consent on behalf of another is as follows:

(1) The person's agent pursuant to an advance health care directive.
(2) The conservator or guardian of the person having the authority to make health care decisions for the person.
(3) The spouse of the person.
(4) An individual as defined in Section 297 of the Family Code.
(5) An adult son or daughter of the person.
(6) A custodial parent of the person.
(7) Any adult brother or sister of the person.
(8) Any adult grandchild of the person.
(9) An available adult relative with the closest degree of kinship to the person.

**Legal guardian**: A person appointed by a court of appropriate jurisdiction.

## 11.2 Basic Requirements

No investigator conducting research under the auspices of PAU may involve a human being as a subject in research without obtaining the legally effective informed consent of the subject or the subject's legally authorized representative (LAR) unless a waiver of consent has been approved by the IRB of record. Except as provided in Sections 11.9 or 11.10 of these procedures, informed consent must be documented using a written consent form approved by the IRB.

The informed consent process involves three key features: (1) disclosing to the prospective research participant information needed to make an informed decision; (2) facilitating the understanding of what has been disclosed; and (3) promoting the voluntariness of the decision about whether or not to participate in the research.

Informed consent is more than just a signature on a form. It is a process of information exchange that includes discussion, questions and answers and (in the absence of a waiver) signing the consent document. The informed consent process is the critical communication link between the prospective research participant and an Investigator. The process begins when the participant/LAR first learns about the research and continues through the completion of the research study. The person obtaining consent must be sufficiently knowledgeable about the study to be able to answer questions and help potential study participants/LARs understand the study. Investigators must obtain consent prior to entering a participant into a study, gathering data about a participant, and/or conducting any procedures required by the research plan, including screening procedures, unless consent is waived by the IRB. See Section 11.9.1 for an exclusion for certain screening and recruitment activities.

If someone other than the investigator conducts the interview and obtains consent, the investigator needs to formally delegate this responsibility, and the person so delegated must have received appropriate training to perform this activity. The person so delegated must be knowledgeable about the research to be conducted and the consenting process, and must have the expertise be able to answer questions about the study including those regarding risks, procedures, and alternatives. The PAU IRB application solicits information regarding who will obtain consent; proposed changes to the personnel authorized to obtain consent must be submitted to the IPAU IRB for approval.

Sample or draft consent documents may be developed by a sponsor or cooperative study group. However, when the Palo Alto University IRB is the IRB of record for the study, the Palo Alto University IRB is the final authority on the content of a consent document that is presented to a potential study participant.

The IRB will evaluate both the consent process and the procedures for documenting informed consent to ensure that adequate informed consent is obtained from participants.

The following procedures describe the requirements for obtaining consent from subjects in research conducted under the auspices of PAU. When the PAU IRB is serving as the IRB of record for external sites or personnel, the below requirements may be adapted as appropriate based upon the local context where the research will occur (e.g., who may serve as a LAR).

### 11.3 Informed Consent Process

1. Before involving a human subject in research, an investigator shall obtain the legally effective informed consent of the subject or the subject's LAR.

2. An investigator shall seek informed consent only under circumstances that provide the prospective subject or the LAR sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence.
3. The information that is given to the subject or the LAR shall be in language understandable to the subject or the LAR.
4. The prospective subject or the LAR must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information.
5. Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or LAR in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension. The key information does not need to be repeated in the remainder of the form and redundancies should be avoided. If the consent form is brief, the whole form may be considered to meet the requirement for a concise and focused presentation of key information.
6. Informed consent as a whole must present information relating to the research in sufficient detail, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or LAR's understanding of the reasons why one might or might not want to participate.
7. No informed consent process may include any exculpatory language through which the subject or the LAR is made to waive, or appear to waive any of the subject's legal rights or releases or appears to release the investigator, the sponsor, Palo Alto University or Palo Alto University employees or agents from liability for negligence.

These informed consent requirements are not intended to preempt any applicable federal, state, or local laws (including tribal laws passed by the official governing body of an American Indian or Alaska Native tribe) that have additional requirements for informed consent to be legally effective.

### 11.3.1 Additional Requirements

Informed consent must be obtained under the following circumstances:

1. Informed consent may only be obtained from subjects who have the legal and mental capacity to give consent. For subjects without that capacity, permission must be obtained from a legal guardian with appropriate authority to make decisions regarding the activities called for in the research or a legally authorized representative (LAR);
2. The informed consent information must be presented in language that is understandable to the subject (or LAR/guardian). To the extent possible, the language should be understandable by a person who is educated to 8th grade level and layman's terms shall be used in the description of the research. The IRB may require or allow different readability standards based upon the characteristics of the target subject population;

3. For subjects with Limited English Proficiency (LEP), informed consent must be obtained in a language that is understandable to the subject (or LAR/guardian). In accordance with this policy, the PAU IRB requires that informed consent discussions include a reliable interpreter when the prospective subject does not understand the language of the person who is obtaining consent, and, in most circumstances, that consent materials are translated;
4. The investigator is responsible for ensuring that each prospective subject is adequately informed about all aspects of the research and understands the information provided.

### 11.4 Determining a potential adult participant's ability to consent to research

A potential research participant has the capacity to consent to his or her own participation in a research activity if he/she demonstrates an appreciation:

1. That the activity is research;
2. Of the risks and benefits of a study;
3. Of the study procedures and requirements;
4. Of the alternatives that are available if not participating; and
5. That, if choosing not to participate, this decision is accepted without penalty

In reaching a decision about participation, it is essential for the potential participant to demonstrate an ability to use this information in a rational manner. Thus, in considering risks, benefits, and available alternatives, participants must show they understand the aspects of these factors that are unique to them as individuals.

See Section 12.8 for further discussion regarding adults who cannot give consent for themselves.

The decision-making capacity of a potential research participant should be evaluated when there are reasons to believe that the potential participant may not be capable of making voluntary and informed decisions about research participation. The investigator and research staff must have procedures in place for assessing and ensuring a participant's capacity to understand and make an informed decision. The IRB evaluates whether the proposed plan to assess capacity to give consent is adequate.

It is often possible for investigators and others to enable persons with some decisional impairments to make voluntary and informed decisions to consent or refuse participation in research. Potential measures include repetitive teaching, group sessions, audiovisual presentations, and oral or written recall tests, follow-up questions to assess understanding, video or audio-taping of consent interviews, second opinions, use of independent consent observers, allowing a waiting period before enrollment, or involvement of a trusted family member or friend in the discussion and decision making process.

Investigators and IRB members must be aware that some participants' decision-making capacity may fluctuate. For participants with fluctuating decision-making capacity or those with decreasing capacity to provide consent, periodic reevaluation of capacity and re-consent or consent for continued participation by a LAR may be necessary.

In the event that a research participant loses or becomes impaired in decision-making capacity after enrollment, and this is not anticipated in the research plan, the investigator is responsible for notifying the IRB. The investigator is responsible for developing a plan for the IRB's consideration that follows the guidelines outlined above for persons with fluctuating or diminishing capacity.

When a participant has the capacity to give consent, informed consent should be obtained and documented in accordance with Section 11.3. When a participant lacks the capacity to give consent, and the IRB has approved inclusion of individuals who cannot provide consent, investigators may obtain consent from the participant's LAR as described in Section 12.8. When consent will be obtained from the participant's LAR, the agreement of the participant should also be sought, if possible. The investigator should provide the IRB with a plan that describes when and how the participant's agreement will be obtained, including provisions that will be taken to promote understanding and voluntariness and how agreement will be documented. Under no circumstances may anyone be forced or coerced to participate.

If the investigator plans to use audio or videotapes, computer video presentations, or written materials to promote understanding, these materials must be provided to the IRB for review. If the investigator intends to use audio or video recordings to document consent or agreement, provisions to ensure the security of the recordings should be described to the IRB.

## 11.5 Elements of Informed Consent

### 11.5.1 Basic Elements of Informed Consent

To be valid, the informed consent process must provide the following basic elements of information to potential study participants or their LAR in a clear and concise manner:

1. A statement that the **study involves research**, an explanation of the **purposes** of the research and the **expected duration** of the subject's participation, a description of the **procedures** to be followed, and identification of any **procedures which are experimental**;
2. A description of any reasonably foreseeable **risks or discomforts** to the subject;
3. A description of any **benefits** to the subject or to others which may reasonably be expected from the research;
4. A disclosure of appropriate **alternative procedures** or courses of treatment, if any, that might be advantageous to the subject;
5. A statement describing the extent, if any, to which **confidentiality** of records identifying the subject must be maintained;
6. **For research involving more than minimal risk**, an explanation as to whether any compensation **and** an explanation as to whether any medical treatments are available

if injury occurs **and**, if so, what they consist of, or where further information may be obtained;

7. An **explanation of whom to contact** for answers to pertinent questions about the research and research subjects' rights, **and** whom to contact in the event of a research-related injury to the subject.

Please note, at PAU we expect both phone and email options to be provided for participants to be able to choose their preferred method of contact for both the study team and the IRB.

8. A statement that participation is **voluntary**, refusal to participate involves **no penalty or loss of benefits** to which the participant is otherwise entitled, and the participant **may discontinue participation at any time** without penalty or loss of benefits to which the subject is otherwise entitled;
9. One of the following statements about any research that involves **the collection of identifiable private information or identifiable biospecimens**:
    i. A statement that **identifiers might be removed** from the identifiable private information or identifiable biospecimens **and that**, after such removal, the information or biospecimens **could be used** for future research studies or distributed to another investigator for future research studies **without additional informed consent** from the subject or the legally authorized representative, if this might be a possibility; or

    ii. A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, **will not be used or distributed** for future research studies.

    In order to fully inform potential participants of potential uses of their data, the PAU IRB expects that option (i) will be utilized in most circumstances. If option (ii) is utilized, **no** additional uses beyond those explicitly described in the consent (*even by the study investigators*) are allowed.

### 11.5.2 Additional elements of informed consent to be applied, as appropriate:

1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;
2. Anticipated circumstances under which the subject may be removed by the investigator without regard to the subject's consent;
3. Any additional costs to the subject that may result from participation in the research;
4. When applicable, the amount and schedule of all payments;
5. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

6. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject;
7. The approximate number of subjects involved in the study.
8. A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;
9. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and
10. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

If the study is funded by NIH, and meets the NIH definition of a 'clinical trial', the following section should be added:

> "A description of this study will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this web site at any time."

### 11.5.3 Additional Considerations regarding Consent

All of the following reflect the expectations of the PAU IRB regarding information included in the consent. Reasons for any deviation(s) from these expectations must be provided in the Initial Submission xForm:

1. Both a phone number and email address for study team should be provided on the consent form, to facilitate subjects using the means they feel most comfortable with to contact the investigators.

2. If the PI is a student, at least one contact method for reaching their faculty advisor must be provided.

3. If the study is intentionally recruiting a vulnerable population (e.g., individuals with substance problems, individuals with mental health problems, individuals experiencing intimate partner violence), referral sources that are appropriate to the population being recruited should be provided in the consent form. Referral sources should not be provided only at the end of study participation, although investigators may provide referrals again at this time.

## 11.6 Subject Withdrawal or Termination

A subject enrolled in a research study may decide to withdraw from the research, or an investigator may decide to terminate a subject's participation in research regardless of whether the subject wishes to continue participating. Investigators must plan for the possibility that subjects will withdraw from research and include a discussion of what withdrawal will mean and how it will be handled in their research plans and consent documents. When seeking informed consent from subjects,

1. The investigator should inform subjects whether the investigator or study sponsor intends to either: (1) retain and analyze already collected data relating to the subject up to the time of subject withdrawal; or (2) honor a research subject's request that the investigator or study sponsor will destroy the subject's data or that the investigator or study sponsor will exclude the subject's data from any analysis.

When a subject's withdrawal request is limited to discontinuation of the primary interventional component of a research study, research activities involving other types of participation for which the subject previously gave consent may continue. Investigators should ask a subject who is withdrawing whether the subject wishes to participate in continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject would distinguish between study-related interventions and procedures and continued follow-up in person, by phone, or via records review.

If a subject withdraws from the interventional portion of the study, but agrees to continued follow-up as described in the previous paragraph, the investigator must obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original consent document). IRB approval of consent documents for these purposes would be required.

If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up, the investigator must not access or gather private information about the subject for purposes related to the study. However, an investigator may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.

### 11.6.1 Posting of Clinical Trial Consent Forms [§ 45 CFR 46.116(h)]

The revised Common Rule includes the following requirement:

> "(1) For each clinical trial conducted or supported by a Federal department or agency, one IRB-approved informed consent form used to enroll subjects must be posted by the awardee or the Federal department or agency component conducting the trial on a publicly available Federal website that will be established as a repository for such informed consent forms.
>
> (2) If the Federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a Federal website (e.g.,

confidential commercial information), such Federal department or agency may permit or require redactions to the information posted.

(3) The informed consent form must be posted on the Federal website after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol." [45 CFR 46.116(h)].

This requirement may be satisfied by either the awardee or the Federal department or agency.

At this time, two publicly available federal websites that satisfy the consent form posting requirement have been identified: ClinicalTrials.gov and a docket folder on Regulations.gov (Docket ID: HHS-OPHS-2018-0021). HHS and other Common Rule departments and agencies are developing instructions and other materials providing more information to the regulated community about this posting requirement.

Additional federal websites that would satisfy the revised Common Rule's clinical trial consent form posting requirement might be identified in the future.

Federal guidance or instructions regarding the implementation of this requirement was not available at the time this SOP went into effect. Until federal guidance or instructions are available, when PAU is the prime awardee, investigators should consult with the HRPP Administrator and Grants Office regarding how to satisfy this requirement.

### 11.7 Documentation of Informed Consent

Except as provided in Section 11.9 and 11.10 of this document, informed consent must be documented by the use of a written consent form approved by the IRB.

1. Informed consent is documented by the use of a written consent form approved by the IRB and signed (including in an electronic format) and dated by the subject or the subject's LAR at the time of consent;
2. For research conducted in accordance with ICH-GCP E6 or in facilities subject to Joint Commission requirements, the name of the person who obtained consent and the date they did so is documented on the written consent form;
3. A written copy of the signed and dated consent form must be given to the person signing the form. The investigator should retain the signed original in the research records. When appropriate, a copy of the consent form is uploaded into the electronic health record;

The consent form must be a written consent document that embodies the basic and required additional elements of informed consent. The investigator shall give either the subject or the subject's LAR adequate opportunity to read the informed consent form before it is signed; alternatively, this form may be read to the subject or the subject's legally authorized representative;

Although the regulations allow for the use of a “short form” consent document, Palo Alto University does not utilize this option.

## 11.8 Special Consent Circumstances

### 11.8.1 Enrollment of persons with limited English-language proficiency

1. **Expected enrollment**: In some studies, the investigator may be able to anticipate enrollment of persons who do not speak or read, or have limited proficiency in, oral or written English. When the target population includes such persons or the investigator and/or the IRB otherwise anticipates that the consent process will be conducted in a language other than English, the IRB requires a translated consent document and other participant materials to be prepared. In order to ensure that translated documents are accurate, the investigator must provide a signed translation accuracy form. The translation accuracy form cannot be completed by someone affiliated with the study due to their conflict of interest. The investigator may choose to wait to provide a translated form with the verification of translation accuracy until all study materials have been approved in English to avoid multiple edits to multiple forms. When a nonEnglish speaking participant enrolls, the participant signs the translated consent document and is given a copy of the signed translated consent document.
2. **Unexpected enrollment:** If a person who does not speak or read, or has limited proficiency in, English presents for possible enrollment, an IRB-approved translated version of the written consent may not be available for use. Investigators should carefully consider the ethical and legal ramifications of enrolling a participant when a language barrier exists. If the participant does not clearly understand the information presented during the consent process or in subsequent discussions, his/her consent may not be informed, and therefore, not effective.
3. **Use of interpreters in the consent process:** Unless the person obtaining consent is fluent in the prospective participant’s language, an interpreter is necessary to facilitate the consent discussion. Someone who is independent of the participant (i.e., not a family member) should assist in presenting information and obtaining consent. Whenever possible, interpreters should be provided copies of the translated consent document before (24 to 48 hours if possible) the consent discussion with the participant.

### 11.8.2 Braille consent

For blind participants who read Braille, the IRB may approve a consent document prepared in Braille. In order to assure that a Braille consent document is accurate, the IRB requires a signed verification of translation accuracy form. If possible, the participant signs the Braille consent document; otherwise oral consent is obtained, witnessed and documented as described under “Oral Consent” (see Section 11.8.4).

### 11.8.3 Consenting in American Sign Language (ASL)

For deaf participants who are fluent in American Sign Language (ASL), the IRB may approve a consent process using ASL and the IRB-approved written consent form. When this process is approved, the individual authorized to obtain consent from the prospective participant must use a certified interpreter fluent in ASL to conduct the consent process and the documentation of the consent process must conform to the requirements set forth in Section 11.7.

### 11.8.4 Oral Consent

When a potential participant is unable to read a written consent form (for example, is blind or illiterate), the IRB may approve an oral consent process, provided the potential participant (1) has the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is explained orally and (2) is able to indicate approval or disapproval to study entry.

For research that is no more than minimal risk, documentation of consent may be waived according to the criteria in Section 11.10.

For greater than minimal risk research, the consent form must be read to the potential participant and the participant must be given an opportunity to ask questions. An audiotape approved by the IRB may also be used. If capable of doing so, the participant signs, or marks an X to signify consent. If that is not possible, the participant provides oral consent. The person obtaining consent and a witness sign the written study consent form with a statement that documents that an oral process was used and, if necessary, that the participant gave oral consent. The consent process is also documented in the participant's research record. A signed copy of the consent form is given to the participant and a copy of the audiotape, if applicable.

## 11.9 Waiver or Alteration of Informed Consent

An IRB may waive the requirement to obtain informed consent, provided the IRB finds and documents that the below criteria are satisfied.

Likewise, an IRB may approve a consent procedure that omits some, or alters some or all, of the basic and additional elements of informed consent (an "alteration"), provided that the IRB finds and documents that the below criteria are satisfied. An IRB **may not** omit or alter any of the basic requirements for informed consent (See Section 11.2).

a) The research or clinical investigation involves no more than minimal risk to the subjects;

b) The research or clinical investigation could not practicably be carried out without requested waiver or alteration;

c) If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;

d) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

e) Whenever appropriate, the subjects or LARs will be provided with additional pertinent information after participation.

This option applies to both FDA-regulated and DHHS-conducted or supported research.

**Waiver or Alteration of Consent in Research Involving Public Benefit and Service Programs:**

An IRB may waive the requirement to obtain informed consent, provided the IRB finds and documents that the below criteria are satisfied.

Likewise, an IRB may approve a consent procedure that omits some, or alters some or all, of the basic and additional elements of informed consent (an "alteration") (See Sections 11.5.1 and 11.5.2), provided that the IRB finds and documents that the below criteria are satisfied. An IRB **may not** omit or alter any of the general requirements for informed consent (See Section 11.2).

(a) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:

1. Public benefit or service programs;
2. Procedures for obtaining benefits or services under those programs;
3. Possible changes in or alternatives to those programs or procedures; or
4. Possible changes in methods or levels of payment for benefits or services under those programs; and,

(b) The research could not practicably be carried out without the waiver or alteration.

This option **does not** apply to FDA-regulated research.

In order to approve a request from an investigator to waive the requirement for informed consent, or to omit or alter one or more basic or additional element of consent the investigators may be asked to provide justification, or additional information or documentation, to support that the above criteria are satisfied.

### 11.9.1 Screening, Recruitment or Determining Eligibility

An IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's legally authorized representative, if either of the following conditions are met:

1. The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or

2. The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

The above does not negate the requirements of other rules, such as HIPAA, when applicable. It also does not negate the requirement to obtain consent, or a waiver of consent, before involving a subject (including the use of their identifiable private information or biospecimens) in other research activities.

NOTE: Although this provision is not in **FDA regulations**, the FDA does not consider records review or oral communication with the subject prior to obtaining consent to be part of the clinical investigation, therefore waivers are not required.

### 11.10 Waiver of Documentation of Informed Consent

The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all participants if it finds **any** of the following:

1. The only record linking the participant and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality (e.g., domestic violence research where the primary risk is discovery by the abuser);

   **Note:** Participants must be asked whether they want documentation linking them with the research, and their wishes must govern. (When the research is completed entirely online and this option is the *sole* basis for granting the waiver of documentation, subjects must be asked if they want documentation linking them with the research, and their wishes will govern. They will be reminded of the risks of including their identifying information with their responses.)

   This option **does not** apply to FDA-regulated research.

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.

   **Note 1.** Procedures such as non-sensitive surveys, questionnaires and interviews generally do not require written consent when conducted by non-investigators (e.g., marketing surveys, telemarketing).

   This option **does** apply to FDA-regulated research (most commonly in the context of <u>minimal risk screening activities</u> that are necessary to determine eligibility for enrollment in a clinical trial).

OR

3. If the subjects or LARs are members of a distinct cultural group or community in which signing forms is not the norm, the research presents no more than minimal risk or harm to subjects, and there is an appropriate alternative mechanism for documenting that informed consent was obtained.

   This option **does not** apply to FDA-regulated research.

Unless the IRB has granted a full waiver of the requirement to obtain informed consent, investigators who seek and receive approval for a waiver of documentation of consent still must perform an adequate consent process.

In cases in which the documentation requirement is waived, the IRB requires the investigator to provide in the application materials a written summary of the information to be communicated to the subjects, and the IRB considers whether to require the investigator to provide participants with a written statement regarding the research. This is usually required by the PAU IRB.

The IRB's determination will be documented in the IRB record and communicated to the investigator.

## 12 Vulnerable Research Participants

When some or all of the participants in a research study conducted under the jurisdiction of Palo Alto University are likely to be vulnerable to coercion or undue influence or have diminished decision-making capacity, the research must include additional safeguards to protect the rights and welfare of these participants. The IRB must ensure that all of the regulatory requirements for the protection of vulnerable participants are met and that appropriate additional protections for the vulnerable population are in place.

### 12.1 Definitions

**Children.** Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research is conducted. According to California law, a person may consent to his or her own medical care at the age of eighteen.

California law also allows an emancipated minor to consent for his or her own medical care. According to California Family Code 7002, an emancipated minor is defined as an individual under the age of 18 who either (i) is or has been married; (ii) is on active duty with the armed forces of the United States; or (iii) has received a declaration of emancipated pursuant to Section 7122. California law allows any adult or emancipated minor to consent to participate in research. Legally emancipated minors may participate in research at PAU without the consent of a parent or guardian, if University legal counsel has advised that the evidence of legal emancipation provided by the minor to the investigator is sufficient.

Unemancipated minors may participate in research with the consent of a parent or guardian.

**NOTE**: For research conducted in jurisdictions other than California, the research must comply with the laws regarding the legal age of consent in the relevant jurisdiction(s). Palo Alto University's Legal Counsel must be consulted with regard to the laws in other jurisdictions.

**Guardian.** A guardian is an individual who is authorized under applicable state or local law to give permission on behalf of a child to general medical care.

In California, a "Guardian" is defined as a judicially appointed guardian or conservator having authority to make a health-care decision for an individual.

**NOTE:** For research conducted in jurisdictions other than California, the research must comply with the laws regarding guardianship in the relevant jurisdiction(s). Palo Alto University's Legal Counsel must be consulted with regard to the laws in other jurisdictions.

**Fetus.** A fetus means the product of conception from implantation until delivery.

**Dead fetus.** A fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.

**Delivery.** A delivery is a complete separation of the fetus from the woman by expulsion or extraction or any other means.

**Neonate.** A neonate is a newborn.

**Viable**. As it pertains to the neonate, viable means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.

**Nonviable neonate.** A nonviable neonate means a neonate after delivery that, although living, is not viable.

**Pregnancy.** A pregnancy encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.

**Prisoner.** A prisoner is any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

### 12.2 Involvement of Vulnerable Populations

If the IRB reviews research that involves categories of participants vulnerable to coercion or undue influence, the review process should include one or more individuals who are knowledgeable about or experienced in working with these participants. The IRB may include one or more individuals who are knowledgeable about or experienced in working with individuals from these populations or it may seek such expertise through the use of consultants.

45 CFR 46 has additional subparts designed to provide extra protections for vulnerable populations, which also have additional requirements for IRBs.

> Subpart B - Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research
>
> Subpart C - Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects
>
> Subpart D - Additional Protections for Children Involved as Subjects in Research

DHHS-conducted or supported research that involves any of these populations must comply with the requirements of the relevant subparts. Research funded by other federal agencies may or may not be covered by the subparts.

In its FWA, Palo Alto University limits its commitment to apply Subparts B, C, and D to nonexempt human subjects research conducted or supported by DHHS or any other federal agency that requires compliance with the Subpart(s) (B, C, or D) applicable to the research.

The following policies and procedures, which are based on Subparts B, C, and D, apply to all research regardless of funding. The individual sections describe how the subparts apply specifically to DHHS-funded research.

## 12.3 Responsibilities

1. The investigator is responsible for identifying the potential for enrolling vulnerable participants in the research proposal, including the possible inclusion of participants who may have impaired decisional capacity and who are being asked to participate in a research study with greater than minimal risk.
8. The IRB shall include representation, either as members or through the use of consultants, of individual(s) who are knowledgeable about or experienced working with the vulnerable populations involved in the research proposal under review.
9. The IRB reviews the investigator's justifications for including vulnerable populations in the research to assess appropriateness for inclusion in the research proposal.
10. The IRB must ensure that appropriate additional safeguards have been included in each study to protect the rights and welfare of vulnerable subjects at the time of initial review of the research proposal.
11. Information reviewed as part of the continuing review process should include the number of participants considered to be members of specific vulnerable populations.

## 12.4 Procedures

### Initial Review of Research Proposal:

1. The investigator identifies the intent to enroll vulnerable participants in the proposed research; provides justification for their inclusion in the study; and describes safeguards to protect the participant’s rights and welfare.
12. The IRB evaluates the proposed safeguards, including the proposed plan for obtaining consent from a legally authorized representative, if applicable, and agreement from vulnerable participants, when possible; determines the need for additional protections and considers, if appropriate, the use of a data and safety monitoring board, consent monitor or participant advocate.

**Continuing Review and Monitoring**. At Continuing Review the investigator should identify the number and categories of vulnerable participants enrolled and any problems that arose relevant to their rights and welfare.

## 12.5 Research Involving Pregnant Women, Human Fetuses and Neonates

According to the Palo Alto University Federalwide Assurance (FWA), Subpart B of 45 CFR 46 applies only to DHHS-funded research; the funding-source specific requirements are noted in the appropriate sections.

For research involving greater than minimal physical risk to these populations, PAU may cede review to an IRB with experience in the assessment of such risks, or may obtain a consultant with appropriate, applicable expertise. PAU’s IRB is unlikely to have sufficient expertise to review studies that present more than minimal physical risks to pregnant women, fetuses, and neonates. Please see Appendix A for details regarding research involving Pregnant Women or Fetuses.

## 12.6 Research Involving Prisoners

### 12.6.1 Applicability

*Prisoner* means any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

For research not conducted or supported by DHHS, where the risk to prisoners is no more than minimal (as defined in Section 12.6.2), no additional safeguards are required under these policies and procedures. However, the IRB may determine that additional safeguards or restrictions are warranted for a specific study.

For research involving more than minimal risk, and for research conducted or supported by DHHS (unless the research qualifies for exemption and only incidentally includes prisoners (See Section 6.2, the requirements outlined in this section apply.

As applicable, investigators must obtain permission from and abide by the requirements of correctional authorities and state or local law.

### 12.6.2 Minimal Risk

Minimal risk, in studies involving prisoners, means 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 <u>of healthy persons</u>.

### 12.6.3 Composition of the IRB

In addition to satisfying the general membership requirements detailed in other sections of these policies and procedures, when reviewing research involving prisoners, the IRB must also meet the following requirements:

1. A majority of the IRB (exclusive of prisoner members) must have no association with the prison(s) involved, apart from their membership on the IRB;
2. At least one member of the IRB must be a prisoner, or 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 need satisfy this requirement; and
3. The prisoner representative must be a voting member of the IRB. A comment may be added to the roster indicating that the prisoner representative will only count towards quorum when s/he is in attendance and reviewing studies involving prisoners.

If Palo Alto University were selected as a site for a multi-center study involving prisoners it could also opt to rely upon a properly constituted IRB from an institution participating in the research for the review §46.304(b).

### 12.6.4 Review of Research Involving Prisoners

Please see Appendix B.

## 12.7 Research Involving Children

The following applies to all research involving children, regardless of funding source. The requirements in this section are consistent with Subpart D of 45 CFR 46, which applies to DHHS-funded research.

For research involving greater than minimal physical risk to this population, PAU may cede review to an IRB with experience in the assessment of such risks, or may obtain a consultant with appropriate, applicable expertise.

### 12.7.1 Allowable Categories

In addition to the IRB's normal duties, research involving children must be reviewed by the IRB to determine if it fits within and is permissible under one or more federally-defined categories. Each procedure or intervention that the child will undergo for the research must be taken into consideration, and, if the research includes more than one study group assignment (e.g., placebo vs. active, investigational agent vs. comparator) a component analysis must be conducted by the IRB and the category determination must be made for each group assignment. The categories are as follows:

1. **[45 CFR 46.404] Research not involving greater than minimal risk.** Research determined not to involve greater than minimal risk to child participants may be approved by the IRB only if the IRB finds and documents that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians as set forth in Section 12.7.2.
2. **[45 CFR 46.405] Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual participant.** Research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual participant, or by a monitoring procedure that is likely to contribute to the participant's well-being, may be approved by the IRB only if the IRB finds and documents that:
    - The risk is justified by the anticipated benefit to the participants;
    - The relation of the anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative options; and
    - Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 12.7.2.
3. **[45 CFR 46.406] Research involving greater than minimal risk and no prospect of direct benefit to the individual participant, but likely to yield generalizable knowledge about the participant's disorder or condition.** Research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual participant, or by a monitoring procedure which is not likely to contribute to the well-being of the participant, may be approved by the IRB only if the IRB finds and documents that:
    - The risk represents a minor increase over minimal risk;
    - The intervention or procedure presents experiences to participants that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
    - The intervention or procedure is likely to yield generalizable knowledge about the participants' disorder or condition which is of vital importance for the understanding or amelioration of the disorder or condition; and

- Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 12.7.2.

4. **[45 CFR 46.407] Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate serious problems affecting the health or welfare of children.** When the IRB does not believe that the research meets the requirements of any of the above categories, and the IRB finds and documents that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, the IRB shall refer the research for further review as follows:

- HHS conducted or supported research in this category will be referred for review by the Secretary of Health and Human Services. However, before doing so the IRB must determine that the proposed research also meets all of the requirements of the Common Rule.
- For research that is not DHHS conducted, the IRB will consult with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, and law). Based on the recommendation of the panel, the IRB may approve the research if:
  - The research in fact satisfies the conditions of the previous categories, as applicable; or
  - All of the following:
    - The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
    - The research will be conducted in accord with sound ethical principles; and
    - Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 12.7.2.

### 12.7.2 Parental Permission and Assent

#### 12.7.2.1 Parental Permission

The IRB must determine that adequate provisions have been made for soliciting the permission of each child's parent or guardian.

Parents or guardians must be provided with the basic elements of consent and any additional elements the IRB deems necessary, as described in Section 11.5.

The IRB may find that the permission of one parent is sufficient for research to be conducted under Categories 1 [45 CFR 46.404] & 2 [45 CFR 46.405] above.  The IRB's determination of whether permission must be obtained from one or both parents will be documented in the reviewer's notes when a study receives expedited review, and in meeting minutes when reviewed by the convened committee.

Permission from both parents is required for research to be conducted under Categories 3 [45 CFR 46.406] & 4 [45 CFR 46.407] above unless

1. One parent is deceased, unknown, incompetent, or not reasonably available; or
2. When only one parent has legal responsibility for the care and custody of the child.

The IRB may waive the requirement for obtaining permission from a parent or legal guardian if:

- The research meets the provisions for waiver in Section 11.9 or
- The IRB determines that the research is designed to study conditions in children for which parental or guardian permission is not a reasonable requirement to protect participants (for example, neglected or abused children), provided that an appropriate mechanism for protecting the children who will participate in the research is substituted, and that the waiver is not inconsistent with Federal, State, or local law. The choice of an appropriate mechanism will depend upon the nature and purpose of the activities described in the protocol/research plan, the risks and anticipated benefits to the research participants, and the child's age, maturity, status, and condition.

Permission from parents or legal guardians must be documented in accordance with and to the extent required by Section 11.7.

#### 12.7.2.2 Assent from Children

The IRB must determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. This judgment may be made for all children to be involved in the study, or for each child, as the IRB deems appropriate.

If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that 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, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the participants are capable of giving assent, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accordance with the applicable regulations.

Because "assent" means a child's affirmative agreement to participate in research, the child must actively show his or her willingness to participate in the research, rather than just complying with directions to participate and not resisting in any way.

The IRB should take into account the nature of the proposed research activity and the age, maturity, and psychological state of the children involved when reviewing the proposed assent procedure and the form and content of the information conveyed to prospective participants. For research activities involving adolescents whose capacity to understand resembles that of adults, the assent procedure should likewise include information similar to what would be provided for informed consent by adults or for parental permission. For children whose age and maturity level limits their ability to fully comprehend the nature of the research activity, but who are still capable of being consulted about participation in research, it may be appropriate to focus on conveying an accurate picture of what the actual experience of participation in research is likely to be (for example, what the experience will be, how long it will take, whether it might involve any pain or discomfort). The assent procedure should reflect a reasonable effort to enable the child to understand, to the degree he or she is capable, what his or her participation in research will involve.

Parents and children will not always agree on whether a child should participate in research. Where the IRB has indicated that the assent of the child is required in order for him or her to be enrolled in the study, dissent from the child overrides permission from a parent. Similarly, a child typically cannot decide to be in research over the objections of a parent. There are individual exceptions to these guidelines but in general, children should not be forced to be research participants, even when permission has been given by their parents.

#### 12.7.2.3 Documentation of Assent

When the IRB determines that assent is required, it also is also responsible for determining whether and how assent must be documented. When the research targets very young children or children unable or with limited capacity to read or write, an oral presentation accompanied perhaps by some pictures with documentation of assent by the person obtaining assent in a research note is likely more appropriate than providing the child a form to sign. In this case, the investigator should provide the IRB with a proposed script and any materials that they intend to use in explaining the research. The assent process, along with the child’s decision, should be documented in the participant’s research record.

When the research targets children who are likely able to read and write, investigators should propose a process and form that is age appropriate and study specific, taking into account the typical child's experience and level of understanding, and composing a document that treats the child respectfully and conveys the essential information about the study. The assent form should:

1. Tell why the research is being conducted;
2. Describe what will happen and for how long or how often;
3. Say it's up to the child to participate and that it's okay to say no;
4. Explain if it will hurt and if so for how long and how often;
5. Say what the child's other choices are;
6. Describe any good things that might happen;
7. Say whether there is any compensation for participating; and 8. Ask for questions.

Illustrations might be helpful, and larger type and other age appropriate improvements are encouraged when they have the potential to enhance comprehension. Studies involving older children or adolescents should include more information and may use more complex language.

#### 12.7.2.4 Children who are Wards

Children who are wards of the State or any other agency, institution, or entity can be included in research approved under 45 CFR 46.406 or 45 CFR 46.407 (Categories 3 & 4 in Section 12.7.1), only if such research is:

1. Related to their status as wards; or
2. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as participants are not wards.

If the research meets the condition(s) above, an advocate must be appointed for each child who is a ward (one individual may serve as advocate for more than one child), in addition to any other individual acting on behalf of the child as legal guardian or in *loco parentis.* One individual may serve as advocate for more than one child.

The advocate must be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

## 12.8 Adults with Impaired Decision Making Capacity

The requirements in this section apply to all research involving adults who cannot provide consent or with impaired decision-making capacity regardless of funding source.

Research involving participants who do not have the ability to provide consent or who have impaired decision-making capacity should only be conducted when the aims of the research cannot reasonably be achieved without their participation. Participation of this population in research cannot be justified solely on their availability or the convenience for the investigator.

When an investigator seeks to include such participants in research, the investigator must disclose this to the IRB and provide justification for why inclusion is necessary. If capacity to consent is questionable, or may fluctuate, investigators should include provisions for determining capacity to provide informed consent (See Section 11.4), and, if appropriate to reevaluate capacity during participation. When capacity to consent may diminish, the procedures should include, when possible and appropriate, designation of a legally-authorized representative (LAR), inclusion of the LAR in the initial consent discussion and process, and documentation of the participant’s agreement, when possible. When the research includes participants who are likely to regain the capacity to consent, the investigator should include provisions to inform the participant regarding his or her participation and to seek consent for ongoing participation, if applicable.

When the IRB reviews research involving greater than minimal risk and the proposed participant population includes adults who cannot provide consent, may have impaired capacity to provide consent, or whose capacity can be expected to fluctuate over time, the IRB review process will include at least one member, or a consultant, who is experienced with or otherwise knowledgeable about the population.

In evaluating research, the IRB must be able to determine that the risks to participants are reasonable not only in relation to any benefits, but also in relation to the importance of the knowledge that may reasonably be expected to result. In considering the risks of research involving participants who are unable to provide informed consent or who have diminished capacity to do so, the IRB should consider whether any components of the research involve risks that are greater for participants with diminished capacity. For example, the population might experience increased sensitivity or discomfort to certain stimuli or may not be able to verbalize or otherwise demonstrate when they are experiencing discomfort or pain.

For research involving greater than minimal physical risk to this population, PAU may cede review to an IRB with experience in the assessment of such risks, or may obtain a consultant with appropriate, applicable expertise.

If the IRB has appropriate, applicable expertise to review a greater than minimal risk study involving adults unable to consent or with impaired decision-making capacity, the IRB will consider the following (as appropriate to the research):

1. Whether the aims of the research can reasonably be achieved without inclusion of the population;
2. Whether the research is likely to improve the understanding of the condition, disease, or issue affecting the impaired population;
3. Whether any experimental procedure or intervention has undergone pre-clinical testing or human testing on other populations and whether the data from that testing supports its use in the proposed research;
4. Whether the procedures or interventions that participants will undergo in the research place them at increased risk and if appropriate mechanisms are in place to minimize risks, when possible;
5. Whether the data and safety monitoring plan, including any stopping rules, is appropriate given the risks of the research and the vulnerability of the population;
6. Whether the procedures for withdrawing an individual participant from the research are appropriate;
7. Whether the recruitment procedures, consent process, and plans for financial compensation support voluntariness and minimize the likelihood of undue influence or coercion;
8. Whether participants will be exposed to financial or other risks that they might not consider acceptable if they had the capacity to provide consent, and whether appropriate mechanisms have been put into place to minimize these risks;
9. Whether procedures for determining capacity to provide consent, and for evaluating capacity on an ongoing basis, if applicable, are appropriate;
10. Whether the procedures for informing participants who regain capacity about their involvement in the research, and for obtaining consent for on-going participation, if applicable, are appropriate;

11. Whether assent should be required when possible, and, if so, if the proposed procedures to obtain and document assent are appropriate;
12. Whether a research participant advocate or consent monitor should be required for some or all participants.

# 13 Reportable Events

Regulations require an organization to have written procedures for ensuring prompt reporting of changes in research activity; unanticipated problems involving risk to participants or others; and any instances of serious or continuing non-compliance to the IRB, organizational officials, and applicable federal agencies. In order to comply with this requirement, Palo Alto University has procedures to review issues that arise during the conduct of research.

The following section provides definitions and procedures regarding issues that arise during the conduct of research that must be reported to the IRB.

## 13.1 Definitions

**Unanticipated problems involving risk to participants or others (UPs):** UPs refer to any incident, experience, outcome, or new information that:

1. Is unexpected
2. Is related or possibly related to participation in the research, and
3. Indicates that participants or others are at a greater risk of harm (including physical, psychological, economic, legal or social harm) than was previously known or recognized.

**Unexpected:** The incident, experience or outcome is not expected (in terms of nature, severity, or frequency) given the research procedures that are described in the study-related documents, such as the IRB-approved research protocol/research plan and informed consent documents; and the characteristics of the population being studied.

**Related:** There is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research.

**Adverse Event (AE):** For the purposes of these policies and procedures, an AE is any untoward or unfavorable (physical or non-physical) occurrence in a human research participant, which is temporally associated with the participant's participation in the research (though not necessarily related to participation in the research). AE's may or may not be anticipated. If they are unanticipated, and are related or possibly related to participation in the research, then they are unanticipated problems involving risk to subjects or others—see above definition. Anticipated AEs (e.g., those identified as a possibility in the approved IRB protocol) are to be documented by the investigator for each subject and must be reported at the time of continuing review.

**Protocol/Research Plan Deviations:** A protocol/research plan deviation is defined as a variation from the IRB approved research plan that happens without prior review and approval of the IRB (e.g., a study visit occurs outside protocol/research plan window, a subject is enrolled who does not meet eligibility criteria, etc.). Depending on the details, protocol/research plan deviations may be determined to be non-compliance (serious, continuing, or otherwise).

**Protocol/Research Plan Exceptions:** Protocol/research plan exceptions are planned deviations from the protocol/research plan. Exceptions are anticipated and must occur with prior approval by the IRB, and agreement from the sponsor (if applicable). If an exception is implemented without IRB approval, it is a deviation, even when it has received sponsor approval.

## 13.2 Procedures

### 13.2.1 Reporting

Investigators must report the following events or issues to the HRPP Office as soon as possible, but no later than 10 working days after the investigator first learns of the event:

1. Changes made to the research that are implemented without prior IRB approval, regardless of the reason, but including changes made to eliminate apparent immediate hazards to the participant(s);
2. Adverse events (either local or external) involving direct harm to participants enrolled by the investigator (i.e., local adverse events), which in the opinion of the investigator or sponsor, may represent an unanticipated problem involving risk to participants or others;
3. An unanticipated event related to the research that exposes participants to potential risk but that does not involve direct harm to participants;
4. An unanticipated event related to the research that results in actual harm or exposes individuals other than the research participants (e.g., investigators, research assistants, students, the public, etc.) to potential risk;
5. New information that indicates an increase to the risks or decrease to potential benefits of the research;
6. New information that may impact the willingness of participants to continue in the research;
7. A breach of confidentiality;
8. Incarceration of a participant in a study not approved to enroll prisoners;
9. Complaint of a participant when the complaint involves the health, safety, or rights of the participant or indicates unexpected risks, possible non-compliance, or cannot be resolved by the research team;
10. Protocol/research plan deviations, with the exception of minor deviations. Minor deviations (deviations that do not impact participant safety, compromise the integrity of study data, and/or affect the participant’s willingness to participate in the research) are to be reported at the time of continuing review;
11. Sponsor or lead investigator/coordinating center notifying PAU of a UP at another site, or an imposed suspension or termination of some or all research activities;

12. Any other event that indicates participants or others might be at risk of serious, unanticipated harms that are reasonably related to the research.

### 13.2.2 Submission of Reports

Investigators or the study team must complete the Reportable Events form in IRB Manager. This form will contain the following:

a. Detailed information about the event or issue, including relevant dates;
b. Any corrective and preventative actions, planned or already taken, to ensure that the issue or problem is corrected and will not occur again;
c. An assessment of whether any participants or others were placed at risk as a result of the event or suffered any harm (e.g., physical, social, financial, legal, or psychological) and any plan to address these consequences;
d. If a report from a sponsor/lead investigator, or coordinating center is the basis for the report of a possible unanticipated problem involving risks to participants or others, the report should be accompanied by an analysis from that entity detailing (1) how the event or problem meets the definition of a UP; (2) proposed studywide corrective actions or modifications to the research along with a timeline for anticipated completion of the actions; and (3) whether or not the problem has been reported as a UP to any relevant federal agencies;
e. If a sponsor, lead investigator or coordinating center suspends or terminates some or all research activities, the report should be accompanied by information from that entity detailing (1) why the suspension or termination was enacted; (2) if it was due to a possible UP (in which case the information in “d” above must be included); (3) any impact on participants or others and actions to be taken to protect participants; (4) any plan to inform participants of the suspension or termination and other pertinent information; and (5) whether the suspension or termination has been reported to any relevant federal agencies;
f. Other relevant information;

Reports are screened by the HRPP Administrator and immediately forwarded to the Chair, or designee, if s/he believes that intervention may be required to protect participants or others from serious harm.

Upon receipt of a report or complaint from someone other than the investigator or study staff on behalf of the investigator, the HRPP Administrator will notify the Investigator when appropriate. When an IRB staff member receives a complaint or report, they will initiate the Reportable Event from IRB staff xForm as soon as practicable.

### 13.2.3 IRB Procedures for Handling Reportable Events

1. Upon receipt of a written report of an event from an investigator, the HRPP

Administrator or their designee checks for completeness. If any applicable information (as detailed above) is missing or incomplete, the investigator is contacted to obtain additional information.

2. The IRB Chair, HRPP Administrator, and/or other experienced member(s) designated by the IRB Chair or HRPP Administrator receives and reviews the report. The reviewer(s) make the initial determination as to whether the event is as an unanticipated problem and/or non-compliance (See Section 14 for procedures for unanticipated problems, and Section 15 for serious or continuing non-compliance).
3. Based on the information received from the investigator, the IRB Chair, HRPP Administrator, or designee may suspend the research to ensure protection of the rights and welfare of participants. Suspension directives made by the IRB Chair or designee are reported to a meeting of the convened IRB and follow Palo Alto University notification procedures for IRB suspensions.
4. The HRPP Administrator, IRB, or the IRB Chair (or designee) has the authority to require submission of more detailed information from the investigator, the sponsor, or the study coordinating center about any event occurring in a research study as a condition of the continuation of the IRB's approval of the research.
5. If the IRB Chair or designee determines that the problem reported does not meet the definition of an unanticipated problem or serious or continuing non-compliance, the reviewer considers whether any corrective or preventative actions planned or already taken are sufficient and whether modifications to the research plan, consent document, or corrective action plan may be necessary, and refer the matter to the convened IRB for review, if appropriate. The results of the review are recorded in IRB Manager and communicated to the investigator.
6. If the reviewer determines that the event may be an unanticipated problem, or serious or continuing non-compliance, the report is reviewed at a convened IRB meeting and follows notification procedures for UPs.

# 14 Unanticipated Problems Involving Risks to Participants or Others

Palo Alto University complies with DHHS regulations that require organizations to have written policies on reporting unanticipated problems involving risks to participants or others (also referred to as UPs, UAPs, and UPIRTSOs) to the IRB, organizational officials and relevant federal agencies and departments.

This section provides definitions and procedures for the reporting of UAPs to the Palo Alto University IRB.  Investigators conducting research under the oversight of an external IRB must comply with the reporting requirements of the external IRB and the internal reporting requirements outlined in Section 9.

In conducting its review of protocol deviations, noncompliance, subject complaints, and other reportable events, the IRB will also consider whether the event or issue was caused by, contributed to, or otherwise related to an UAP.

## 14.1 Procedures

Except as noted below, all definitions and procedures outlined in Section 13 apply.

### 14.1.1 Reporting

Investigators must report the following events or issues to the IRB as soon as possible but within **7 working days** after the investigator first learns of the event using the “Reportable Event” xForm in IRB Manager.

If investigators are uncertain but believe that the event might represent an UAP, a report should be submitted.

Examples of UAPs include:

1. A single occurrence of a serious, unexpected event that is uncommon and strongly associated with the research procedures;
2. A single occurrence, or more often a small number of occurrences, of a serious, unexpected event that is not commonly associated the research procedures, but uncommon in the study population;
3. Multiple occurrences of an AE that, based on an aggregate analysis, is determined to be an unanticipated problem. There should be a determination that the series of AEs represents a signal that the AEs were not just isolated occurrences and involve risk to human subjects (e.g., a comparison of rates across treatment groups reveals higher rate in the treatment arm versus a control). A summary and analyses supporting the determination should accompany the report;
4. An AE that is described or addressed in the protocol or informed consent documents, but occurs at a specificity or severity that is inconsistent with prior observations. A discussion of the divergence from the expected specificity or severity should accompany the report;
5. A serious AE that is described or addressed in the investigator’s protocol or informed consent documents, but for which the rate of occurrence in the study represents a clinically significant increase in the expected rate of occurrence (ordinarily, reporting would only be triggered if there were a credible baseline rate for comparison). A discussion of the divergence from the expected rate should accompany the report;
6. AEs involving direct harm to subjects enrolled by the local investigator which in the opinion of the investigator or sponsor, may represent an UAP;
9. Any other AE or safety finding (e.g., based on animal or epidemiologic data) that indicates subjects or others might be at risk of serious, unanticipated harms that are reasonably related to the research. These would cause the sponsor to modify the investigator’s brochure, study protocol, or informed consent documents, or would prompt other action by the IRB to ensure the protection of human subjects. An explanation of the conclusion should accompany the report.

10. Reports (including reports from DSMBs/DMCs) that indicate that risks are greater than previously known or that indicate that the research should be modified, suspended, or halted.
11. Sponsor or lead investigator/coordinating center-imposed suspension or termination of some or all research activities;
12. An unanticipated event related to the research that exposes subjects or others to potential risk but that does not involve direct harm;
13. A breach of confidentiality or loss of research data (e.g., a laptop or thumb drive is lost or stolen);
14. An unanticipated event related to the research that results in actual harm or exposes individuals other than the research subjects (e.g., investigators, research assistants, students, the public, etc.) to potential risk;
15. New information that indicates increased risk, new risk(s), or decrease to potential benefit from what was previously understood. Examples include:

a. An interim analysis or safety monitoring report indicates that the frequency or magnitude of harms or benefits may be different than initially presented to the IRB;

b. A report or publication that indicates the risks, benefits, or merit of the research are different from what was previously understood.

#### 14.1.2 Review Procedures

1. Upon receipt of the Event Report, the IRB staff pre-reviews the submission and, if needed, contacts the investigator for corrections or additional information.

2. The IRB Chair or designated reviewer receives and reviews the report and makes the initial determination as to whether the event represents a UP. The reviewer has access to all study documents, including the complete study file, the current protocol, the currently approved consent/permission/assent document(s), previous UP reports and the investigator's brochure (if applicable). If needed, the Chair or designee may request additional information from the investigator, sponsor, or others (including study committees, such as data monitoring committees, data safety monitoring boards, or steering committees).

A. If the reviewer determines that the event does not meet the definition of a UP, they will determine whether any additional actions are necessary to ensure the protection of human subjects. As warranted, the reviewer may refer the matter to the convened IRB for review. The reviewer can require actions described above in Section 13. The results of the review will be recorded in review notes in IRB Manager and communicated to the investigator.

B. If the reviewer determines that the event may be an UP, the report will be referred for review by the convened IRB. The convened IRB will determine whether the event is an UP and whether any additional actions are necessary to ensure the protection of human subjects. If needed, the IRB may request additional information from the investigator, sponsor, or others. All IRB members have access to the report and supporting documentation and all study materials electronically. The results of the review will be recorded in the IRB minutes and communicated to the investigator.

1. Based upon the circumstances, the IRB may take any of the following actions, or others, to ensure the protection of human subjects:
   a. Require modifications to the protocol/research plan
   b. Revise the review frequency for continuing review
   c. Require a modification to the consent process
   d. Require a modification to the consent/permission/assent document(s)
   e. Require additional information be given to current participants, for example, when the event may relate to a participant's rights, welfare, or willingness to continue participation
   f. Require additional information be given to participants who have completed the study
   g. Require additional training of the investigator and/or study staff
   h. Require re-consent of participants currently enrolled
   i. Require additional monitoring of the research
   j. Require monitoring the consent process
   k. Report or refer to appropriate parties (e.g., legal counsel, research compliance, risk management, Institutional Official) for additional review
   l. Suspend approval
   m. Terminate approval
   n. Other actions as appropriate given the specific circumstances
2. If the IRB finds that the event is an UP, the IRB will follow the procedures for reporting to regulatory. Agencies, sponsors, and organizational officials in Section 17. When appropriate, a preliminary report may be submitted while more information is obtained to inform the determination or actions. Reports that have already been reported to the federal oversight agency (e.g., by a Sponsor, Coordinating Center, or Single IRB (sIRB) do not also need to be reported by Palo Alto University.

The IRB notifies the investigator in writing of its findings, with copies to the Department Chair, the IO, the Grants Office (if study is externally funded) in addition to any reports noted in Section 17. If the study is suspended or termination, all procedures in Section 8.

# 15 Non-compliance

This section provides definitions and procedures for the reporting and review of known or suspected noncompliance for research under the oversight of the Palo Alto University IRB.

Research under the oversight of an external IRB must comply with the reporting requirements of the external IRB and the internal reporting requirements outlined in Section 9.

In conducting its review of protocol deviations, unanticipated problems, subject complaints, and other reportable events, the IRB will also consider whether the event or issue was caused by, contributed to, or otherwise related to noncompliance.

### 15.1 Definitions

**Non-compliance**: Non-compliance is defined as any failure to follow applicable federal, state, or local laws, or institutional policies governing human subject protections, or the requirements or determinations of the IRB, including the requirements of the approved investigational plan (i.e., protocol deviations).

Noncompliance can result from performing an act that violates these requirements or failing to act when required. Non-compliance may be minor or sporadic or it may be serious or continuing.

**Minor non-compliance:** Minor non-compliance is defined as non-compliance that, in the judgment of the IRB, does not increase risks to participants or others, does not compromise the scientific integrity of the study, and does not affect participants' willingness to participate in the research.

**Serious non-compliance:** Serious non-compliance is defined as non-compliance that, in the judgment of the convened IRB, increases risk of harm to subjects, adversely affects the rights, welfare or safety of subjects or others, or adversely affects the integrity of the data or the research. Willful violation of regulations and/or policies may also constitute serious noncompliance.

**Continuing non-compliance:** Continuing non-compliance is defined as a pattern of noncompliance which continues after it has been determined that non-compliance occurred, including inadequate effort to take corrective actions or comply with IRB requirements within a reasonable timeframe.

**Apparent Non-Compliance** is an event that appears to constitute noncompliance, but the IRB has not yet made a formal assessment of the event.

**Finding of Non-Compliance:** Finding of Non-Compliance is defined as an allegation of noncompliance that is proven true, or a report of non-compliance that is clearly true (for example, audit finding of an unsigned consent document, or admission by an investigator that the protocol/research plan was willfully not followed. A finding of non-compliance must be categorized as minor, serious, or continuing.

### 15.2 Reporting

Investigators and their study staff are required to report instances of possible non-compliance to the IRB through the submission of a Reportable Events Form in IRB Manager. The investigator is responsible for reporting possible non-compliance by study personnel. Any individual or employee may report observed or apparent instances of non-compliance. This may be accomplished by calling the IRB, providing an email summary, or a written document outlining the non-compliance. An IRB staff person will submit the “Reportable Events Form for IRB Staff” when they are made aware of an apparent instance of non-compliance by someone other than the study team. The reporting party is responsible for making the report in good faith, maintaining confidentiality and cooperating with any IRB and/or organizational review of the report.

If an individual, whether investigator, study staff or other, is uncertain whether there is cause to report non-compliance, he or she may contact the HRPP Administrator or the IRB Chair directly to discuss the situation informally.

Reports of alleged serious or continuing non-compliance must be submitted to the HRPP Office within 10 working days of discovery. The report must include a complete description of the alleged non-compliance, including any personnel involved.

Reports may be made anonymously.

## 15.3 Review of Apparent Non-compliance

All allegations of non-compliance are reviewed by the HRPP Administrator, IRB Chair, or designee. The reviewer reviews the report or allegation and may request additional information or an audit of the research in question.

When the HRPP Administrator, IRB Chair, or designee determines that non-compliance did not occur because the incident was within the limits of an approved protocol/research plan for the research involved, the determination is reported in writing to the investigator and, if applicable, the reporting party. The determination letter is copied to any parties notified of the allegation at the outset.

If in the judgment of the HRPP Administrator, IRB Chair, or designee, the report or allegation represents non-compliance, the non-compliance is processed according to Section 15.4 (Review of Findings of Non-compliance).

If in the judgment of the HRPP Administrator, IRB Chair, or designee, an allegation or finding of non-compliance warrants suspension of the research before completion of any review or investigation to ensure protection of the rights and welfare of study participants, the IRB Chair may suspend the research as described in Section 8 with subsequent review by the IRB.

If the HRPP Administrator, IRB Chair, or designee determines that additional expertise or assistance is required to complete the review or investigation and may request assistance from the HRPP Office or form an *ad hoc* committee to assist with the review and fact gathering process. When an *ad hoc* committee assists in the review process, the Chair or designee is responsible for assuring that minutes of the meeting are generated and kept to help support any determinations or findings made by the *ad hoc* committee.

## 15.4 Review of Findings of Non-compliance

### 15.4.1 Minor Non-compliance:

When the IRB Chair or designee determines that non-compliance occurred, but the noncompliance does not meet definition of serious or continuing non-compliance, the determination is reported in writing to the investigator and, if applicable, the reporting party. The Chair or designee reviews any corrective and preventive actions taken or proposed by the investigator and determine if the actions are sufficient or if additional actions may be necessary. In the event that additional actions may be warranted, the matter may be referred to the convened IRB for review.

### 15.4.2 Serious or Continuing Non-compliance

When the IRB Chair or designee determines that non-compliance has occurred and that the noncompliance may meet the definition of serious or continuing non-compliance, the report of noncompliance is referred for review by the IRB at the next available convened meeting. The Chair or designee may call an emergency IRB meeting should the circumstances warrant.

All initial findings of potential serious or continuing non-compliance referred to the IRB are reviewed at a convened meeting.

The IRB may:

1. Find that there is no issue of non-compliance
2. Find non-compliance that is neither serious nor continuing and that an adequate corrective and/or preventive action plan is in place
3. Find serious and/or continuing non-compliance and require a corrective and/or preventive action plan or modification of a proposed plan
4. Find that additional information is required to make a final determination. The committee determines if the additional information requires review by the full committee or a subcommittee thereof; if the latter, a report is written by the subcommittee for review by the full committee for final determination.

### 15.4.3 Final Review

Upon a finding of serious or continuing non-compliance, the IRB may take one or more of the following actions:

1. Request a corrective and/or preventive action plan from the investigator
2. Verify that participant selection is appropriate
3. Observe the informed consent process
4. Require additional data and safety monitoring of the research activity
5. Request a directed audit of the study or specific areas of concern
6. Request a status report after each participant receives intervention
7. Modify the continuing review cycle/approval period
8. Require additional investigator and staff education

9. Require oversight by a senior investigator
10. Restrict, suspend or terminate the investigator's research privileges
11. Require notification of the non-compliance to currently enrolled participants (for example, if the non-compliance might affect their willingness to continue participation)
12. Require modification(s) to the protocol/research plan and/or consent/permission/assent form(s).
13. Require notification of the non-compliance to participants whose participation has ended
14. Require re-consent of current participants
15. Suspend the study (See below)
16. Terminate the study (See below)
17. Other actions deemed appropriate by the IRB

Where the IRB determines that the non-compliance also meets the definition of an unanticipated problem involving risks to participants or others, it is also handled according to Section 14.

The investigator is informed of the IRB determination and the basis for the determination in writing. If the IRB determines that the non-compliance was serious or continuing, the results of the final review are reported as described in Section 17.

### 15.5 Apparent IRB Noncompliance

When there has been apparent serious or continuing noncompliance on the part of the IRB (e.g., repeated failure to make a required determination), the HRPP Director will gather the relevant facts and report the matter, with any recommendations, to the IO. The IO may take actions as needed to further investigate the matter (e.g., a directed audit) prior to determining whether the apparent noncompliance is serious or continuing. The IO may also require corrective and preventive actions as warranted to remedy the matter and prevent recurrence. Serious or continuing noncompliance on the part of the IRB will be reported as necessary following the procedures outlined in Section 17.

## 16 Complaints

The HRPP and IRB will be responsive and sensitive to the complaints or concerns expressed by subjects or others and will respond to all complaints or concerns in a confidential and timely manner. The PI and all other research team members are responsible for the safety and welfare of all subjects enrolled in their studies. When investigators or team members hear complaints or concerns from subjects, they will try to resolve them.

Investigators conducting research under the oversight of the PAU IRB report complaints unable to be resolved by the investigator using the Reportable Events xForm in IRB Manager. All complaints, including those resolved by the investigator, should be summarized at the time of continuing review in the Continuing Review xForm, when continuing review is applicable.

Investigators conducting research under the oversight of an external IRB must comply with the reporting requirements of the external IRB and the internal reporting requirements outlined in Section 9.

Investigators are encouraged to contact the HRPP Administrator or IRB Chair when they are having difficulty resolving a complaint or concern, and whenever circumstances warrant (e.g., immediate attention is needed).

When the HRPP or IRB office is the direct recipient of complaints or concerns, the staff will do the following:

1. Document the complaint or allegation. When appropriate, the staff may request that the subject submit the complaint in writing.
2. Reassure the subject that the HRPP/IRB will take all necessary measures to inquire into the circumstances and to address the issue.
3. Provide written confirmation of receipt of the complaint to the subject if the subject is willing to provide contact information.
4. Convey the information to the IRB of record in a timely manner.
5. When appropriate, contact the investigator for additional information or to assist with resolution.
6. When appropriate, contact other resources to assist with information-gathering or resolution.

For research under the oversight of the PAU IRB, the HRPP Administrator, IRB Chair, or designee will consider the complaint or concern and take any reasonable steps necessary to investigate and/or resolve the issue, if appropriate, prior to review and consideration by the IRB.

Upon receipt of the complaint, the HRPP Administrator, Chair, or designee makes a preliminary assessment whether the complaint warrants immediate suspension of the research project. If a suspension is warranted, the procedures in Section 8 are followed.

If the complaint may meet the definition of non-compliance, it is considered an allegation of non-compliance according to Section 15.

If the complaint may meet the definition of an unanticipated problem involving risk to participants or others, it is handled according to Section 14.

If the complaint is actually a query from a research participant regarding study procedures or payments not received it is forwarded to the investigator/study team for handling.

A report will be provided to the IRB at the next available meeting if the research is subject to convened IRB review, or provided to the designated expedited reviewer if the research is eligible for expedited review. When reviewing complaints, the IRB will consider whether the complaint was the result of, or related to, an UAP or noncompliance, and, if so, will follow the relevant procedures. The IRB Chair or designated expedited reviewer may refer any complaint for review by the convened IRB. The IRB minutes, or reviewer comments for expedited reviews, will reflect the action(s) taken and, if necessary, notice to the appropriate officials and/or agencies.

The HRPP will maintain written copies of complaints and concerns and will document the investigation and resolution. The complainant will be notified promptly following resolution of the complaint or concern, when appropriate, if contact information has been provided. If the HRPP or IRB receives a complaint, or identifies information while investigating a complaint, that is indicative of possible misconduct in research, PAU's Research Integrity Officer will be notified immediately.

# 17 Reporting to Regulatory Agencies and Organizational Officials

Federal regulations require prompt reporting to appropriate institutional officials and, as applicable, the federal department or agency head (e.g., OHRP), of (i) any unanticipated problems involving risk to participants or others; (ii) any serious or continuing non-compliance with this policy or the requirements or determinations of the IRB; and (iii) any suspension or termination of IRB approval. Palo Alto University IRB complies with this requirement as outlined below.

When research is under the oversight of an external IRB, the terms of the agreement with that IRB will guide reporting.

Reports that have already been reported to the applicable federal oversight agency (e.g., by a Sponsor, Coordinating Center, or sIRB) do not also need to be reported by Palo Alto University. The Palo Alto University IO and any other appropriate parties will be informed of such reports by the HRPP/IRB Office when the matter involves local subjects or significantly impacts the conduct of the research at Palo Alto University.

## 17.1 Procedures

IRB staff will initiate these procedures as soon as the IRB takes any of the following actions:

1. Determines that an event may be considered an unanticipated problem involving risks to participants or others
2. Determines that noncompliance was serious or continuing
3. Suspends or terminates approval of research

1) The HRPP Administrator or designee prepares reports or letters that include the following information:
    a. Reason for the report (Unanticipated problem involving risks to participants or others, serious or continuing non-compliance, suspension or termination of IRB approval of research);
    b. Name of the institution(s) conducting the research;

   c. Title of the research project and/or grant proposal in which the problem occurred;
   d. Name of the investigator on the project;
   e. Number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement);
   f. A detailed description of the problem including the findings of the organization and the reasons for the IRB's decision;
   g. Actions the institution is taking or plans to take to address the problem (e.g., revise the protocol/research plan, suspend enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring etc.);
   h. Plans, if any, to send a follow-up or final report by a specific date, upon completion of an investigation or when a corrective action plan has been implemented; 2) The IRB Chair and the IO review the letter and recommend modifications as needed.

3) The IO is the signatory for the report or letter.
4) The HRPP Administrator or designee sends a copy of the report to:
   a. The Institutional Official
   b. The IRB Chair
   c. The following federal agencies:
      - OHRP, if the study is subject to DHHS regulations or subject to a DHHS FWA.
      - FDA, if the study is subject to FDA regulations.
      - If the study is conducted or funded by any Federal Agency other than DHHS that is subject to "The Common Rule", the report is sent to OHRP or the head of the federal agency, as required by the agency.
      - If the study is conducted or supported by a federal agency that has not adopted the Common Rule, and reporting is required, the report is sent to the party identified by the agency

      Reports are not submitted to federal departments or agencies such as OHRP or FDA unless the research is subject to federal regulations or another mandate that necessitates such reporting.

   d. Investigator
   e. Sponsor, if applicable
   f. Investigator's Department Chair
   g. Others as deemed appropriate by the HRPP Director, IRB Chair, and Institutional Official

The HRPP Administrator ensures that all steps of this policy are completed within 30 working days of the determination. For more serious actions, the Administrator expedites reporting. If additional time is needed to gather facts, or determine corrective actions, a preliminary report will be submitted within 30 days, to be followed by a final report as described above.

# 18 Investigator Responsibilities

Investigators are responsible for the conduct of research and the protection of human subjects involved in their research. If tasks are delegated to appropriately trained and qualified members of the research team, investigators must maintain oversight for the conduct of those to whom they delegate responsibility and retain ultimate responsibility for the research.

## 18.1 Investigators

The research team is made up of 'investigators', differentiated as follows, along with their responsibilities in the conduct of research involving human participants.

### 18.1.1 Principal Investigators (PI)

The Palo Alto University IRB recognizes one PI for each study. With limited exception, as addressed below, the PI has the ultimate responsibility for all research activities. At Palo Alto University the PI is required to be a full-time faculty or staff member (including post-doctoral fellows), or an affiliate-faculty member with a full-time faculty member identified as the Co-PI. This is the ONLY instance in which a Co-PI is recognized at Palo Alto University.

Where the activity is a student dissertation, or other student-designed research, the faculty mentor identified on the submission form is the individual with ultimate responsibility for the research activity in question.

Studies that require expertise or skills beyond those held by the PI or faculty mentor must either be modified or have expertise and skills supplemented by the inclusion of one or more additional qualified co-investigators.

### 18.1.2 Co-Investigators, Study Coordinators, and Research Assistants

Co-investigators, Study Coordinators, and Research Assistants are individuals other than the PI who is substantively involved in the conduct of the research study. Such involvement could include:

- Obtaining information about living individuals by intervening or interacting with them for research purposes;
- Obtaining identifiable private information about living individuals for research purposes;
- Obtaining the voluntary informed consent of individuals to be enrolled in the research; and
- Studying, interpreting, or analyzing identifiable private information or data for research purposes.

## 18.2 Responsibilities

**Investigators who conduct research involving human participants must:**

1. Conduct research in accordance with the ethical principles in the Belmont Report;
3. Have a research plan that is scientifically sound and minimizes risk to participants;
4. Ensure that the study includes a plan for the just, fair, and equitable recruitment and selection of participants;
5. When some or all of the participants are likely to be vulnerable to coercion or undue influence (e.g., children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons), include additional safeguards in the study to protect the rights and welfare of these participants;
6. Ensure that the study includes adequate provisions for the monitoring of participants and data to ensure participant safety;
7. Ensure that there are adequate provisions to protect the privacy interests of participants;
8. Ensure that there are adequate provisions to protect data confidentiality and the interests of participants, including an information security plan that considers the collection, storage, maintenance, analysis, transmission, and destruction of data and other identifiable information, when applicable;
9. Have sufficient resources necessary to protect human participants, including:
    a. Access to a population that would allow recruitment of the required number of participants;
    b. Sufficient time to conduct and complete the research;
    c. Adequate number of qualified staff to conduct the research;
    d. Adequate facilities to conduct the research;
    e. Necessary equipment to conduct the research;
    f. A plan to ensure proper supervision of the research, including a plan for periods of absence or decreased availability;
    g. Availability of medical, psychological, or other support that participants might require during or as a consequence of participation in the research;
10. Assure that all procedures in a study are performed with the appropriate level of supervision and only by individuals who are licensed or otherwise qualified to perform such under the laws of California and Palo Alto University policies;
11. Assure that all study personnel are educated in the regulatory requirements regarding the conduct of research and the ethical principles upon which they are based;
12. Assure that all study personnel are adequately trained and informed about the research and their specific duties and functions;

13. Promptly report any changes in study personnel, including investigators, to the IRB for review and approval (investigators and staff may not begin work on the research until IRB-approved);
14. Protect the rights, safety, and welfare of research participants;
15. Ensure that the information in the consent/permission/assent form(s) is consistent with that in the protocol;
16. Obtain and document informed consent and ensure that no human research participant is involved in the research prior to obtaining consent or permission from the legally authorized representative, unless a waiver of the requirement has been approved by the IRB;
17. Have a procedure to receive questions, complaints, or requests for additional information from participants and respond appropriately;
18. Ensure that all information provided to the IRB is accurate and complete so that the IRB may fulfill its responsibilities to review the research and make the required determinations;
19. Ensure that all research involving human participants receives IRB review and approval or a determination of exemption in writing before research begins;
20. Ensure that all research involving human participants is reviewed by other organizational components and committees, as applicable;
21. Comply with all IRB decisions, conditions, and requirements;
22. Ensure that studies receive continuing IRB review and approval;
23. Report unanticipated problems, deviations, complaints, non-compliance, suspensions, terminations, and any other reportable events to the IRB;
24. Notify the IRB if information becomes available that suggests a change to the potential risks or benefits of the research;
25. Obtain IRB review and approval before changes are made to the research unless a change is necessary eliminate apparent immediate hazards to participants;
26. Notify the IRB when a study has concluded by completing a Study Closure form in IRB Manager, including information regarding final study enrollment and a summary of findings.
27. Retain records for the time period and in the manner required by applicable regulations, contractual agreements and organizational policies.

### 18.3 Investigator Records

Investigators must comply with all sponsor record-keeping requirements, if applicable, and maintain the following research records:

### 18.3.1 Study Records

- Individual participant records
- Recruitment material
- Documentation of consent process (who, what, when, and how)
- Signed consent forms
- Unanticipated Problem Reports
- Reports of Participant complaints
- Results of all procedures conducted on the participant, including final visit (if no final visit, reason why: e.g., removal from study, withdrawal from study, death)

### 18.3.2 Regulatory Records

- All IRB-approved versions of the protocol/research plan
- All correspondence to and from the IRB
- All correspondence with the sponsor and others regarding the study
- Continuing review progress reports
- Modification Requests

### 18.3.3 Record Retention

Palo Alto University's Record Retention policy, which includes provisions for ownership of data, must be followed. Study records must be retained in accordance with regulatory, organizational, and sponsor or grantor requirements, but no less than three (3) years following completion of the research. All records must be maintained securely with limited access. Disposal of study records must be done in such a manner that no identifying information can be linked to research data.

## 18.4 Investigator Concerns

Investigators who have concerns regarding Palo Alto University's HRPP or IRB(s) should convey them to the Institutional Official or other responsible party, as appropriate, who will convey the concern to the IO. The IO considers the concern, and, if deemed necessary, seeks additional information. The IO may convene the parties involved, including the investigator, or a subcommittee to investigate and decide if procedural or policy modifications are warranted. In addition, the IRB Chair and/or the HRPP Administrator are available to address investigators' questions, concerns and suggestions.

# 19 Sponsored Research

It is Palo Alto University policy that any sponsored research conducted under the jurisdiction of Palo Alto University is conducted in accordance with federal guidelines and ethical standards.

The following describe the procedures to ensure that all sponsored research meets this requirement.

### 19.1 Definitions

**Sponsor:** Sponsor means the company, institution, individual donor, or organization responsible for the initiation, management or financing of a research study.

**Sponsored research:** Sponsored research means research funded through a grant or contract that involves a specified statement of work (e.g., the research proposal), including clinical trials involving investigational drugs, devices or biologics.

### 19.2 Responsibility

Contracts and other funding agreements with sponsors will be reviewed for the following by the Grants Office in consultation with the HRPP Office, as necessary:

1. All contracts with a sponsor have a written agreement with the Sponsor that addresses medical care for research participants with a research-related injury, when appropriate.
2. In studies where sponsors conduct research site monitoring visits or conduct monitoring activities remotely, the sponsor contract have a written agreement with the sponsor that the Sponsor promptly (no longer than 30 days) reports findings that could affect the safety of participants or influence the conduct of the study to Palo Alto University.
3. When the sponsor has the responsibility to conduct data and safety monitoring, the sponsor contracts have a written agreement with the sponsor that addresses provisions for data monitoring to ensure the safety of participants and for providing data and safety monitoring reports to Palo Alto University.
4. Sponsor contracts have a written agreement with the sponsor about plans for disseminating findings from the research and the roles that investigators and Sponsors play in the publication or disclosure of results.
5. When participant safety could be directly affected by study results after the study has ended, the sponsor contracts have a written agreement with the sponsor that the investigator or Palo Alto University will be notified of the results in order to consider informing participants.
6. Payment in exchange for referral of prospective participants from investigators (physicians) (“finder’s fees”) is not permitted. Similarly, payments designed to accelerate recruitment that are tied to the rate or timing of enrollment (“bonus payments”) are also not permitted.

## 20 Conflict of Interest in Research

Openness and honesty are indicators of integrity and responsibility, characteristics that promote quality research and strengthen the research process. It is Palo Alto University policy to preserve public trust in the integrity and quality of research by reducing actual or perceived conflict of interest (“COI”) in the conduct of research. COI in research is any interest that competes with an organization’s or individual’s obligation to protect the rights and welfare of research participants, the integrity of a research study, or the credibility of the research program. A conflict of interest can be financial or non-financial. A conflict of interest should be eliminated when possible and disclosed and effectively managed when it cannot be eliminated.

## 20.1 Researcher Conflicts of Interest

Pursuant to the Palo Alto University Policy on Conflicts of Interest, the Palo Alto University Assistant Provost of Research Assessment and Institutional Effectiveness (RAIE) serves as the Deciding Institutional Official (DIO) for Conflict of Interest. The DIO collaborates with Palo Alto University’s HRPP Office and IRB to ensure that COIs of investigators and research staff (‘researchers’) are identified and a proposed management plan is reviewed and approved by the IRB before it approves relevant research activities.

### 20.1.1 Procedures

#### 20.1.1.1 Disclosure of Researcher COI

For IRB purposes, researcher conflict review occurs at the time of new study submission, continuing review, and amendments to identify and add new study personnel or to disclose a new or changed interest. The researcher/study personnel with the conflict must report the potential conflict in the Initial Submission xForm or Modification xForm as appropriate. In the event a conflict that requires disclosure or management is identified, the study team collaborates with the DIO and the IRB, to create a written summary of the conflict and a conflict management plan (‘CMP’). If the DIO and/or the DIO’s appointed ad hoc COI review committee has not completed the review, the IRB defers the research study review or prohibits participation by the researcher with a potential COI until the CMP can be reviewed and approved by the IRB.

#### 20.1.1.2 Evaluation of COI

The IRB reviews COI and CMP to determine:

- Whether the COI affects the rights or welfare of research participants;
- Whether the COI might adversely affect the integrity or credibility of the research or the research program; and
- Whether the CMP effectively protects research participants and the integrity and credibility of the research and the research program.

During its review the IRB considers:

- How the research is supported or financed;
- The nature and extent of the conflict;
- The role and responsibilities of the conflicted individual in the design, conduct, and reporting of the research; and

- The ability of the conflicted individual to influence the outcome of the research.

#### 20.1.1.3 Management of COI

The IRB has final authority to determine whether the research, the COI, and the CMP, if any, allow the research to be approved, and can require additional measures to manage a COI.

For example, in addition to the CMP, the IRB may require:

1. Disclosure of the COI to research participants during the consent process and/or in the consent document;
2. Modification of the research plan or safety monitoring plan;
3. Monitoring of research by a third party;
4. Disqualification of the conflicted party from participation in all or a portion of the research;
5. Appointment of a non-conflicted PI;
6. Divestiture of significant financial interests; and
7. Severance of relationships that create actual or potential conflicts.

In the event the conflict cannot be effectively managed, the IRB may disapprove the research, or prohibit the individual with the conflict from participation in the research.

## 20.2 IRB Member Conflict of Interest

No IRB member or alternate may participate in the review of any research in which the member has a conflict of interest (COI), except to provide information as requested. It is the responsibility of each IRB member to disclose any COI related to a study submitted for review and recuse him/herself from the deliberations and vote by leaving the room.

The IRB staff ensures that IRB members and alternates are not assigned to conduct reviews of studies for which the member has a conflict and ensures appropriate recusal during convened meetings.

IRB members, alternates, or consultants may be considered to have a conflicting interest requiring recusal when they, or an immediate member of their family, have any of the following:

1. Involvement in the design, conduct, or reporting of the research;

28. Significant financial interests related to the research being reviewed, as described in the Palo Alto University Conflict of Interest Policy; or

29. Any other situation where an IRB member believes that another interest conflicts with his or her ability to deliberate objectively on a study.

At the beginning of each IRB meeting the IRB Chair reminds members that they must recuse themselves from the discussion and vote of a specific research study in which they have a conflict. If a conflicted member is participating by conference call, videoconference or web meeting, the member’s participation (connection) is suspended for discussion and voting.

IRB members with a conflicting interest are not counted towards quorum for the particular review and are not present for the discussion. Recusals of members with COIs are recorded in the minutes.

### 20.3 Institutional Conflict of Interest

Pursuant to the Palo Alto University Policy on Institutional Conflicts of Interest, the Palo Alto University Compliance Committee serves as the Conflict of Interest Committee (“COI Committee”). As a matter of policy, Palo Alto University will not participate in a human subjects’ research project when it has an institutional financial interest. An exception to this policy may be made only when the DIO determines that circumstances exist to merit an exception and a conflict management plan is adopted to maintain research integrity and serve the best interests of participants enrolled in the research. Palo Alto University’s HRPP Office and IRBs collaborate with the COI Committee to ensure that institutional COI is identified and managed before the IRB completes its review of any research application.

## 21 Outreach

Palo Alto University is committed to ensuring that research participants, prospective research participants, and members of the community have the opportunity to understand and offer input and concerns regarding Palo Alto University’s human research protection program, and the research that is conducted under its auspices.

The following procedures describe how Palo Alto University fulfils that commitment.

### 21.1 Responsibility

The HRPP Administrator and IO ensure the following:

### 21.2 Outreach Resources and Educational Materials

1. The HRPP Office website includes information on how to contact Palo Alto University to ask questions, express concerns, or provide feedback about specific research projects or research in general along with a listing of relevant research-related links.
2. All consent documents contain the contact information for the IRB Office at Palo Alto University, for current and potential research participants to ask questions, offer input, and express concerns.
30. Palo Alto University periodically provides presentations related to research to community organizations.

### 21.3 Evaluation

Each year the HRPP Administrator, in consultation with the IO and/or IRB Chair(s), as appropriate, reviews:

1. The specific community outreach activities in the past year;
31. Feedback provided via the “Contact Us” mechanism on the HRPP Office website, via and contact information in consent documents;
32. Feedback provided from other sources (unaffiliated IRB members, investigators, research staff, students, etc.).

The results of the review are used to evaluate the outreach activities and make changes as appropriate. The review is also used to identify additional resources that may be needed to meet the outreach needs of the research community.

# 22 Information Security

Palo Alto University has established standards and safeguards to protect research participant information. It is the responsibility of investigators to familiarize themselves with and comply with these standards. Investigators are required to comply with PAU’s Network and Computer Policies (https://www.paloaltou.edu/computer-and-network-acceptable-use-policy).

Palo Alto University has established standards and safeguards to protect research participant information. All PAU issued laptops have been encrypted to ensure that data on the device isn't compromised in the event the device is loss or stolen. All passwords should meet complexity requirements to minimize the risk of being compromised. When choosing a password to protect your device, be sure to use a password with the following characteristics. Once a study is complete it is recommended that the identifiable research data be securely deleted. Please contact support@paloaltou.edu if you need assistance.

- Do not share your password with anyone.
- Passwords must have at least six characters.
- Passwords can’t contain the user name or parts of the user’s full name, such as his first name.
- Passwords must use at least three of the four available character types: lowercase letters, uppercase letters, numbers, and symbols

It is the responsibility of investigators to familiarize themselves with and comply with these standards.

The use of personal laptops, desktops, portable/USB drives, and other non-Palo Alto University devices for storage of identifiable research data is discouraged. When a non-Palo Alto University computer or device must be used for the purposes of storing, even temporarily, or transmitting identifiable research data, it must be password protected and encrypted. Additionally, any potential or known breach of a device or of research data must be immediately reported to the IRB, Office of Integrity and Compliance, and CIO so that appropriate steps can be taken to assess the situation, protect the information, and comply with regulations. Lost or stolen Palo Alto University devices must also be reported to the police.

# 23 Special Topics

## 23.1 Community Based Research

Community based research (CBR) is research that is conducted as a partnership between academic investigators and members of a community. In CBR projects, the community participates fully in all aspects of the research process. *Community* is often self-defined, but general categories of community include geographic community, a community of individuals with a common problem or issue, or a community of individuals with a common interest or goal.

Where research is being conducted in communities, investigators are encouraged to involve members of the community in the research process, including the design and implementation of research and the dissemination of results when appropriate. The Palo Alto University HRPP Office assists investigators in developing such arrangements.

The most significant community involvement is in a subset of CBR called Community Based Participatory Research (CBPR) where there is an equal partnership between academic investigators and members of a community, with the community members actively participating in all phases of the research process, including the design and implementation of research and the dissemination of results when appropriate.

Questions to be considered as CBR studies are developed, and issues that the IRB considers when reviewing CBR include, but are not limited to:

- How is the community involved or consulted in defining the need for the proposed research (i.e., getting the community’s agreement to conduct the research)?
- How is the community involved or consulted in generating the study research plan?
- How are research procedures, including recruitment strategies and consent processes assessed to ensure sensitivity and appropriateness to various communities (e.g., literacy issues, language barriers, cultural sensitivities, etc.)?
- How is the community involved in the conduct of the proposed research?
- How are community members who participate in the implementation of the research trained and supervised?
- How have “power” relationships between investigators and community members on the research team, and in recruitment strategies been considered to minimize coercion and undue influence?
- What are the risks and benefits of the research for the community as a whole?
- How will boundaries between multiple roles (e.g., investigator, counselor, peer) be maintained (i.e., what happens when the investigator/research staff is the friend, peer, service provider, doctor, nurse, social worker, educator, funder, etc.)?
- How are research outcomes disseminated to the community?

- Is there a partnership agreement or memorandum of understanding signed by Palo Alto University or the Palo Alto University investigator and the community partner(s) that describes how they work together?

When CBR studies are proposed, the above information will be included in the submission materials. When CBR studies are being reviewed, the IRB Chair will review the above information with the IRB before the IRB reviews the study. When the IRB reviews CBR studies, it will include, either as members or consultants, individuals with expertise in community based research.

### 23.2 International Research

The Palo Alto University IRB reviews all international human research over which it has jurisdiction to assure adequate provisions are in place to protect the rights and welfare of research participants. All policies and procedures that are applied to research conducted domestically are applied to international research, as appropriate. Approval of research is permitted if “the procedures prescribed by the foreign institution afford protections that are at least equivalent to those provided in [45 CFR 46 101 (h)].”

For **federally conducted or supported research**, approval of research for foreign institutions or sites “engaged” in research is only permitted if the foreign institution or site holds an FWA with OHRP and local IRB review and approval is obtained.

Approval of research for foreign institutions or sites “not engaged” in research is only permitted if one or more of the following circumstances exist:

- *When the foreign institution or site has an established IRB/EC*:
    - o The investigator must obtain approval to conduct the research at the "not engaged" site from the site’s IRB/IEC or provide documentation that the site’s IRB/EC has determined that approval is not necessary for the investigator to conduct the proposed research at the site.
- *When the foreign institution or site does not have an established IRB/IEC*:
    - o A letter of cooperation must be obtained demonstrating that the appropriate institutional or oversight officials permit the research to be conducted at the performance site.
- IRB approval to conduct research at the foreign institution or site is contingent upon receiving documentation of the performance site’s IRB/EC determination, or letter of cooperation, as applicable.

The Palo Alto University IRB seeks sufficient knowledge of the local research context by requesting approval for the project from local IRBs or ethics committees (which may or may not be OHRP-registered) and/or local letters of support. The source of this information depends on the nature of the study, the country and the resources available to the investigator. Where there is a local IRB/IEC, Palo Alto University’s IRB must receive and review the foreign institution or site’s IRB/IEC review and approval of each study prior to beginning the research at the foreign institution or site. When appropriate, the IRB communicates and coordinates with the local institutions or ethics committees.

Investigators planning research in other countries are strongly encouraged to contact the HRPP Administrator and/or IRB Chair as soon as possible to help identify sources of local review.

Investigators are also encouraged to review OHRP's International Compilation of Human Research Standards and to search their database of registered IRBs by country.

In settings where there are no IRBs/IECs, Palo Alto University's IRB may require additional verification and information from people outside the particular research project who are familiar with the customs, practices, or standards of care where the research takes place, including other applicable committees, other Palo Alto University investigators with knowledge of the region, or a consultant who is an expert on the region, prior to approval. These individuals may either provide a written review of a particular research plan or attend an IRB meeting to provide the Palo Alto University IRB with recommendations based on their expertise.

#### 23.2.1.1 IRB Responsibilities

In addition to IRB review considerations discussed elsewhere in this manual, the IRB will consider the following when reviewing transnational research:

1. The qualifications of the investigator and research staff to conduct research in that country, including knowledge of relevant laws, regulations, guidance, and customs.
2. Whether the consent process and consent documents are appropriate for the language(s) of participants and communication with the participant population, and that arrangements are made to be able to communicate with participants throughout the study (e.g., to ask and answer questions).
3. How modifications to the research will be handled.
4. How complaints, non-compliance, protocol/research plan deviations, and unanticipated problems involving risks to participants or others will be handled.
5. How post-approval monitoring will be managed.
6. Whether the investigator has obtained the appropriate host country permissions to conduct research (e.g., institutional, governmental or ministerial, IRB, local or tribal).
7. When applicable, whether the investigator has provided an appropriate plan, and any necessary supporting documentation, to comply with the requirements of country law for investigational articles.
8. Mechanisms for communicating with the investigator and research staff when they are conducting the research in other countries.

#### 23.2.1.2 Investigator Responsibilities

The investigator conducting transnational research is responsible for:

1. Ensuring that the resources and facilities are appropriate for the nature of the research.
2. Verifying the qualifications of the investigators and research staff for conducting research in that country(ies).
3. Obtaining all appropriate host country permissions to conduct research (e.g., institutional, governmental or ministerial, IRB, local or tribal).
4. Complying with the requirements of country law; including, when applicable, requirements for research involving investigational articles and requirements for data management and privacy such as EU GDPR;
5. Ensuring that the consent process and consent document are appropriate for the culture(s) and language(s) of participants, and that arrangements are made to be able to communicate with participants throughout the study (e.g., to ask and answer questions).
6. Ensure that the following activities occur:
    a. Initial review, continuing review, and review of modifications
    b. Post-approval monitoring of the conduct of the research in accordance with the plan approved by the IRB
    c. Handling of complaints, non-compliance, and unanticipated problems involving risk to participants or others.
7. Not relying upon an IRB or EC that does not have policies and procedures for the activities listed above.
8. Ensuring that reportable information such as complaints, non-compliance, protocol/research plan deviations, and unanticipated problems involving risks to participants or other are communicated to the IRB.
9. Notifying the IRB promptly if a change in research activities alters the performance site's engagement in the research (e.g., performance site "not engaged" begins to obtain consent of research participants, etc.).
10. Ensuring that there are mechanisms in place for communicating with the IRB when they are conducting the research in other countries.

Note that the IRB will assist investigators to the best of our ability in identifying and ensuring compliance with the requirements of host country law, but that this is ultimately the responsibility of the investigator.

### 23.2.1.3 Consent Documents

The informed consent documents must be in a language understandable to the proposed participant. The IRB will review the proposed document of the exact content contained in **the foreign language informed consent document** in the IRB application (Initial or Amendment). All documents, including verification **of translation accuracy**, are part of the IRB file.

### 23.2.1.4 Monitoring of Approved International Research

The IRB is responsible for the ongoing review of international research conducted under its jurisdiction through the continuing review process as applicable (see Sections 6 and 7.8) in accordance with all applicable federal regulations. When the IRB and a local ethics committee are both involved in the review of research, there is a plan for coordination and communication with the local IRB/IECs.

The IRB requires documentation of regular correspondence between the Palo Alto University investigator and the foreign institution or site and may require verification from sources other than the Palo Alto University investigator that there have been no substantial changes in the research since its last review.

## 23.3 Data Sharing

### 23.3.1 Moving data to a new institution

When an investigator is permanently leaving PAU to work at another institution, they must file a Data Transfer agreement prior to removing data from PAU. The investigator must include with this form:

(1) If the project was supported by a grant, an agreement that original research records must remain at PAU;
(2) If the project was not supported by a grant, either an agreement to maintain the original records at PAU or an agreement to maintain copies of research records at PAU;
(3) The name of the person of office that will be responsible for maintaining either original research records or copies of the records;
(4) The nature of all data (physical data vs electronic records); and
(5) Whether the research records include any identifiable data.

The PI must explain how they will protect the confidentiality of the data during and after transfer to a new institution.

### 23.3.2 Sharing De-identified Data

Sharing de-identified data furthers the goals of transparency and replicability in science. For research conducted under the 2018 regulations, study team members may request to share deidentified data outside the study team under the following conditions:

(a) identifying information was never collected

(b) the consent form included appropriate notice regarding use of de-identified data (see Section 11.5.1).

The PI must submit the Request to Share De-identified Data xForm prior to sharing the data with an individual outside the study team or prior to posting on a public repository. With this xForm, the PI must describe methods of de-identification, a full list of variables that will be shared (e.g., a data codebook), a list of all people or sites the data will be shared with, and provide any relevant data sharing agreements.

## 23.4 Research Repositories and Research Involving Coded Private Information

### 23.4.1 Coded Human Data or Biological Specimens

Palo Alto University IRB policy is based on the OHRP guidance document entitled, “Guidance on Research Involving Coded Private Information or Biological Specimens” (October 16, 2008 http://www.hhs.gov/ohrp/policy/cdebiol.html). This document:

1. Provides guidance as to when research involving coded private information or specimens is or is not research involving human subjects, as defined under HHS regulations for the protection of human research subjects (45 CFR Part 46).
2. Reaffirms OHRP policy that, under certain limited conditions, research involving **only** coded private information or specimens is not human subjects research.
3. Clarifies the distinction between (a) research involving coded private information or specimens that does not involve human subjects and (b) human subjects research that is exempt from the requirements of the HHS regulations.

For purposes of this policy, coded means that: (1) identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertains has been replaced with a number, letter, symbol, or combination thereof (i.e., the code); and (2) a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

**Guidance:**

Obtaining identifiable private information or identifiable specimens for research purposes constitutes human subjects research. Obtaining identifiable private information or identifiable specimens includes, but is not limited to:

1. Using, studying, or analyzing identifiable private information or identifiable specimens that have been provided to the investigator from any source; and
2. Using, studying, or analyzing identifiable private information or identifiable specimens that were already in the possession of the investigator.

Private information or specimens are considered to be individually identifiable when they can be linked to specific individuals by the investigator(s) either directly or indirectly with a code.

Research involving **only** coded private information or specimens does **not** involve human subjects per the Common Rule definition if both of the following conditions are met:

1. The private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals;

**and**

2. The investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because:

    1. The investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased (note that the HHS regulations do not require the IRB to review and approve this agreement);

    2. There are IRB‑approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; or
    3. There are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.

In some cases an investigator who obtains coded private information or specimens about living individuals under one of the conditions cited in 2(a)‑(c) above may (1) unexpectedly learn the identity of one or more living individuals, or (2) for previously unforeseen reasons now believes that it is important to identify the individual(s). If, as a result, the investigator knows, or may be able to readily ascertain, the identity of the individuals to whom the previously obtained private information or specimens pertain, then the research activity now involves human subjects. Unless this research is determined to be exempt (See Section 5), IRB review of the research is required and informed consent required unless the IRB approves a waiver. (See Section 11.9).

### 23.4.2 Who Should Determine Whether Coded Private Information or Specimens Is Human Subjects Research

The investigator submits the Request for Human Subjects Research Determination Form in IRB Manager for review by the HRPP Office and/or IRB Chair if they believe the study is not human subjects research. If the study is not human subjects research, it will be registered as such in IRB Manager and the investigator will be informed.

### 23.4.3 Data or Biological Sample Repositories

A repository is a collection of information or biospecimens whose organizers:

- Receive information or biospecimens from one or more sources
- Maintain the information or biospecimens over time
- Control access to and use of information or biospecimens by multiple individuals and/or for multiple purposes, which may evolve over time

These policies and procedures apply to both information and biospecimen repositories. For simplicity, both are referred to as samples.

There are two types of repositories, non-research repositories and research repositories:

### 23.4.3.1 Non-research Repositories

Non-research repositories are created and maintained for purposes that are totally unrelated to research (e.g., public health surveillance).

Even though these repositories are not created for research purposes, they may contain information that is of interest to researchers. The creation (or operation) of non-research databases or repositories does not involve human subject research and does not require IRB oversight. However, IRB oversight is required for research involving identifiable private information from non-research databases and repositories (including data/tissue banks and registries).

- When research involves identifiable private information or identifiable biospecimens, each research use must receive prospective IRB review and either notice of exemption with limited IRB review or approval and continuing IRB oversight.
- Researchers should submit an application for IRB review and receive notice of exemption with limited IRB review or IRB approval before initiating the research.
- The application should include any available information about the circumstances under which the information or specimens were originally collected.
- The IRB may require researchers to obtain informed consent of participants for research involving identifiable information or biospecimens contained in non-research databases or repositories. The IRB can waive the requirement for informed consent if the research meets the regulatory criteria for waiver.

### 23.4.3.2 Research Repositories

Research repositories are created and maintained specifically for research purposes (e.g., databases to identify prospective participants).

Research repositories may involve three components:

- Data collection;
- Data storage and management; and ● Use.

<u>Data collection</u>

If the data were collected for research purposes or are associated with information that can identify the donor, informed consent must be obtained from the donor unless appropriately waived by the IRB. The PAU IRB is not approving research using data collecting under Exempt Categories 7 and 8 (relying upon broad consent) at this time.

The consent document should include: ●

A clear description of

  - the specific types of research to be conducted (if known; or, if unknown, this should be explained);

    - the conditions under which data are released to recipient-investigators; and
    - procedures for protecting the privacy of participants and maintaining the confidentiality of data
- A statement regarding future withdrawal of the data from the study (i.e., whether participants may, in the future, request that their data be destroyed or that all personal identifiers be removed from data).

  Other information (such as the length of time that data will be stored, participants' access to information learned from the research, and secondary uses of the data) should be provided as appropriate.

Repositories should have data submission policies to ensure that the data are collected in an ethical manner, with informed consent and IRB approval.

Sample Storage and Data Management

Repositories should have written policies on:

- Data and tissue submission requirements
    - Informed consent
    - IRB review
- Physical and procedural mechanisms for the secure receipt, storage, and transmission of information and biospecimens
- Policies on release of information and biospecimens, including:
    - Coding
    - Release of identifiers
    - Certificates of Confidentiality and Privacy Certificates

Use of Information or Biospecimens

Recipient-investigators should have a written data use agreement with the repository. The data use agreement should specify under what conditions the data are being released to the recipientinvestigator(s). The terms under which the data are released may determine whether the recipient-investigator’s research requires IRB oversight.

#### 23.4.3.3 IRB Oversight

Operation of a research repository and its data management center under the jurisdiction of Palo Alto University is subject to oversight by the Palo Alto University IRB. A proposal to establish a repository is submitted to the IRB using the Initial Application form, specifying the conditions under which information and biospecimens will be accepted and shared, and ensuring adequate provisions to protect the privacy of participants and maintain the confidentiality of data. The IRB also reviews and approves the data collection protocol and informed consent document for distribution to sample collectors and their local IRBs. The PAU IRB will not approve a proposal to establish a repository that relies upon the use of broad consent.

### 23.5 Certificate of Confidentiality (CoC)

Certificates of Confidentiality (CoC) protect research information by prohibiting certain disclosures and conditioning others upon consent from the subject. The protections and requirements of CoCs are outlined in **42 U.S.C. 241(d)** and in written policies and requirements of certain Federal agencies such as **NIH**, and **CDC** and are summarized below.

Certificates of Confidentiality (CoC) protect research information by prohibiting certain disclosures and conditioning others upon consent from the subject. The protections and requirements of CoCs are outlined in 42 U.S.C. 241(d) and in written policies and requirements of certain Federal agencies such as NIH and CDC and are summarized below.

CoC's are obtained as follows:

- CoCs are issued automatically when research is conducted or supported by NIH and falls within the scope of the NIH policy.
- CoCs are issued automatically when research is conducted or supported by the CDC and involves the collection of identifiable, sensitive information.
- Research that is not supported by NIH or CDC may still have the protections afforded by CoCs through successful application to the NIH, FDA, HRSA, SAMHSA, or other authorized Federal agencies or departments.

Additional information about CoCs and the application process for research not covered by the NIH policy is available on the NIH CoC Website.

#### 23.5.1 Definitions

**Identifiable, sensitive information** means information that is about an individual and that is gathered or used during the course of biomedical, behavioral, clinical, or other research and

1. Through which an individual is identified; or
2. For which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

#### 23.5.2 Protections and Requirements

When a CoC is issued, whether automatically or under an approved application, the person(s) engaged in the research must not disclose or provide the name of a subject or any information, document, or biospecimen that contains identifiable, sensitive information about the subject and that was compiled for the purposes of the research:

1. In any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, unless the disclosure is made with the consent of the individual to whom the information, document, or biospecimen pertains; or
2. To any other person not connected with the research, unless:
    a. Required by Federal, State, or local laws (e.g., adverse event reporting to the FDA, transmissible disease reporting required under State law), but excluding proceedings as described in "1" above;
    b. Necessary for the medical treatment of the subject to whom the information, document, or biospecimen pertains and made with the consent of the subject;
    c. Made with the consent of the individual to whom the information, document, or biospecimens pertains; or
    d. Made for the purposes of other scientific research that is in compliance with applicable Federal regulations governing the protection of human subjects in research.

#### 23.5.2.1 Additional Protections

Identifiable, sensitive information protected under a CoC, and all copies thereof, are immune from the legal process, and shall not, without the consent of the individual to whom the information pertains, be admissible as evidence or used in any action, suit, or other judicial, legislative, or administrative proceeding.

Identifiable, sensitive information that has been collected under a CoC, and all copies thereof, are protected for perpetuity.

Nothing in the rule (42 U.S.C. 241(d)) may be construed to limit the access of a subject to information about himself or herself collected during the research.

When consent is obtained, the consent should inform subjects that a CoC is in place and describe the protections and limitations.

### 23.5.3 NIH and CDC Policy

The NIH Policy on CoCs applies to *"all biomedical, behavioral, clinical, or other research funded wholly or in part by the NIH, whether supported through grants, cooperative agreements, contracts, other transaction awards, or conducted by the NIH Intramural Research Program, that collects or uses identifiable, sensitive information"* that was commenced or ongoing on or after December 13, 2016.

The CDC requirements for CoCs apply to *"CDC supported research commenced or ongoing after December 13, 2016 and in which identifiable, sensitive information is collected, as defined by Section 301(d)."*

CoCs are automatically granted, and the requirements of such must be complied with, whenever a NIH or CDC funded activity falls within the scope of the NIH policy or CDC's requirements. Investigators and institutions are responsible for determining when research with NIH or CDC support are covered by a CoC.

NIH and CDC expands upon 42 U.S.C. 241(d) by explaining that NIH and CDC consider research in which identifiable, sensitive information is collected or used, to include:

- Human subjects research as defined in 45 CFR 46, including research determined to be exempt (except for exempt research when the information obtained is recorded in such a manner that human subjects cannot be identified or the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects);
- Research involving the collection or use of biospecimens that are identifiable to an individual or for which there is at least a very small risk that some combination of the biospecimen, a request for the biospecimen, and other available data sources could be used to deduce the identity of an individual;
- Research that involves the generation of individual level, human genomic data from biospecimens, or the use of such data, regardless of whether the data is recorded in such a manner that human subjects can be identified or the identity of the human subjects can readily be ascertained; or
- Any other research that involves information about an individual for which there is at least a very small risk, as determined by current scientific practices or statistical methods,
- that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual, as defined in subsection 301(d) of the Public Health Service Act.

### 23.5.4 NIH and CDC CoC Determination

At PAU, Grants Office staff will, in consultation with the investigator(s) (or Program or Project Director, if applicable), determine if the NIH policy or CDC requirements applies to research with NIH or CDC involvement or support. The questions outlined in the NIH policy and CDC requirements will be used to guide the analysis. When it has been determined that the NIH policy or CDC requirements do not apply, investigators (or Program or Project Directors, if applicable) are responsible for consulting with the Grants Office whenever they are proposing changes to the NIH or CDC supported activity that may impact or change the analysis. The NIH policy and CDC requirements include additional responsibilities and requirements for internal controls and for ensuring that recipients of identifiable, sensitive information protected by a CoC understand that they are also subject to the requirements of subsection 301(d) of the Public Health Service Act. For additional information see the PAU HRPP Guidance on CoCs.

### 23.5.5 Application Procedures for non-NIH Research

Any person engaged in human subjects research that collects or uses identifiable, sensitive information may apply for a CoC. For most research, CoCs are obtained from NIH, an investigator may apply for a CoC through the NIH Institute or Center funding research in a scientific area similar to the project.

When a researcher is conducting a research project that is covered by the Agency for Healthcare Research and Quality (AHRQ) confidentiality statute (42 U.S.C. section 299c-3(c)), a CoC is not needed (AHRQ notice NOT-HS-18-012). While the AHRQ statute does not define "identifiable", AHRQ applies the PHS Act definition of "identifiable, sensitive information". Investigators should consult with AHRQ when they believe that data might be considered "nonidentifiable" or when otherwise uncertain whether a research project falls within the scope of the statute.

When a researcher is conducting a research project that is covered by the Department of Justice (DoJ) confidentiality statute, 28 CFR 22, and/or a NIJ Privacy Certificate, a CoC may not be needed. Investigators should consult with DoJ/NIJ to determine whether a CoC should be obtained.

If there is an Investigational New Drug Application (IND) or an Investigational Device Exemption (IDE), the sponsor can request a CoC from the FDA. When FDA funds or conducts research, a CoC is automatically issued.

CoCs may also be issued by other Federal agencies and departments, such as SAMSHA or HRSA.

For more information, see the NIH CoC Website.

### 23.5.6 IRB Review

Investigators are responsible for clearly representing in the IRB submission that a CoC is in place, or that an application for CoC has been submitted or is pending. When the CoC application is in process or pending, the IRB may condition final approval upon its receipt.

For studies that are already underway, investigators must submit a Modification Request in IRB Manager, along with updated consent language (if applicable) when a CoC is applied for, or when automatically issued under the NIH policy or CDC requirements.

When reviewing research under a CoC, the PAU IRB will evaluate whether the research plan is consistent with the obligations to protect information and specimens under a CoC and, when consent will be obtained, whether the proposed consent language or other form of notification properly discloses the CoC and appropriately describes the associated protections and limitations. Sample consent language is available on the NIH CoC Website.

When research is not under a CoC, the IRB may require an investigator to apply for a CoC if the research includes identifiable, sensitive information and the IRB determines that a CoC is necessary to minimize risks and adequately protect subjects' privacy and the confidentiality of subjects' information or specimens.

## 23.6 Palo Alto University Students and Employees as Research Participants

When Palo Alto University students and/or employees are being recruited as potential research participants, investigators must ensure that there are additional safeguards for these participants. The voluntary nature of their participation must be primary and without undue influence on their decision. Investigators must emphasize to participants that their academic status, grades, or employment will not be affected by their participation decision.

**To minimize coercion, investigators should avoid, whenever possible, the use of their students and employees in research procedures that are neither therapeutic nor diagnostic. Investigators should solicit student and employee participants through means such as bulletin board notices, flyers, advertisements in newspapers, and announcements in classes or laboratories other than their own. When entering a classroom to recruit students and conduct research, e.g., administer a survey, investigators should do so at the end of the class period to allow non-participating students the option of leaving the classroom (unless other arrangements have been made), thereby alleviating pressure to participate.**

### 23.6.1 Human Subject Research and Course Projects

Learning how to conduct ethical human subject research is an important part of a student's educational experience. Research activities that are designed as part of a course requirement for purposes of a learning experience only and **not "**designed to develop or contribute to generalizable knowledge" **may** not require IRB review and approval if all of the following conditions are true:

- Results of the project are viewed only by the course instructor and discussed within the classroom for teaching and learning purposes.
- Results of the project are not made public through presentation (outside of the classroom) and are not published in paper or electronic format (e.g., cannot be made available on the internet, cannot be published in a journal, etc.).
- Procedures involve no more than minimal risk.
- Vulnerable populations are not targeted (e.g., children under age 18, prisoners, persons who are cognitively impaired, etc.).
- Data collected are recorded in such a manner that participants are not identifiable (i.e., images in videotapes and photographs and voices on audiotape are not identifiable).
- When appropriate, informed consent is obtained.

#### 23.6.1.1 Responsibility of the Course Instructor

The course instructor is responsible for ensuring the protection of human subjects (including ensuring a process is in place for obtaining voluntary consent from research participants when appropriate), and for monitoring the students' progress.

When designing a project, students should be instructed on the ethical conduct of research and on the preparation of the IRB application, when such is required. Instructors and students should:

1. Understand the principles of the Belmont Report and their application;
2. Develop appropriate consent documents and an appropriate consent process;
3. Plan appropriate strategies for recruitment;
4. Identify and minimize potential risks to participants or others;
5. Assess the risk-benefit ratio for the project;
6. Establish and maintain strict guidelines for protecting privacy and confidentiality; and
7. Allow sufficient time for IRB review, if applicable, and completion of the project.

In making a determination of whether or not a class research project requires IRB review, the instructor is encouraged to contact the HRPP Office for assistance or submit a request for a human subjects research determination following the procedures outlined in Section 5.

#### 23.6.1.2 Individual Research Projects Conducted by Students

Independent study projects, senior theses, undergraduate research projects, Masters and advanced degree research, and similar exercises that meet the regulatory definition of human subjects' research must be submitted for IRB review prior to the enrollment of participants or data collection. This includes human subject research activities that ultimately contribute to part or all of a thesis, dissertation, or other type of publication or presentation. IRB review/approval cannot occur after a study has begun.

Students may serve as principal investigators. A full time faculty member must be identified as mentor and has overall responsibility for the conduct of the study.

Students, Advisors, Faculty Sponsors, and Instructors should contact the HRPP Office with any questions.

### 23.6.2 Independent Study, Theses and Dissertations

These research activities, including research done as part of a course of study, that meet the regulatory definition of human subjects research must be submitted for IRB review prior to the enrollment of participants or data collection. IRB review/approval cannot occur after a study has begun.

Students may serve as principal investigators. A full time faculty member must be identified as mentor, and has overall responsibility for the conduct of the study. Students, Advisors, Faculty Sponsors and Instructors should contact the HRPP Office with any questions.

## 23.7 Use of Student Education Records in Research

This section provides a brief summary of the Family Educational Rights and Privacy Act (FERPA) and Protection of Pupil Rights Amendment (PPRA) and provides general guidance for researchers when accessing students' records and for IRB members to consider when reviewing research studies that include access and/or use of student education records.

### 23.7.1 Family Educational Rights and Privacy Act (FERPA)

The Family Educational Rights and Privacy Act (FERPA) is a Federal law that protects the privacy of student education records at educational entities that receive funds from the federal Department of Education (ED).

#### 23.7.1.1 Definitions

Educational Records: Educational records are defined as records, files, documents, and other materials that contain information directly related to a student and are maintained by their educational institution or by a person acting for that institution. Education records may be paper and electronic records and may include:

- Grades
- Class lists
- Student course schedules
- Disciplinary records
- Student financial records
- Payroll records for employee who are employed as a direct result of their status as student (e.g. work study, assistantships, resident assistants)

#### 23.7.1.2 Rights under FERPA

In general, schools must have written permission from the parent or eligible student to release any information from a student's education record. However, FERPA allows schools to disclose personally identifiable information from an education record of a student without consent if the disclosure is to organizations conducting studies for, or on behalf of, educational agencies or institutions to:

1. Develop, validate, or administer predictive tests;
2. Administer student aid programs; or
3. Improve instruction. [34 CFR 99.31(a)(6)]

A written agreement with the receiving organization is required, including:

1. The purpose, scope, and duration of the study(ies);
2. The information to be disclosed;

3. A requirement that the receiving organization uses the personally identifiable information from the educational records only for the purpose(s) of the study as stated in the agreement;
4. A requirement that the receiving organization conducts the study in a manner that does not permit personal identification of students and parents by anyone other than representatives of the organization with legitimate interests; and
5. A requirement that the receiving organization destroys or returns all personally identifiable information when the information is no longer needed for the purposes for which the study was conducted and that specified the time period in which the information must be returned or destroyed.

Education records may be released without consent under FERPA if all personally identifiable information has been removed including:

1. Students' names and other direct identifiers, such as students' Social Security Numbers or student numbers;
2. Indirect identifiers, such as the name of students' parents or other family members, the students' or families addresses, and personal characteristics or other information that would make the students' identities easily traceable, and dates and places of birth and mothers' maiden names;
3. Biometric records, including measurable biological or behavioral characteristics that can be used for automated recognition of an individual, including fingerprints, retina and iris patterns, voiceprints, DNA sequence, facial characteristics, and handwriting; and
4. Other information that, alone, or in combination, is linked or linkable to a student that would allow a reasonable person in the school community, who does not have personal knowledge of the relevant circumstances, to identify to student with reasonable certainty.

#### 23.7.1.3 Procedures

At PAU, when FERPA applies, investigators must provide the IRB with information describing how they will ensure compliance with the rule. A letter of support or other documentation from the school supporting the conduct of the research should be provided. The investigator must explain in the Initial Submission form whether written consent to disclose student information will be obtained. The IRB will review the information provided to verify compliance, including verification that permission for the use of the records will be obtained or that permission is not required under an allowed use or exception.

### 23.7.2 Protection of Pupil Rights Amendment (PPRA)

The Protection of Pupil Rights Amendment (PPRA) affords parents of elementary and secondary students certain rights regarding the conduct of surveys, collection and use of information for marketing purposes, and certain non-emergency physical/medical exams. PPRA applies to the programs and activities of a state educational agency (SEA), local educational agency (LEA), and any other recipient of ED funds. These rights transfer from parents to students when they reach the age of 18 or are an emancipated minor. This section is not intended to address PPRA as a whole, rather it addresses PPRA requirements as they most commonly relate to research.

### 23.7.2.1 Definitions:

**Instructional Material** means instructional content that is provided to a student, regardless of its format, including printed or representational materials, audio-visual materials, and materials in electronic or digital formats (such as materials accessible through the Internet). The term does not include academic tests or academic assessments.

**Invasive Physical Examination** means any medical examination that involves the exposure of private body parts, or any act during such examination that includes incision, insertion, or injection into the body, but does not include a hearing, vision, or scoliosis screening.

**Personal Information** means individually identifiable information including: (1) a student's or parent's first and last name; (2) a home or other physical address (including a street name and the name of a city or town); (3) a telephone number; or, (4) a Social Security Number.

**Research or Experimentation Program or Project** means any program or project in any program that is designed to explore or develop new or unproven teaching methods or techniques.

### 23.7.2.2 Rights under PPRA

When **research is funded by ED**, no student can be required to submit **without prior consent** to a survey that concerns one or more of the following protected areas:

1. Political affiliations or beliefs of the student or the student's parent;
2. Mental and psychological problems of the student or his or her family;
3. Sex behavior and attitudes;
4. Illegal, anti-social, self-incriminating, and demeaning behavior;
5. Critical appraisals of other individuals with whom the student has close family relationships;
6. Legally recognized privileged and analogous relationships, such as those of lawyers, physicians, and ministers;
7. Religious practices, affiliations, or beliefs of the student or student's parent; or
8. Income, other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under a program.

Parents have the right to **receive notice and an opportunity to opt a student out** of:

1. Any other survey that concerns any of the above protected areas, **regardless of funding**;
2. Any non-emergency, invasive physical exam or screening required as a condition of attendance, administered by the school or its agent, that is not necessary to protect the health and safety of a student, except for hearing, vision, or scoliosis screenings, or any physical exam or screening permitted or required under state law; and
3. Activities involving collection, disclosure, or use of personal information collected from students for marketing or to sell or otherwise distribute the information to others. (This does not apply to the collection, disclosure, or use of personal information collected from students for the exclusive purpose of developing, evaluating, or providing educational products or services for, or to, students or educational institutions.)

   Note: In the event parents do not allow children to participate, investigators should make accommodations for children not participating keeping in mind that these children should not be made to feel excluded from activities.

Parents also have the **right to inspect** upon request and before administration or use:

1. Surveys that concern any of the protected areas and surveys created by third parties;
2. Instruments used to collect personal information from students for any of the above marketing, sales, or other distribution purposes;
3. Any instructional material used as part of the educational curriculum for the student; and
4. Instructional material, including teachers' manuals, films, tapes, or other supplementary instructional material, which will be used in conjunction with any research or experimentation program or project.

### 23.7.2.3 Procedures

At PAU, when PPRA applies, investigators should review the school's PPRA policies and must provide the IRB with information describing how they will ensure compliance with the rule and the school's policies. A letter of support or other documentation from the school supporting the conduct of the research and its compliance with PPRA should be provided. The IRB will review the information provided to verify compliance.

## 23.8 Oral History

A decision whether oral history or other activities solely consisting of open ended qualitative type interviews are subject to the policies and regulations outlined in an institution's FWA and DHHS regulations for the protection of human research subjects (45 CFR 46) is based on the prospective intent of the investigator and the definition of "research" under DHHS regulations at 45 CFR 46.102(d): "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."  The evaluation of such activities hinges upon whether:

The activity involves a prospective research plan that incorporates data collection, including qualitative data, and data analysis to answer a research question; and

The activity is designed to draw general conclusions (i.e., knowledge gained from a study may be applied to populations outside of the specific study population), inform policy, or generalize findings.

In order to be subject to the Palo Alto University human research protection policies, the activity must meet both of the above standards. This determination is made according to the procedures described in Section 5.

General principles for evaluating Oral History activities:

1. Oral history activities, such as open ended interviews, that ONLY document a specific historical event or the experiences of specific individuals, without intent to draw conclusions or generalize findings, do not constitute "research" as defined by DHHS regulations 45 CFR 46.

   Example: An oral history video recording of interviews with holocaust survivors is created for viewing in the Holocaust Museum. The creation of the video tape does not intend to draw conclusions, inform policy, or generalize findings. The sole purpose is to create a historical record of specific personal events and experiences related to the Holocaust and provide a venue for Holocaust survivors to tell their stories.

2. Systematic investigations involving open-ended interviews that are designed to develop or contribute to generalizable knowledge (e.g., designed to draw conclusions, inform policy, or generalize findings) constitute "research" as defined by DHHS regulations at 45 CFR 46.

   Example: An open ended interview of surviving Gulf War veterans to document their experiences and to draw conclusions about their common experiences, inform policy, or generalize findings.

3. Oral historians and qualitative investigators may want to create archives for the purpose of providing a resource for others to do research. Because the intent of the archive is to create a repository of information for other investigators to conduct research as defined by 45 CFR 46, the creation of such an archive constitutes research under 45 CFR 46.

   Example: Open ended interviews are conducted with surviving Negro League baseball players to create an archive for future research. The creation of such an archive constitutes research under 45 CFR part 46 because the intent is to collect data for future research.

Investigators are advised to consult with the HRPP Office regarding whether their oral history project requires IRB review.

## 23.9 Genetic Studies

Research that generates or uses genetic information may create special risks to human subjects and their relatives. These involve medical, psychosocial, legal and economic risks, such as the possible loss of privacy, insurability, and employability, and may result in stigmatization and discrimination. Information about one's own genetic make-up may also provide information about family members.

In studies involving genetic testing or analysis of genetic information, several questions should to be addressed to ensure that potential risks are well understood and that the rights and interests of subjects and their family members are carefully considered and planned for. For example:

1. Is the testing intrinsic to the study? If not, has participation in the genetic testing component been provided as an opt-in?
2. Will test results be given? Is there an appropriate plan for return of results?
3. Does the subject or family member be provided the option to receive or not receive results? How will this decision be recorded?
4. Could the results provide information about individual disease risk? Disease risk for family members?
5. Could other clinically relevant information or incidental findings be uncovered by the study? Is there a plan for the management of such findings?
6. Will testing that could produce clinically relevant information occur in a CLIA-certified lab? If not, are there tests available that could validate or support findings?
7. Could a change in a family relationship be disclosed, such as mistaken paternity?
8. Could/will the research provide information about the origins, ancestry, or natural history of families, indigenous peoples, tribal populations, or other populations? What are the possible risks?
9. Could/will the research generate information that could place subjects or family members at risk or be stigmatizing?
10. Could/will the research generate information of other value or importance to subjects/families?
11. Do any practical limitations exist on the subject's right to withdraw from the research, withdraw data, and/or withdraw biological materials (e.g., specimens, cell lines, extracted genomic DNA)?
12. How will the information and/or biological materials be protected and who will have access?
13. What is the potential for re-identification of individual subjects (e.g., through the combination of their genetic information and/or materials with other sources of information (e.g., public records))? What measures can be taken to mitigate these risks?

14. Is a Certificate of Confidentiality (CoC) in place or should one be considered? (See Section 23.4)
15. Will the specimens, cell lines, or genetic information be stored and/or made available for future research? Is this provided as an opt-in when not intrinsic to the study? (See Section 26.7)

Investigators should carefully consider the above and other factors relevant to their specific study when developing the protocol, consent process, and consent form. The President's Bioethics Commission, the National Academies of Sciences, Engineering, and Medicine, and others have produced reports, recommendations, and materials that investigators and the IRB may find helpful in protocol development and review, including:

- Returning Individual Research Results to Participants: Guidance for a New Research Paradigm
- Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts
- Privacy and Progress in Whole Genome Sequencing
- Genetics Research and American Indian and Alaska Native Communities ● National Human Genome Research Institute:
    - Human Subjects Research in Genomics o Return of Research Results o Data Sharing and Privacy
    - Informed Consent for Genomics Research

In addition to the ethical considerations, investigators must ensure that research involving genetic testing or use of genetic information is consistent with applicable law (e.g., GINA, HIPAA, EU GDPR, state law) and policy (e.g., NIH).

### 23.9.1 Genetic Information Nondiscrimination Act (GINA)

GINA generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against individuals based on their genetic information. This law protects individuals, including research subjects, in the following ways:

- Health insurance companies and health plans are generally prohibited from requesting or requiring genetic information of an individual or their family members, including genetic information generated from research;
- If health insurance companies and health plans do receive such genetic information, they may not use it to make decisions regarding coverage, rates, or preexisting conditions; and
- Employers with 15 or more employees generally may not use genetic information for hiring, firing, promotion, or other decisions regarding terms of employment.

GINA's protections do not extend to life insurance, disability insurance, or long-term care insurance. Thus, GINA does **not** protect individuals from genetic discrimination in seeking life insurance, disability insurance, or long-term care insurance nor does it protect individuals from discrimination by employers with fewer than 15 employees.

GINA defines genetic information as information about:

- An individual's genetic tests;

- Genetic tests of an individual's family members;
- Genetic tests of any fetus of an individual or family member who is a pregnant woman, and genetic tests of any embryo legally held by an individual or family member utilizing assisted reproductive technology;
- The manifestation of a disease or disorder in an individual's family members (family history); or
- Any request for, or receipt of, genetic services or participation in clinical research that includes genetic services (genetic testing, counseling, or education) by an individual or an individual's family members.

GINA includes a "research exception" that allows health insurers and health plans who are engaged in research to request, but not require, that an individual undergo a genetic test so long as certain requirements are satisfied. Additional information on GINA and this exception are available on this OHRP website.

The PAU IRB will consider the protections and limitations of GINA when it assesses the risks of research generating or using genetic information and the adequacy of the measures to protect privacy and maintain confidentiality. Generally, the IRB will also require that the protections and limitations of GINA are disclosed in the consent process when applicable. Sample language for GINA is provided in PAU's template consent form.

## 23.10 Case Reports Requiring IRB Review

In general, an anecdotal report on up to 3 patients seen in one's own practice and a comparison of these patients to existing reports in the literature is not research and does not require IRB approval. Going beyond 3 patients in one's own practice or beyond one's own practice to seek out and report cases seen by other clinicians creates the appearance of a systematic investigation with the intent to contribute to generalizable knowledge and therefore is considered research and requires IRB approval.

### 23.10.1 Definitions

**Single Case Report:** The external reporting (e.g., publication, poster, or oral presentation) of an interesting clinical situation or medical condition of a single patient. Case reports normally contain detailed information about an individual patient and may include demographic information and information on diagnosis, treatment, response to treatment, follow-up after treatment, as well as a discussion of existing relevant literature. The patient information used in the report must have been originally collected solely for non-research purposes as the result of a clinical experience.

**Case Series.** The external reporting (e.g., publication, poster, or oral presentation) of an interesting clinical situation or medical condition in a series of patients (i.e., more than one patient). Case series usually contain detailed information about each patient and may include demographic information and information on diagnosis, treatment, response to treatment, followup after treatment, as well as a discussion of existing relevant literature. The information used in the report must have been originally collected solely for non-research purposes as the result of a clinical experience.

## 23.11 Over-Enrollment Policy

When an investigator enrolls more subjects than the number approved by the IRB, this is considered "over-enrollment" of subjects. If this happens, the investigator has engaged in a protocol deviation. Over-enrollment sometimes occurs in very innocuous ways, but it can also reflect a failure to adequately monitor and supervise the project.

The IRB Office maintains a log to track over-enrollment under each investigator for compliance purposes. If a repetitive pattern is observed, the IRB may consider whether the repeated overenrollment constitutes continuing non-compliance and may take further appropriate action as noted in Section 15.4.2.

### 23.11.1 Over-enrollment in Minimal Risk Research

If the over-enrollment of subjects is ≤10% of the total enrollment number previously approved by the IRB, the investigator is not required to file a reportable events form with the IRB; however, this protocol deviation must be reported in the Continuing Review or Annual Report. If data collection is ongoing, a modification to approve a larger sample must be submitted.

If the over-enrollment is > 10% above the number previously approved by the IRB, the investigator must submit a "Reportable Event" (RE) form (see Section 13). The RE form must indicate the date investigator became aware of the over-enrollment; the reason for overenrollment, how the data of over-enrolled subjects will be handled (used in data analysis or discarded), and corrective measures taken by the investigator to prevent such non-compliance in future studies.

### 23.11.2 Over-Enrollment in Studies that Present More than Minimal Risk

Any over-enrollment in any study that presents greater than minimal risk is a Reportable Event and must be reported immediately to the IRB (see Section 13).

## 23.9 Deception in Human Subjects Research

Deception involves misleading participants as to the true nature of the study procedures or leaving information about the study out of the consent form. The PI should clearly outline that the proposed research involves deception in their Initial Submission form. Deception must be justified and must not involving deceiving the subject regarding risk.

Deception is present any time some elements of consent are not disclosed (e.g., the full purpose of the study must be withheld for the research to be valid). The investigator must therefore request in their submission a waiver of elements of informed consent, which must be reviewed by the IRB for compliance with federal criteria for such waiver. The PI must provide a script to be used during the debriefing session after the subject's participation in the research study and utilize this to debrief subjects. After debriefing, the PI must ask participants if they would like their study information withdrawn and withdraw the study information should this be requested by the research participant. Compensation provided in the study must not be contingent upon agreeing to allow the use of one's data after the debriefing.

The PI may request an exception to the requirement that participants be allowed to withdraw their data during the debriefing. A data and principle-based justification for the exception must be provided.

Studies involving deception are necessarily minimal risk, and therefore can be reviewed by expedited or exempt review procedures if they otherwise meet the criteria and categories for expedited or exempt review.

### 23.10 Human Research Protection Program (HRPP) Policies and Procedures

Policies and procedures for the Human Research Protection Program are available on the following Web site: https://sites.google.com/a/paloaltou.edu/irb/.

## 24 Contact information for the Human Research Protections Program

The HRPP Office is in Room# F-11 on the Calvin Campus.

**IRB Office:**
Phone: 650-433-3870
Address: 1791 Arastradero Road, Palo Alto CA 94304 Email:
IRB@paloaltou.edu

**Institutional Official:**

Rowena G. Gomez, PhD
Assistant Provost of Research Assessment and Institutional Effectiveness (RAIE)
1791 Arastradero Road, Palo Alto, California, 94304
Email: rgomez@paloaltou.edu

# 25 APPENDIX A: Research Involving Pregnant Women, Human Fetuses, and Neonates

## 25.1 Research Involving Pregnant Women or Fetuses

### 25.1.1 Research Not Conducted or Supported by DHHS

For research not funded by DHHS where the risk to the pregnant women and fetus is no more than minimal, no additional safeguards are required and there are no restrictions on the involvement of pregnant women in research.

Pregnant women or fetuses may be involved in research not funded by DHHS **involving more than minimal risk** to pregnant women and/or fetuses if all of the following conditions are met:

1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
13. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus;
14. Any risk is the least possible for achieving the objectives of the research;
15. If the research holds out the prospect of direct benefit to the pregnant woman or the prospect of a direct benefit both to the pregnant woman and the fetus, then the consent of the pregnant woman is obtained in accord with the provisions for informed consent;
16. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the provisions for informed consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.
17. Each individual providing consent under paragraph 4 or 5 of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
18. For children (as defined in Section 12.1) who are pregnant, assent and permission are obtained in accord with the requirements of state law and the IRB;
19. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
20. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
21. The IRB may allow individuals whose normal responsibilities include determining the viability of fetuses to be engaged in the research, if their involvement in the determination of viability for an individual fetus cannot be avoided. Confirmation of the determination regarding viability will be sought from a qualified individual who is not otherwise engaged in the research whenever possible prior to beginning the research. The opinion of the independent qualified individual will be documented and made available

upon request to the IRB or HRPP representative. When advance confirmation is not possible, the investigator will obtain it as soon as s/he can after enrollment, but in all cases within 3 business days. The circumstances that prohibited prospective confirmation of viability and the outcome of the subsequent consultation are reported to the IRB within 5 business days.

### 25.1.2 Research Conducted or Supported by DHHS

For DHHS-conducted or supported research, 45 CFR Subpart B applies to all non-exempt human subject research involving pregnant women, fetuses, and neonates.

Pregnant women or fetuses may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
22. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
23. Any risk is the least possible for achieving the objectives of the research;
24. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, then the consent of the pregnant woman is obtained in accord with the provisions for informed consent;
25. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the provisions for informed consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest;
26. Each individual providing consent under paragraph 4 or 5 of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
27. For children (as defined in Section 12.1) who are pregnant, assent and permission are obtained in accord with the provisions of permission and assent in Section 12.7.2;
28. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
29. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

30. Individuals engaged in the research will have no part in determining the viability of a neonate.

## 25.2 Research involving Neonates of Uncertain Viability or Nonviable Neonates

### 25.2.1 Research Not Conducted or Supported by DHHS

Neonates of uncertain viability and nonviable neonates may be involved in research **involving more than minimal risk** if all of the following conditions are met:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
2. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
3. The IRB may allow individuals whose normal responsibilities include determining the viability of neonates to be engaged in the research, if their involvement in the determination of viability for an individual neonate cannot be avoided. In such cases, confirmation of the determination regarding viability must be made by a qualified individual who is not otherwise engaged in the research whenever possible prior to beginning the research. The opinion of the independent qualified individual will be documented and made available upon request to the IRB or HRPP representative. When advance confirmation is not possible, the investigator will obtain it as soon as she/he can after enrollment, but in all cases within 3 business days. The circumstances that prohibited prospective confirmation of viability and the outcome of the subsequent consultation will be reported to the IRB within 5 business days.
4. The requirements for Neonates of Uncertain Viability or Nonviable Neonates (see below in this section) have been met, as applicable.

   **Neonates of Uncertain Viability.** Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research unless the following additional conditions have been met:

   The IRB determines that:

(a) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or

(b) The purpose of the research is the development of important knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and

5. The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with the provisions of permission and assent, except that the consent

of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

**Nonviable Neonates.** After delivery, nonviable neonates may not be involved in research unless all of the following additional conditions are met:

1. Vital functions of the neonate will not be artificially maintained;
2. The research will not terminate the heartbeat or respiration of the neonate;
3. There will be no added risk to the neonate resulting from the research;
4. The purpose of the research is the development of important knowledge that cannot be obtained by other means; and
5. The legally effective informed consent of both parents of the neonate is obtained in accord with the provisions of permission and assent, except that the waiver and alteration of the provisions of permission and assent do not apply.

However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate <u>will not</u> suffice to meet the requirements of this paragraph.

### 25.2.2 Research Conducted or Supported by DHHS

Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
6. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
7. Individuals engaged in the research will have no part in determining the viability of a neonate.
8. The requirements for Neonates of Uncertain Viability or Nonviable Neonates (see below in this section) have been met, as applicable.

**Neonates of Uncertain Viability.** Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research unless the following additional conditions have been met:

The IRB determines that:

1. The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or

2. The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and\
3. The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with the provisions of permission and assent, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

**Nonviable Neonates.** After delivery, nonviable neonates may not be involved in research unless all of the following additional conditions are met:

1. Vital functions of the neonate will not be artificially maintained;
2. The research will not terminate the heartbeat or respiration of the neonate;
3. There will be no added risk to the neonate resulting from the research;
4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
5. The legally effective informed consent of both parents of the neonate is obtained in accord with the provisions of permission and assent, except that the waiver and alteration of the provisions of permission and assent do not apply.

However, if either parent is unable to consent because of unavailability or incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph.

### 25.3 Viable Neonates

After delivery, a viable neonate may be included in research only to the extent permitted by and in accord with the requirements for Research Involving Children (i.e., a viable neonate is a child for purposes of applying federal regulations and Palo Alto University policies).

### 25.4 Research Involving, After Delivery, the Placenta, the Dead Fetus or Fetal Material

Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities.

If information associated with material described above in this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research participants and all pertinent sections of these policies and procedures are applicable.

## 25.5 Research Not Otherwise Approvable

### 25.5.1 Research Not Conducted or Supported by DHHS

If the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and the research is not approvable under the above provisions, then the IRB will consult with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law). Based on the recommendation of the panel, the IRB may approve the research if:

(1) The research in fact satisfies the conditions detailed above, as applicable; or
(2) All of the following:
    (a) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates;
    (b) The research will be conducted in accord with sound ethical principles; and
    (c) Informed consent will be obtained in accord with the provisions for informed consent and other applicable sections of this manual.

### 25.5.2 Research Conducted or Supported by DHHS

DHHS conducted or supported research that falls in this category must be approved by the Secretary of Health and Human Services. If the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and the research is not approvable under the above provisions, then the research will be sent to OHRP for DHHS review.

# 26 APPENDIX B: Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects

## 26.1 Initial Review of Research Proposal

1. The prisoner representative must review research involving prisoners, focusing on the requirements outlined in Subpart C and these policies.
2. The prisoner representative must receive all review materials pertaining to the research (same as primary reviewer).
3. The prisoner representative must be present at a convened meeting when the research involving prisoners is reviewed. If the prisoner representative is not present, research involving prisoners cannot be reviewed or approved. The prisoner representative may attend the meeting by phone, video-conference, or webinar, so long as the representative is able to participate in the meeting as if they were present in person at the meeting.
4. The IRB must be familiar with the specific conditions in the local prison(s) or jail site(s) that are pertinent to subject protections, before approving the proposal for the local site (45 CFR 46.107(a)).

## 26.2 Modifications to Research

1. Minor modifications to research involving prisoners may be reviewed using the expedited procedure described below.
2. Modifications reviewed by the convened IRB must use the same procedures for initial review including the responsibility of the prisoner representative to review the modification and participate in the meeting (as described above).

## 26.3 Continuing Review

Continuing review will follow the same procedures as initial review including the responsibility of the prisoner representative to review the continuing review materials and participate in the meeting (as described above).

## 26.4 Expedited Review

1. Research **involving interaction** with prisoners may be reviewed by the expedited procedure if a determination is made that the research involves no greater than minimal risk for the prison population being studied and the research falls within the categories of research eligible for expedited review. Whenever possible, the prisoner representative will be consulted to verify that they agree that the research is minimal risk and to conduct (if designated by the IRB Chair as an expedited reviewer) or participate in the expedited review as a consultant. Review of modifications and continuing review will follow these same procedures;

2. Research **that does not involve interaction** with prisoners (e.g., records review) may be reviewed by the expedited procedure if a determination is made that the research involves no greater than minimal risk for the prison population being studied. Review by a prisoner representative is not required. The prisoner representative may review the research as a reviewer (if designated by the IRB Chair as an expedited reviewer) or consultant. Review of modifications and continuing review will follow these same procedures.

### 26.5 Incarceration of Enrolled Subjects

1. If a subject becomes a prisoner while enrolled in a research study that was not reviewed according to these procedures, the investigator must promptly notify the IRB and the IRB shall:
   a. Confirm that the subject meets the definition of a prisoner; and
   b. Consult with the investigator to determine if it is in the best interests of the subject to continue participation in the study, in part or in full, and if so, if there are specific study activities which are in the best interests of the subject that should continue until the IRB is able to review the research applying the standards and requirements for research involving prisoners.
2. If the subject should continue, one of two options are available:
   a. Keep the subject enrolled in the study and review the research applying the standards and requirements for research involving prisoners. If some of the requirements cannot be met or are not applicable (e.g., procedures for the selection of subjects within the prison), but it is in the best interests of the subject to remain in the study, keep the subject enrolled and, if the research is DHHSconducted or supported, inform OHRP of the decision along with the justification; or
   b. Remove the subject from the study and keep the subject on the study intervention under an alternate mechanism such as compassionate use or off-label use.
3. If a subject is incarcerated temporarily while enrolled in a study:
   a. If the temporary incarceration has no effect on the study (i.e., there is no need for study activities involving the prisoner subject to take place during the temporary incarceration), keep the subject enrolled.
   b. If the temporary incarceration has an effect on the study, follow the guidance outlined above.

### 26.6 Additional Duties of the IRB

In addition to the responsibilities of the IRB described in other sections of this manual, the IRB will review research involving prisoners and approve such research only if it finds that:

1. The research falls into one of the following **permitted categories** [45 CFR 46.306(a)(2)]:

   a. Study of 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 subjects;
   b. Study of 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 subjects;
   c. Research on conditions particularly affecting prisoners as a class (for example, research on diseases or social and psychological problems much more prevalent in prisons) provided that the study may proceed only after the DHHS Secretary has consulted with appropriate experts in penology, medicine, and ethics, and published notice in the Federal Register of his/her intent to approve the research;
   d. Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols/research plans approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the DHHS Secretary has consulted with appropriate experts in penology, medicine, and ethics, and published notice in the Federal Register of his/her intent to approve the research; or
   e. The research qualifies under the HHS Secretarial waiver that applies to certain epidemiological research (68 FR 36929, June 20, 2003). The criteria for this category are that the research must have as its sole purpose (i) to describe the prevalence or incidence of a disease by identifying all cases, or (ii) to study potential risk factor associations for a disease.
2. Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;
3. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
4. Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the investigator provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research proposal;
5. The information is presented in language which is understandable to the subject population;
6. Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is

clearly informed in advance that participation in the research will have no effect on his or her parole; and

7. Where the IRB finds there may be a need for follow-up examination or care of subjects after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing subjects of this fact.

## 26.7 Certification to DHHS

Under 45 CFR 46.305(c), the institution responsible for conducting research involving prisoners that is conducted or supported by DHHS shall certify to the Secretary (through OHRP) that the IRB has made the seven findings required under 45 CFR 46.305(a) and receive OHRP authorization prior to initiating any research involving prisoners. Certifications, and requests for DHHS Secretarial consultation, do not need to be submitted to OHRP for research not conducted or supported by DHHS.

For all DHHS-conducted or supported research, PAU will send to OHRP a certification letter to this effect, which will also include the name and address of the institution and specifically identify the research study in question and any relevant DHHS grant application or protocol/research plan. DHHS-conducted or supported research involving prisoners as subjects may not proceed until OHRP issues its authorization in writing to PAU on behalf of the Secretary.

Under its authority at 45 CFR 46.115(b), OHRP requires that the institution responsible for the conduct of the proposed research also submit to OHRP a copy of the research proposal so that OHRP can determine whether the proposed research involves one of the categories of research permissible under 45 CFR 46.306(a)(2), and if so, which one.

The term “research proposal” includes:

1. The IRB-approved protocol; any relevant DHHS grant application or proposal;
2. Any IRB application forms required by the IRB; and
3. And any other information requested or required by the IRB to be considered during initial IRB review.

OHRP also encourages the organization to include the following information in its prisoner research certification letter to facilitate processing:

1. The OHRP Federalwide Assurance (FWA) number;
2. The IRB registration number for the designated IRB; and
3. The date(s) of IRB meeting(s) in which the study was considered, including a brief chronology that encompasses:
    a. The date of initial IRB review; and

b. The date of Subpart C review, if not done at the time of initial IRB review.