



**University of California, Irvine
Human Research Protections
Standard Operating Policies and Procedures**

Policy Number: 1

Title: Institutional Commitment and IRB Authority

**Date of Last Revision: 01/29/09; 08/19/10; 05/24/11; 06/18/12; 05/01/13; 01/12/15;
01/28/15; 05/01/16; 08/01/16, 02/14/17, 06/07/17, 08/24/17, 11/27/18, 02/25/19;
01/05/22; 03/09/22; 12/04/23**

Policy:

The University of California, Irvine (UCI) commits to upholding its Assurance and to registering its boards with the Office for Human Research Protections (OHRP). UCI supports review by one Institutional Review Board for multi-site clinical trials and collaborative research (single IRB review or sIRB).

- A. UCI agrees to uphold the ethical principles of the *Belmont Report*.
- B. UCI will apply OHRP regulations (45 CFR 46, including all Subparts) to all federally-funded proposed research involving human participants. Commensurate protections are in place for all other human subject research conducted at or under the jurisdiction of UCI.
- C. UCI agrees to apply additional regulations such as, the U.S. Food and Drug Administration (FDA) Human Subject Regulations (21 CFR 50, 56, 312 and 812) and the Health Insurance Portability and Accountability Act of 1996 (HIPAA), when applicable, to research involving human participants.
- D. Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practices and the applicable regulatory requirements.
- E. Safeguarding the rights and welfare of human participants in research and other research activities is a general Institutional policy delegated by the Chancellor through the Vice Chancellor for Research. The Vice Chancellor for Research is the Institutional Official (IO). The IO is responsible to exercise appropriate administrative oversight to assure that UCI's policies and procedures designed for protecting the rights and welfare of human participants are effectively applied in compliance with its Assurance.

I. IRB Registration

- A. Through a Federalwide Assurance (FWA), an institution commits to the Department of Health and Human Services (HHS) that it will comply with the requirements in the HHS Protection of Human Subjects regulations at 45 CFR part 46. The Federalwide Assurance (FWA) is the only type of assurance currently accepted and approved by OHRP.
- B. UCI's FWA is 00004071. The FWA is maintained electronically and is available on the UCI Human Research Protection Program's (HRP) website: <https://research.uci.edu/human-research-protections/>.
- C. Human subjects research that takes place under the legal name of UCI (The Regents of the University of California as described in Article IX, Section 9 of the California Constitution (University of California, Irvine))

are covered under UCI's FWA and subject to HRP policies and procedures.

- D. UCI's faculty, staff, and students, which comprise its schools, departments, divisions, institutes and facilities, are subject to the FWA and subject to HRP policies and procedures. This includes any research for which an Assurance or another formal agreement (e.g., MOU) identifies UCI's Institutional Review Board (IRB) as the IRB of record.
- E. IRBs are operated by IRB Organizations (IORGS). UCI's IORG is 0000236.
- F. IORGs allow for registration of IRBs. The individual UCI IRB registration numbers are:
 - 1. IRB A: 00000393
 - 2. IRB B: 00000394
 - 3. IRB C: 00000395
 - 4. IRB E: 00008624
 - 5. IRB WB: 00011147
- G. A list of IRB members is available from the main UCI Human Research Protections website.
- H. IRB Registration is effective for three years. Updates are required as specified through the IORG website. As an example, IRB registration must be updated within 90 days after changes occur regarding the contact person who provided the IRB registration information and/or the IRB chairperson.

II. **Structure of the Human Research Protections Unit**

- A. The UCI Office of Research Administration (ORA) is an administrative unit of the Office of Research. Research Protections (RP) and Sponsored Projects are divisions of OR. Human Research Protections (HRP) is a unit within Research Protections. HRP facilitates and promotes the ethical involvement of human subjects in research by providing administrative support to the IRBs, and consultative services to Investigators and their research staff. The UCI HRP staff facilitates the IRB review and approval of human subjects research in accordance with applicable federal and state regulations, and UC/UCI policies and procedures.
- B. The Director of HRP has operational and HRP personnel management responsibilities. The Director reports to the Associate Vice Chancellor for Research Administration. The Assistant Director of HRP is part of the management team that supports the operational goals of the unit.

III. **Structure of the Institutional Review Board**

- A. The IRB Committees are official University Regulatory Committees. The IRB Committees serve UCI as a whole, rather than a particular school or department, and any institution for which UCI's IRB is designated as the IRB of record in an Assurance filed with OHRP with a corresponding MOU.
- A. UCI's Assurance presently designates five (5) OHRP-registered IRB Committees. Designation of additional IRB Committees under the Assurance requires prior notification of and approval by OHRP.
 - 1. Three Committees review biomedical research studies that are designed primarily to increase the scientific base of information about

- normal or abnormal physiology and development, and studies intended to evaluate the safety, efficacy, and usefulness of drugs, biologics, devices, medical products, procedures or interventions.
2. One Committee reviews social and behavioral sciences studies that are designed primarily to contribute to behavioral, educational, psychological, and social science knowledge.
 3. One Committee primarily reviews matters of alleged non-compliance related to human subject research conducted by a UC Irvine personnel. This committee may also review unanticipated problem reports that involve matters of potential non-compliance and transactional items when needed to support ongoing research.

IV. Responsibilities of the IRB to Provide Oversight in accordance with the Federalwide Assurance

- A. Approval by the IRB is required prior to the initiation of all human subjects research.
- B. Except for research exempted or waived in accordance with 45 CFR 46.101(b) or 45 CFR 101(i), all federally human subjects research will be reviewed, prospectively approved, and, subject to continuing oversight and review at least annually by the IRB.
- C. The IRB has the authority to:
 1. Approve, require modifications in (to secure approval), or disapprove all research activities covered by this policy.
 2. Require that information given to subjects as part of informed consent is in accordance with 45 CFR 46.116 and 21 CFR 50.25. The IRB may require that information, in addition to that specifically mentioned in 45 CFR 46.116, be given to the subjects when the information would meaningfully add to the protection of the rights and welfare of subjects.
 3. Require documentation of informed consent or waive documentation in accordance with 45 CFR 46.117 and 21 CFR 50.27.
 4. Grant permission for the use of surrogate consent, in accordance with California Health and Safety Code 24178.
 5. Observe or have a third party observe the consent process and the research.
 6. Suspend, place restrictions on, or terminate approval of research activities that are not being conducted in accordance with applicable federal regulations, state statutes, and/or UC/UCI policies and procedures, or that has been associated with unanticipated problems involving risk to subjects or others.
- D. Federally funded human subject research that qualifies as Exempt research in accordance with 45 CFR 46.104, will be reviewed by an experienced HRP staff member or IRB Chair to confirm exempt status and registered for three years.
- E. Exempt confirmation may be made by additional, various mechanisms at UCI. See Policy # 12.
- F. UCI Exempt research activities are subject to the same subject protections and ethical standards as outlined in *The Belmont Report*. All exempt research is subject to applicable UCI and UCI IRB policies and procedures.

- G. Research reviewed and approved by the IRB may be subject to review and disapproval by officials of UCI, or any institution for which the UCI IRB is designated as the IRB of record in accordance with an Assurance or a signed MOU or IRB Authorization Agreement with the UCI. However, if the UCI IRB does not grant IRB approval or suspends or terminates IRB approval, these decisions may not be overturned anyone at a higher level.
- V. **Single IRB Review of Multi-Site Clinical Trials and Cooperative Research**
- A. UCI supports the use of a single Institutional Review Board (sIRB) for multi-site research to enhance and streamline the IRB review process. sIRB eliminates duplicative IRB review thereby minimizing unnecessary administrative burdens and systemic inefficiencies while assuring human subjects protections. Other institutional regulatory requirements such as Conflict of Interest, Radiation Safety, Human Stem Cell Research Oversight and Institutional Biosafety must reviewed and approved at UCI.
 - B. UCI IRB can serve as the IRB of Record for an external site engaged in non-exempt research as well as cede IRB review to a non-UCI IRB. To ensure that appropriate regulatory requirements are addressed as part of the IRB review process, typically, international sites are excluded from these agreements.
 - C. When the UCI IRB serves as the IRB of Record it is accepting the responsibility of oversight of the conduct of the research for a particular study site.
 - D. The terms and responsibilities of the IRB of record, the ceding Institution are documented in an IRB Authorization Agreement for a single protocol or a Memorandum of Understanding (MOU) or IRB Master Agreement for multiple research cooperative agreement. Agreements may include UCI serving as the Privacy Board for institutions that do not have such a committee.
 - E. UCI IRB currently has several reciprocal Master Agreements whereby any institution signed on the agreement may serve as the IRB of Record. See HRPP Policy # 4.
- VI. **Transferring IRB Oversight / Continuity**
- A. To prevent lapses in human subject protection, it is generally preferred that the same IRB retain oversight responsibility throughout the conduct of a study, if possible. That said, sometimes transfers to another IRB for subsequent review and oversight is desired or necessary (e.g., sponsor request, workload redistribution – temporary or permanent, unexpected, adverse events such as natural disaster).
 - B. When transferring IRB oversight, the original IRB works closely with the clinical investigator, the receiving IRB, and the sponsor, as appropriate, throughout the transfer process to assures continuous IRB oversight with no lapse in either IRB approval or the protection of human subjects, and with minimal disruption of research activities.
 - C. The breadth and duration of the IRB transfer process may vary depending on the reason for the transfer, the entities involved, and the number and type of studies being transferred.

- D. When transferring ongoing research to another IRB, UCI will assure that the terms and responsibilities of the Reviewing IRB and UCI as the ceding institution are documented in an IRB Master Agreement.
- E. In general, the IRB transfer process involves:
 - 1. Identifying the studies to be transferred;
 - 2. Ensuring the availability and retention of pertinent research records;
 - 3. Establishing an effective date for transfer of oversight, including IRB records, for the clinical investigation(s) and other types of studies;
 - 4. Receiving IRB conducts a review of the studies (new or continuing review), as appropriate, before it accepts responsibility for the studies;
 - 5. Confirming or establishing the date for the next continuing review;
 - 6. Determining whether the consent form needs to be revised;
 - 7. Notifying the Original IRB, the investigator, and sponsor; and
 - 8. Updating IRB registration information, as applicable

References:

45 CFR 46

21 CFR 50 and 56, 312, 812

45 CFR 160 and 164

California Health and Safety Code Sections 24170-24179.5

Declaration of Helsinki

NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research

University Policy on Protection of Human Subjects in Research (issued September 2, 1981)

UCI Office of Research Continuity Plan – March 2014

UCI Research Policy for the Protections of Human Subjects in Research

The Belmont Report

Procedure Number: 1.A**Title: Procedure for Institutional Oversight of Assurance****Procedure:**

This procedure outlines the UCI Institutional Review Board responsibilities in maintaining the UCI Federalwide Assurance.

I. Lead Researcher (LR) Responsibilities;

- A. Obtains the appropriate knowledge regarding human subjects protections, ethics, federal regulations, training, and monitoring to conduct their proposed research,
- B. Assures that the research team is adequately trained and knowledgeable regarding human subjects protections, ethical considerations, and Federal regulations applicable to the proposed research,
- C. Complies with the training, monitoring, and human research guidance as outlined in the Assurance and IRB policies and procedures,
- D. Assures that when UCI is ceding IRB review, the study or clinical trial is registered with UCI IRB,
- E. Complies with the determinations and requirements of the IRB of record and follows the policies of the IRB of record,
- F. Reports Unanticipated Problems Involving Risks to Subjects or Others, and potential Serious Noncompliance or Continuing Noncompliance instances to the IRB of record and to UCI IRB when UCI is ceding review

II. Department Chair Responsibilities;

- A. The IRB relies on the Department Chair or Organized Lead Unit Director to help assess the new human subject protocol and provide an assurance to the following points:
 - 1. The Lead Researcher (and Faculty Sponsor) is competent to perform (and supervise) the study,
 - 2. The research is appropriate in design (i.e., the research uses procedures consistent with sound research design, the study design can be reasonably expected to answer the proposed question, and the importance of the knowledge expected to result from the research is known),
 - 3. There are adequate resources and funds available to support the performance of this research.

III. Institutional Official (IO) Responsibilities;

- A. Allocates the Office of Research budget,
- B. Ensure that the Human Research Protections unit and the IRB has sufficient resources, including IRBs appropriate for the volume and types of human research to be reviewed, so that reviews are accomplished in a thorough and timely manner,
- C. Speak for and legally commit the institution to adherence to the requirements of the federal regulations regarding the involvement of human subjects in biomedical and social-behavioral research,
- D. Assures institutional compliance with the Assurance, federal regulations, state statutes, and UC/UCI policies and procedures,

- E. Appoints and may remove IRB Chairs, Vice Chairs and IRB Members for service on the UCI IRBs,
 - F. Review and sign federal assurances and addenda,
 - G. Ensures ongoing authority and autonomy of the IRBs to perform their function,
 - H. Provides adequate resources for maintenance of human subject protection at UCI, including HRP staff, facilities, resources and equipment,
 - I. Reports to the Executive Vice Chancellor, communicates with the Vice Chancellor, the Vice Chancellor for Health Affairs, the Deans of the Schools and other campus officials regarding human subjects protection issues,
 - J. Suspends or terminates IRB approval of research,
 - K. Disapproves research approved by the IRB
- IV. **Associate Vice Chancellor for Research Administration (AVCRA) for Research Responsibilities;**
- A. Oversees and manages the activities of the OR to promote responsible and ethical conduct in research and to ensure cooperation among individuals and offices that support research and other sponsored activities,
 - B. Creates the Human Research Protection Program budget,
 - C. Reviews and authorizes sIRB MOUs,
 - D. Appoints IRB Chairs, Vice Chairs and IRB Members for service on the UCI IRBs
- V. **IRB Committee Responsibilities;**
- A. Reviews all human subjects research activities and document its findings regarding ethical considerations, scientific merit in regard to the risk/benefit profile, adherence to federal regulations, state statutes, and IRB policies and procedures,
 - B. Reviews and monitors ongoing research for adherence to the federal regulations, state statutes, and IRB policies and procedures,
 - C. Has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. The IRB's action of suspension or termination shall be reported promptly to the investigators, appropriate institutional officers, and the Secretary of HHS,
 - D. When UCI is ceding IRB review, the IRB subcommittee (or designee) may confirm the appropriateness of ceding research that involves greater than minimal risk
- VI. **Director of Research Protections Responsibilities;**
- A. Assures that UCI's Federalwide Assurance and IRB registration is updated or renewed as required.
 - B. Assures that UCI maintains standard policies and procedures (SOPPs) reflecting the current practices of the IRB in conducting reviews and approvals under its Assurance.
 - 1. These policies and procedures will be maintained and kept current by UCI's Human Research Protections staff. The SOPPs will be re-

- reviewed at least every three years. All revision dates will be listed under the revision date section for each policy and procedure.
2. As appropriate, procedures are developed and revised by the Human Research Protections' Director or designee. Changes in policy are to be discussed and confirmed by the IRB Chairs, the Associate Vice Chancellor for Research, and the Human Research Protections Management. Changes are provided at the Research Protections Working Group.
 3. All procedures are to be approved by the Director of Human Research Protections.
- C. Oversees program implementation and management and communicates to the IO or their designee any human research protections issues that are likely to present risks or other concerns to the institution,
 - D. Coordinates, on behalf of the IRB, prompt reporting to the IO and to governmental oversight entities of unanticipated problems involving risks to subjects or others, serious or continuing non-compliance with Federal regulations or IRB requirements, and suspension or termination of IRB approval,
 - E. Maintains, as the official institutional record, all documents pertaining to UCI's Assurance and compliance activity,
 - F. Overall responsibility for management and supervision of all HRP personnel,
 - G. Reviews and negotiates sIRB agreements (IAAs and MOUs). The Director or designee has the authority to sign IAAs (single protocol agreements),
 - H. Appoints (or designee) IRB Chairs, Vice Chairs and IRB Members for service on the UCI IRBs
- VII. Annually, the budget for the IRB and the HRP will be reviewed by the Vice Chancellor for Research, the Associate Vice Chancellor for Research Administration and the Director of Human Research Protections and modified as necessary to accommodate the volume and type of research reviewed, space, facilities and staff.

Policy Number: 2

Title: Activities Subject to IRB Jurisdiction

Date of Last Revision: 01/29/09, 10/18/10, 01/28/15, 05/01/16, 03/12/19, 05/03/21, 01/07/22, 12/04/23

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board to have jurisdiction over all human subjects research subject to its Federalwide Assurance (FWA).

I. Review and Approval of Human Subjects Research

- A. All human subjects research, clinical investigations, and all other activities, which in part involve human subject research, regardless of sponsorship, must be reviewed and approved by UCI's IRB or by an IRB designated as the IRB of record. An IRB is designated as the IRB of record when UCI has entered into an IRB Authorization Agreement or a Memorandum of Understanding with the IRB.
 - 1. No intervention or interaction with human subjects in research, including advertising, recruitment, and/or screening, may begin until the IRB or IRB designees have reviewed and approved the research.
 - 2. Whether a proposed activity constitutes human subject research can be determined by the Human Research Protections (HRP) staff. (See Policy # 16.)
 - 3. Researchers may make their own assessment utilizing Quali Research Protocols (KRP), the IRB submission system, available from the main HRP webpage at: <https://research.uci.edu/human-research-protections/>.
- B. UCI's FWA defines its jurisdiction over the review of human subjects research. Regardless of sponsorship, the IRB or a designated IRB must review all human subjects research if any of the following apply:
 - 1. The research is conducted by or under the direction of any UCI employee (i.e., faculty, staff, student) or agent in connection with their institutional responsibilities;
 - 2. The research uses UCI property, facilities, or resources to support or carry out the activity;
 - 3. The name of the University of California, Irvine is used in applying for funds (intra or extramural);
 - 4. The name of the University of California, Irvine is used in explanations and/or representations to subjects;
 - 5. The UCI employee or agent plans to use their University of California, Irvine association in any dissemination, publication or public presentation resulting from the research;
 - 6. The research involves the use of non-public information maintained by UCI to identify or contact human subjects or prospective subjects.
- C. The State of California IRB reviews research involving California issued death records (certificates and indices). (See Policy # 29.)
- D. If an Investigator begins a non-research activity and later finds that

analysis of the private identifiable data would contribute to generalizable knowledge, the Investigator must submit an application to the IRB for approval prior to analysis of the data for research purposes or prior to publication or presentation with the intent to contribute to generalizable knowledge (e.g., journal article, poster session, public speech, presentation, or project report).

- E. Only faculty with paid appointments of 50% or more, Emeriti faculty, and Academic Administrators may serve as Lead Researchers on research proposals. Students, volunteer (i.e., non-salaried) faculty members and staff may also assume the Lead Researcher (LR) role as long as they have a formal affiliation with UCI and have a Faculty Sponsor (FS) who fulfills the Lead Researcher eligibility criteria.

II. **Failure to Obtain IRB Approval**

- A. The implications of engaging in activities that qualify as human subjects research therefore requiring IRB review and approval without obtaining such approval are significant. Results from such studies may not be published or presented unless IRB approval had been obtained prior to collecting the data. The IRB will determine whether the data may be used to satisfy thesis or dissertation requirements.
- B. Investigators who request approval to continue human subjects research under 45 CFR 46 and/or under 21 CFR 50 and 56 that was not previously reviewed, or request approval to use data that was collected without IRB approval, face the possibility that the IRB will recommend withdrawal or request that the Investigator administratively withdraw their application, as the IRB cannot give post-hoc (retroactive) approval.
- C. The IRB may not approve applications where the Investigator has attempted to circumvent IRB policies and procedures regarding human subjects research by collecting data as non-research and then applying to use it as existing data. It is therefore in the Investigator's best interest to carefully consider the likelihood that they will want to use the data for research purposes in the future, and to err on the side of inclusion and seek IRB approval prior to commencing the work.
- D. General Counsel of the Regents of the UC has stated that: "If a principal investigator conducts an activity involving human subjects but does not obtain the approval of the campus Human Subjects committee or designated IRB, the Regents would not be obligated to defend or indemnify the principal investigator if legal action were instituted by the subject."

III. **Exempt Human Subjects Research**

Exempt confirmation may be made by various mechanisms at UCI. (See Policy # 12.)

IV. **Confirmation that Activities do not Constitute Human Subjects Research**

Confirmation that activities do not constitute human subject research are determined by the investigator. (See Policy # 16.)

References:

45 CFR 46

21 CFR 50 and 56
21 CFR 812
University Policy on Protection of Human Subjects in Research
UCI Research Policy for the Protections of Human Subjects in Research
2018 Common Rule 45 CFR 46

Procedure Number: 2.A**Title: Procedure for Activities Subject to IRB Jurisdiction****Procedure:**

This procedure provides guidance on the types of activities that are subject to review and approval by the UCI Institutional Review Board.

I. Lead Researcher (LR) Responsibilities

- A. The LR submits an IRB Application, which includes a description of their activity for review and obtains a determination of exemption or approval prior to the initiation of human subjects research.
 - i. The LR may submit an Exempt Self-Determination application. (See Policy # 12.)
- B. If unsure if the activity constitutes human subject research, the LR may also make their own assessment utilizing KRP and the Non-Human Subject Research Determination application.

II. IRB Responsibilities

- A. The IRB reviews the proposed activity in accordance with applicable regulatory, institutional and IRB policies and procedures.
- B. If a human subjects research study has been completed without prior IRB approval, the IRB Chair or Committee requests withdrawal of the application for research and notifies the LR of the regulatory requirements regarding prospective IRB approval of human subjects research. The LR and Faculty Sponsor, if applicable, may be notified that the data not be used for any publications, presentations, thesis, or dissertation requirements.
- C. If the IRB Chair or Committee determines that an Investigator has attempted to circumvent IRB policies and procedures regarding human subjects research by collecting data as non-research and then applying to use them as existing data the IRB Chair or Committee may request that the application for research be withdrawn. The LR and Faculty Sponsor, if applicable, may be notified that the data may not be used for any publications, presentations, thesis, or dissertation requirements.

III. Human Research Protections (HRP) Staff Responsibilities

- A. The HRP staff processes the research protocol in accordance with applicable IRB policies and procedures.

TABLE 1

TYPE	DESCRIPTION	IRB REVIEW REQUIRED
Clinical Investigation	Experiments using a test article on one or more human subjects that are regulated by the Food and Drug Administration or support applications for research or marketing permits for products regulated by the Food and Drug Administration. Products regulated include foods, including dietary supplements that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products.	YES
Standard Diagnostic or Therapeutic Procedures	The collection of data about established and accepted diagnostic, therapeutic procedures, or instructional methods for dissemination or contribution to generalizable knowledge.	YES
	An alteration in patient care or assignment for research purposes.	YES
	A diagnostic procedure added to a standard treatment for the purpose of research.	YES
	An established and accepted diagnostic, therapeutic procedure or instructional method, performed only for the benefit of a patient but not for the purposes of research.	NO
Novel Procedures, Treatment, or Instructional Methods	A systematic investigation of innovations in diagnostic, therapeutic procedure, or instructional method in multiple participants in order to compare to standard procedure. The investigation is designed to test a hypothesis, permit conclusions to be drawn, thus to develop or contribute to generalizable knowledge.	YES
	The use of innovative interventions that are designed solely to enhance the wellbeing of an individual patient and have a reasonable expectation of success. The intent of the medical or	NO

TYPE	DESCRIPTION	IRB REVIEW REQUIRED
	behavioral science practitioner is to provide diagnosis, preventive treatment, or therapy to the particular individual.	
Repositories (e.g., storage of data and/or biospecimens for future research)	A storage site or mechanism by which identifiable human tissue, blood, genetic material, or data are stored or archived for research by multiple Investigators or multiple research projects.	YES
	Storage of human tissue, blood, genetic material, or data that has been de-identified by UCI/UCIMC personnel at the time of collection.	YES May qualify as “non-human subject research”
UCI functioning as the Coordinating Center for a Multi-center Research Project	UCI is <i>NOT</i> an enrolling site and the UCI LR has agreed to serve as the coordinating center for a multi-center trial, which may include activities such as data collection, data analysis, reporting of an unanticipated problem involving risk to participants or others to regulatory authorities, and/or oversight of the research at participating sites.	YES LR should be aware of additional responsibilities
	UCI <i>IS</i> an enrolling site and the UCI LR has agreed to serve as the coordinating center for the multi-center trial, which may include activities such as data collection, data analysis, reporting of an unanticipated problem involving risk to participants or others to regulatory authorities, and/or oversight of the research at participating sites.	YES LR should be aware of additional responsibilities
Emergency Use of an Investigational Drug or Device	1. This does not limit the physician’s ability to deliver emergency care. The physician may deliver such care, but the data derived from such care may not be used in any prospectively conceived research. 2. Emergency use involving investigational drugs, devices or biologics must meet the Food and Drug Administration (FDA) requirements.	IRB NOTIFICATION REQUESTED PRIOR TO USE
	Sponsor requires IRB approval to release drug/device in emergency use situation.	YES

TYPE	DESCRIPTION	IRB REVIEW REQUIRED
Educational Activities/Field Study Courses/Research Methods Classes	Activities designed for educational purposes only. The data will not contribute to generalizable knowledge or will not result in a master's thesis, or doctoral dissertation.	NO
Case Studies	Retrospective review of no more than three (3) patients' medical records with intent to document a specific situation or the experience of the individuals without intent to form a research hypothesis, draw conclusions or generalize findings. Data published will be de-identified (i.e., none of the 18 PHI identifiers).	NO
	Retrospective review of more than three (3) patient's medical record(s).	YES
	Retrospective review of a patient's medical records for use in an educational setting. The data will be de-identified.	NO
Ethnographic Research	The Investigator or their staff will participate, overtly or covertly, in people's daily lives for an extended period of time. They will be watching what happens, listening to what is said, asking questions and collecting data to create a broader understanding of a particular environment, ethnic group, gender, etc.	YES
Internet Research	Use of internet websites (e.g., Amazon Turk, Twitter, Facebook, chat rooms) are used to conduct research regarding a particular topic. This may include the completion of questionnaires/surveys, cognitive tasks, or the collection of personal data, etc.	YES

TYPE	DESCRIPTION	IRB REVIEW REQUIRED
Public Health Surveillance Activities	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).	NO
Oral Histories	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.	NO
	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)	YES
	Oral historians and qualitative investigators may want to create archives for the purpose of providing a resource for others to do research. The intent of the archive is to create a repository of information for other investigators to conduct human research.	YES

TYPE	DESCRIPTION	IRB REVIEW REQUIRED
Quality Assurance and Quality Improvement Activities	Evaluations of a specific project, process, or resource utilization review, etc. where the primary intent (design) of the activity is solely for internal assessment or improvement.	NO
	Activities conducted for the purpose of (a) implementing a practice to improve the quality of patient care, and (b) collecting patient or provider data regarding the implementation of the practice for clinical, practical, or administrative purposes	NO
Pilot Activities	Preliminary activities typically designed to help the Investigator refine data collection procedures. This data is to be included in the publication.	YES
	Activities including those involving only one individual may be subject to the same scrutiny as a full-scale research project. Although the data derived from a pilot activity may not be included in the full-scale research project, the activity would still need IRB review prior to conducting the activity.	YES
Criminal Justice Activities	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.	NO
National Security Activities	Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.	NO

Policy Number: 3

Title: Research Involving Performance Sites

Date of Last Revision: 08/10/05, 11/06/10, 4/20/12, 05/01/16, 01/21/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board to assure that appropriate approvals and/or written agreements are in place when human subjects research involves performance sites. In general, an institution is considered *engaged* in a particular non-exempt human subjects research project when its employees or agents for the purposes of the research project obtain: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research.

I. Performance Sites “Engaged” in Research

- A. Regardless of financial support or funding, UCI’s IRB must assure that all performance sites “engaged” in research have approval from the IRB of Record for the proposed research to be conducted at the site.
- B. The performance site “engaged” in research may have the proposed research reviewed and approved by:
 - 1. its own assurance holding IRB;
 - 2. another designated assurance holding IRB; or
 - 3. UCI IRB providing an approved Memorandum of Understanding (MOU) is on file.
- C. Initiation of research conducted at a performance site “engaged” in research is contingent upon UCI’s IRB receipt and review of the IRB approval from the “engaged” performance site.
- D. It is the responsibility of the IRB of Record and the Assurance holding institution to assure that the resources and facilities are appropriate for the nature of the research under its jurisdiction.

II. Performance Sites “Not engaged” in Research

- A. When performance sites are “not engaged” in research and have an established IRB, the Lead Researcher (LR) must obtain documentation to conduct the research at the “not engaged” site from the site’s IRB (e.g., evidence that IRB approval is not needed for that activity).
- B. When performance sites are “not engaged” in research and the “not engaged” site does not have an established IRB, a letter of cooperation/permission must be obtained demonstrating that the appropriate institutional officials/representatives are permitting the research to be conducted at the performance site.
- C. It is the responsibility of the UCI LR and the performance site “not engaged” in research to assure that the resources and facilities are appropriate for the nature of the research.
- D. It is the responsibility of the UCI LR and/or the performance site “not engaged” in research to notify the UCI IRB promptly if a change in

research activities alters the performance site's engagement in the research (e.g., performance site "not engaged" begins consenting research participants, etc.)

- E. The IRB reserves the right to require the cooperation/permission letter be provided prior to initial IRB approval, once available, at the time of continuing review, or as part of a routine quality improvement review.

References:

45 CFR 46

21 CFR 50 and 56

OHRP Guidance Document: Assurance of Performance Sites, September 1998

OHRP Guidance Document: Engagement of Institutions in Research, October 2008

Procedure Number: 3.A**Title: Procedure for Research Involving Performance Sites****Procedure:**

This procedure outlines the process for assuring approval for "engaged" and "not engaged" performance sites associated with UCI human subject research.

I. Lead Researcher (LR) Responsibilities

- A. The LR will obtain documentation of IRB approval or letter of cooperation / permission for sites "engaged" and "not engaged" in human subjects research with UCI.
- B. The LR will include any IRB approval documentation for "engaged" sites in the initial submission to the IRB. The LR may begin research activities at each site as it is approved by UCI's IRB.
- C. The LR will obtain the IRB approval letters or letters of cooperation/permission for each performance site. It is the responsibility of the LR to maintain current IRB documentation, (e.g., approvals, continuing reviews, updated assurance, investigator qualifications, etc.), throughout the course of the research.
- D. It is the LR's responsibility to assist performance sites that do not have an IRB and are "engaged" in research in securing the appropriate Assurance and IRB approvals.

II. IRB Committee Responsibilities

- A. The Committee needs to determine whether the site is "engaged" versus "not engaged" in research. (See Policy 3.)
- B. Additions of study sites may be reviewed and approved in an expedited manner by the Chairperson or their designee, when appropriate documentation (e.g. IRB approval, Letter of Cooperation, etc.) is provided by the LR.
- C. For performance sites "engaged" in research where UCI has agreed to serve as the IRB of Record through a MOU, the HRP will maintain electronic documentation of this agreement.
- D. As noted above, the IRB reserves the right to require the cooperation/permission letter be provided prior to initial IRB approval, once available, at the time of continuing review, or as part of a routine quality improvement review.

III. The Human Research Protections (HRP) Team Responsibilities

- A. The HRP team (Administrator, Sr. Analyst, and Analyst) under the direction of the Administrator will verify that the appropriate documentation for performance sites has been submitted to the IRB for approval. If omissions in documentation are found, a team member will contact the LR specifying the required documentation needed from the performance site(s).
- B. The HRP team will verify the institution's OHRP Assurance number and IRB registration number with both OHRP and the FDA as applicable for performance sites "engaged" in research, where UCI is relying and the

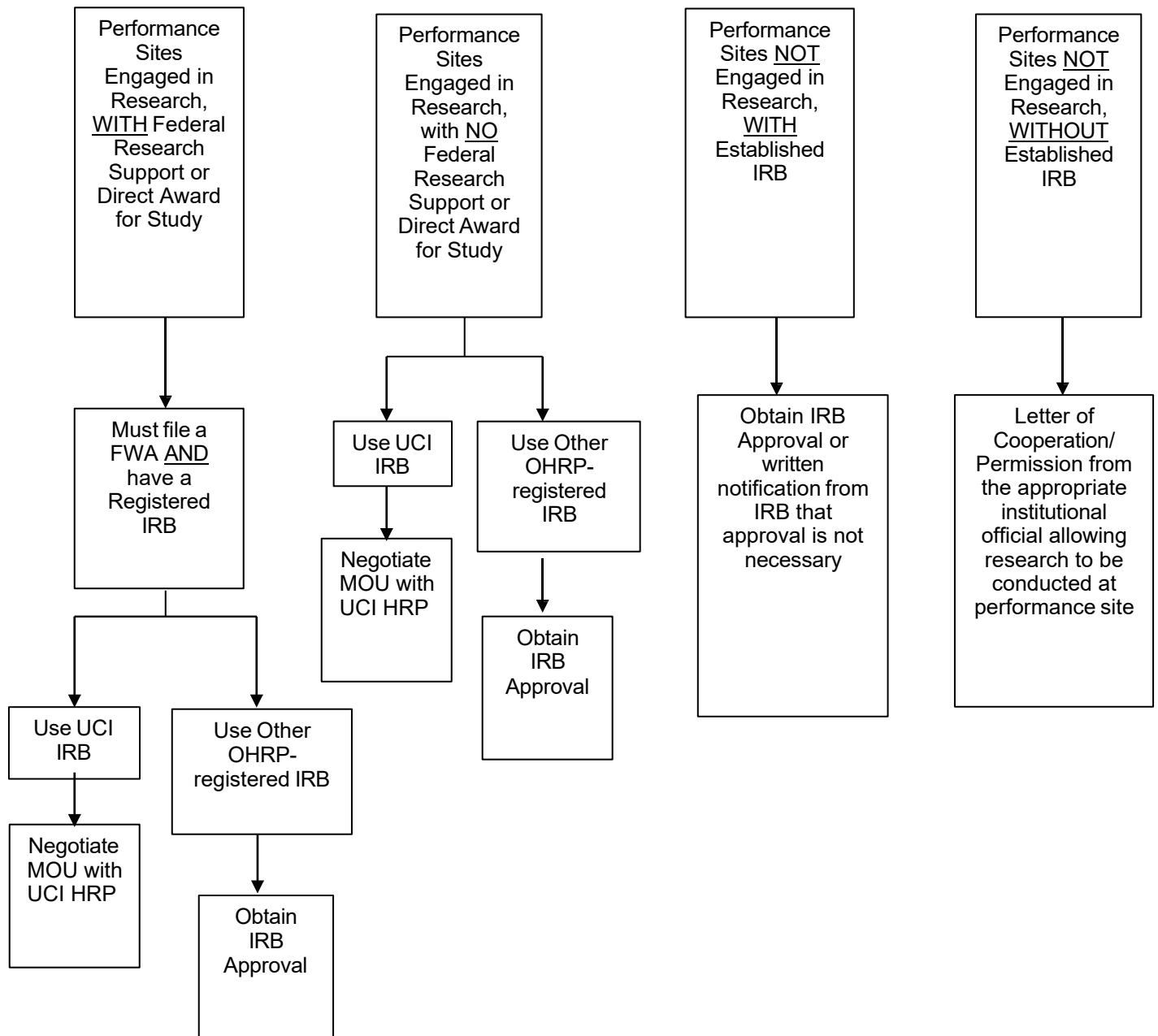
institution is not signed on to the SMART IRB. These numbers are located on the OHRP website.

Attachment:

Collaborating Institution and Performance Site Flow Chart

Examples of Research Activities Meeting Requirements for "Engaged" vs. "Not Engaged."

PERFORMANCE SITES *ENGAGED AND NOT ENGAGED IN RESEARCH



***Engaged in Research.** A performance site becomes “engaged” in human subject research when its employees or agents (i) intervene or interact with living individuals for research purposes; or (ii) obtain individually identifiable private information for research purposes. Further, an institution is automatically considered to be “engaged” in human subject research whenever it receives a direct federal award to support such research. In this case, the awardee institution bears ultimate responsibility for protecting human subjects under the award. See OHRP [Guidance on Engagement of Institutions in Human Subjects Research](#) for more information.

Social/Behavioral
Examples of Research Meeting Requirements for "Engaged" vs. "Not Engaged"

EXAMPLE	IRB DECISIONS BASED ON REGULATIONS
<p>UCI Investigators are allowed to come into the elementary school classroom to observe, audio/video tape, or distribute surveys/questionnaires for research purposes. The students and teachers of the school are consented by UCI Investigators to participate.</p>	<p>The school would be considered "not engaged" in research. The students and teachers of the school are participants in a study for which they have been consented.</p>
<p>A teacher is administering a standardized test at his elementary school as part of an educational requirement. The UCI Investigator is collecting the test scores as part of a UC Irvine research project. The teacher is not administering the informed consent or performing data analysis.</p>	<p>The school would be considered "not engaged" in research. The teacher is performing a task as part of his professional responsibility. The school will release data to the UCI Investigator with parental permission.</p>
<p>An organization performs its own research, which is completed by its own personnel. Investigators at UCI will analyze the data. The data will not have identifiers. However, the UCI Investigator will be included in the publication.</p>	<p>The organization would be "engaged" in research. UCI would be considered "not engaged." The investigator will not analyze data that includes identifiable private information and co-authoring a paper, journal article or presentation does not constitute engagement.</p>
<p>High School teachers and UCI Investigators are paired together to develop a novel math curriculum that will be evaluated in the classroom. The teachers will administer the curriculum while the UCI Investigators will interview the students throughout the process.</p>	<p>Both the schools and UCI would be "engaged in research" as both would be collecting data and involved in the publication of the results.</p>
<p>UCI receives an award and obtains a letter of cooperation from Garden Grove School District to perform research, which involves students. The teachers do not obtain consent from the students but will be administering surveys to the students as part of the research. UCI Investigators obtain informed consent; the teacher is not involved in the planning of the study, the analysis of data, or the publication of results.</p>	<p>UCI would be considered "engaged in research" as UCI received funding to conduct the research. The school is "not engaged" in research as the teacher is not obtaining consent, etc., but is functioning as a contract provider and is performing a task that he/she is trained and qualified to perform. Teachers may also be research subjects, which may require informed consent.</p>

Biomedical
Examples of Research Meeting Requirements for "Engaged" vs. "Not Engaged"

EXAMPLE	IRB DECISIONS BASED ON REGULATIONS
A UCI Investigator is conducting research and consenting subjects for research. Subjects may get their blood and tissue samples taken from a local clinic instead of the UCI site, because of convenience.	The local clinic is "not engaged" in research as they are considered to be a "contract" provider and the participant requested use of the local clinic. A contract provider may only perform commercial services in which they are appropriately qualified (e.g., an appropriately qualified laboratory performs analyses of blood samples for Investigators solely on a commercial basis) or perform other genuinely non-collaborative services meriting neither professional recognition nor publication privileges. UCI is "engaged" in research.
A UCI Investigator has a 5-year research study, which requires a hearing evaluation as part of follow-up. A subject chooses to see their local doctor to obtain the hearing evaluation.	The local doctor would be considered "not engaged" in research as they are providing a service, which is considered standard practice. UCI is "engaged" in research.
A UCI Investigator will contract with an independent MRI center to conduct MRI procedures for research purposes. The MRI center will then send all reports to the Investigator.	The independent MRI center is considered "not engaged" in research. The MRI center is considered a contract provider and providing a service for which they are qualified to perform outside of the research context. UCI is "engaged" in research.
An external clinic (outside UCI) has written permission from the participants to disclose Protected Health Information to a UCI Investigator for research purposes. The data was collected at the external clinic solely for the purpose of routine clinical care.	The external site is "not engaged" in research because they have obtained explicit written permission from the participants to release PHI. UCI is "engaged" in research.
A UCI Investigator receives grant funding from the Federal government. The research is conducted at the OC Health Department with the assistance of OC Health Department employees.	OC Health department would be considered "engaged" in research. UCI is "engaged" in research as the recipient of the funding and as such the UCI IRB must also approve the research. The OC Health Department IRB must also review and approve the research study.
A UCI Investigator is conducting an oncology study in which additional non-UCI sites would follow the protocol and administer the chemotherapy.	Both UCI and non-UCI sites would be considered "engaged" in research as they will be obtaining consent and performing research procedures. All sites require IRB approval from each site's IRB.

Policy Number: 4

Title: Offsite Research, Cooperative Research and Research at UCI-affiliated Institutions

Date of Last Revision: 10/12/07, 11/06/10, 05/01/16, 08/02/19, 09/23/19, 03/11/20, 06/22/20, 10/12/20, 01/21/22, 09/12/22, 05/11/23

Policy:

- I. All human subjects research, including off-site research, cooperative research studies and research at University of California, Irvine (UCI)-affiliated institutions, must be reviewed and approved by UCI's Institutional Review Board (IRB), an independent IRB or other non-UCI IRB as prospectively agreed upon by the UCI IRB or otherwise registered with the UCI IRB, prior to initiation of the research if it satisfies any of the following criteria:
 - A. The research is conducted by or under the direction of any UCI employee (i.e., faculty, staff, or student¹) or agent in connection with his/her institutional responsibilities;
 - B. The research uses UCI property, facilities, or resources to support or carry out the activity;
 - C. The name of the University of California, Irvine is used in applying for funds (intra or extramural);
 - D. The name of the University of California, Irvine is used in explanations and/or representations to subjects;
 - E. The UCI employee or agent plans to use their University of California, Irvine association in any dissemination, publication or public presentation resulting from the research;
 - F. The research involves the use of non-public information maintained by UCI to identify or contact human subjects or prospective subjects;
 - G. UCI receives a direct Federal award to conduct human subject research, even where all activities involving human subjects are carried out by a subcontractor or collaborator; and/or
 - H. The research is conducted in accordance with an Assurance filed with OHRP in which UCI's IRB is designated as the IRB of record through an established Memorandum of Understanding (MOU).

- II. **Memorandum of Understanding (MOU) with Other UC Campuses**

UCI IRB Committees along with IRB Committees at the other UC campuses and UC-managed laboratories have signed a MOU that allows one UC IRB to rely on another UC IRB for review and approval of human-subjects research protocols that are:

 - A. Eligible for expedited review or greater than minimal risk to the subjects and
 - B. Will be conducted concurrently at one or more UC location, or
 1. Involves personally identifiable data or samples from one or more UC location for which investigators at another UC location will be conducting analyses.
 2. The MOU, effective March 21, 2006, is reviewed annually to

¹ See HRPP Policy # 12 for exceptions.

determine whether improvements or amendments to the MOU are needed.

- C. For studies where UCI is the prime awardee for extramural funding, UCI will serve as the UC Reviewing IRB for the other UC campuses.
- D. **In an effort to promote a more streamlined process, where UCI serves as the IRB of record, UCI will utilize the SMART IRB agreement instead of the UC IRB Reliance or MOU. A Letter of Agreement between both institutions is required.**

III. **Children's Hospital of Orange County (CHOC)-Memorial Healthcare Systems (MHS)-UCI (CMU) Agreement for Research**

UCI IRB Committees, CHOC, and MHS have signed an agreement that allows the UCI IRB to rely on the CHOC IRBs for review and approval of human subjects research protocols conducted by UCI researcher (i.e., faculty, staff, or student) that are solely conducted at CHOC. One exception to this provision is when a UCI researcher submits a positive COI Disclosure requiring a UCI COIOC management plan. In this instance, UCI IRB review and oversight is required. Other exceptions shall be determined by the Institutional Official at either UCI, CHOC, or MHS.

- A. **In an effort to promote a more streamlined process, where UCI serves as the IRB of record, UCI will utilize the SMART IRB agreement instead of the UC IRB Reliance or MOU. A Letter of Agreement between both institutions is required.**

IV. **SMART IRB** - the "Streamlined, Multisite, Accelerated Resources for Trials" IRB Reliance platform supported by the National Center for Advancing Translational Sciences (NCATS) to facilitate multi-site clinical trials.

- A. **Important note:** SMART IRB is not an actual IRB that provides regulatory approval. SMART IRB provides a roadmap for institutions to implement the Single IRB Review requirements. Through a flexible master IRB reliance agreement, standard operating procedures, and complementary tools and resources, SMART IRB supports and encourages collaboration and harmonization across the nation.
- B. **In an effort to promote a more streamlined process, where UCI serves as the IRB of record, UCI will utilize the SMART IRB agreement instead of the UC IRB Reliance or MOU. A Letter of Agreement between both institutions is required.**

V. **Fountain Valley Regional Hospital** - UCI has also entered into an MOU wherein UCI serves as the IRB of Record for Fountain Valley Regional Hospital. UCI will also act as its HIPAA Privacy Board.

VI. **Memorandum of Understanding (MOU) with the National Cancer Institute (NCI) Central Institutional Review Boards (CIRBs)**

- A. UCI IRB Committees have established an MOU with the NCI Adult and Pediatric CIRBs. The MOU allows the UCI Committees to rely upon the NCI CIRB for:
 - 1. Review of Cooperative Group Trials from the following cooperative groups: ACOSOG, CALGB, ECOG, GOG, NCCTG, NCIC, NSABP, RTOG, and SWOG, as well as any other studies opened in the Cancer Trials Support Unit.

- VII. **UCI has also entered into MOUs where a non-UCI IRB is designated as the IRB of Record for example:**
- A. National Cancer Institute Central IRB (CIRB) for review and oversight of NCI multi-center, adult cooperative oncology studies.
 - B. StrokeNet Central IRB for review and oversight of small and large clinical trials and research studies to advance acute stroke treatment, stroke prevention, and recovery and rehabilitation following a stroke.
 - C. NeuroNEXT, or Network for Excellence in Neuroscience Clinical Trials, was created to conduct studies of treatments for neurological diseases through partnerships with academia, private foundations, and industry.
 - D. NEALS, or Northeast Amyotrophic Lateral Sclerosis (ALS), is a non-profit group of research institutions who collaboratively conduct clinical research in ALS and other motor neuron diseases.
 - E. Independent IRBs for review and oversight of industry-authored clinical trials, including:
 - 1. Western IRB (WIRB) or its affiliates;
 - 2. Advarra
 - F. UCI continues to enter into IRB Authorization Agreements and MOUs to support single IRB review of multi-site trials and cooperative research.

VIII. **UCI IRB as the IRB of Record or Coordinating Center for Multi-site Research**

The UCI IRB will serve as the IRB of Record for an offsite location when the offsite location is engaged in human research.

- A. **Differences between “IRB of Record” and “Coordinating Center.”**
- 1. When the UCI IRB serves as the IRB of Record, it is accepting the responsibility of research conduct oversight for a particular study or site. The details of such an agreement are outlined in a Memorandum of Understanding, as necessary.
 - 2. When UCI serves as the Coordinating Center (i.e., the UCI investigator is the lead investigator of a multi-site study or UCI is the lead institution of a multi-site study), the UCI investigator is responsible for assuring that IRB approval is granted at the participating sites prior to the initiation of the research at that site. It is important to note that even when UCI serves as the “Coordinating Center,” the UCI IRB is not serving as the IRB of Record for all sites. The Coordinating Center assumes responsibility for assuring that the participating site(s) has received IRB approval.
 - 3. Under rare circumstances, the UCI IRB may be requested to serve as the IRB of Record for a participating site of a multi-center trial in which a UCI Investigator is serving as the “Coordinating Center.” The participating site either may not have an IRB, or due to other circumstances, may request the UCI IRB to serve as their IRB of Record for that particular study at that particular site.

B. **UCI IRB as the IRB of Record**

1. The Senior Director of Human Research Protections (HRP), the Director of HRP or designee, including the IRB Chair/s or IRB Vice Chair/s, the Associate Vice Chancellor, or the Institutional Official will make all final determinations regarding the UCI IRB Committee's willingness to serve as the IRB of Record and Privacy Board for an offsite location "engaged" in research.
2. A Memorandum of Understanding (MOU) is executed when the UCI IRB serves as the IRB of Record for a site that is not a UCI-affiliated site. The MOU outlines specific provisions and responsibilities for each party entering into the agreement. The OHRP IRB Authorization template is one example of a MOU that may be used.
3. The UCI IRB will not accept an "Unaffiliated Investigator Agreement" in order to serve as the IRB of Record. All agreements for the UCI IRB to serve as the IRB of Record for a performance site "engaged" in research must be detailed in a MOU and an executed agreement negotiated by UCI Sponsored Projects when federal funds are involved.
4. Conditions for the UCI IRB to serve as the IRB of Record:
 - a. UCI investigator will be conducting research at the offsite institution. The institution engaged in human research does not have an IRB and will rely solely on the UCI IRB for review of human subjects research activities; *or*
 - b. The performance site engaged in human research may or may not have an IRB of Record but will rely on the UCI IRB for a specific research project.
 - c. The research shall be conducted in collaboration with UCI; and
 - d. The UCI Investigator has a formal affiliation with UCI.
 - e. **In general, the relying institution is not an international site.**
5. When federal funds are involved, the performance site engaged in research requesting UCI IRB to serve as the IRB of Record must:
 - a. File a Federalwide Assurance (FWA); and
 - b. Conduct the research in accordance with the terms and conditions specified in the executed agreement negotiated by UCI Sponsored Projects.
6. The UCI investigator must provide all necessary information pertaining to local research activities conducted at an offsite location in the UCI IRB protocol and in accordance with UCI IRB policies and procedures.
7. The UCI IRB and offsite location will maintain an approved Federalwide Assurance (FWA) and provide verification of such during the negotiation of the MOU.
8. Investigators will comply with all oversight activities deemed appropriate by the UCI IRB, Federal oversight agencies and/or Federal funding agencies at all sites (e.g., monitoring, auditing).
9. **As noted above, where a cooperative institution has an IRB and UCI is requested to serve as the IRB of record, UCI will require the use of the SMART IRB.**

10. **Requests for collaborating sites to rely on the UCI IRB must be made via a formal amendment to the UCI IRB approved study. Reliance agreements where UCI serves as the IRB of record will not be considered at initial review due to the amount of time involved as this often protracts the initial IRB approval timeframe for the UCI site.**
 11. **Regarding HIPAA: When collaborative sites have their own Privacy Board, the UCI IRB (which serves as the Privacy Board at UCI) will not serve as the Privacy Board for the relying institution.**
- C. Communication with other IRBs**
1. **The UCI investigator must provide all necessary information regarding local contact information in the UCI IRB application.**
 2. The UCI investigator or representative from the offsite location must provide to the IRB and keep current the names, addresses, and phone numbers of local contact persons who can make decisions regarding IRB issues.
 3. UCI requires that the offsite location, relying on the UCI IRB as the IRB of Record, communicate any audit findings or other problems associated with the conduct of research to UCI IRB. Findings or problems include but are not limited to: unanticipated problems involving risk to participants or others, complaints from research participants, or any serious or continuing non-compliance issues.
 4. The UCI IRB will report promptly to the appropriate institutional officials of the offsite location all actions taken by the UCI IRB regarding (a) any serious or continuing noncompliance by investigators and (b) any suspension or termination of IRB approval in accordance with the UCI IRB policies and procedures.
- D. Coordinating Center for Multi-site Research**
1. The UCI investigator must provide all necessary information regarding participating sites in the UCI IRB application.
 2. The UCI IRB will acknowledge the existence of any Coordinating Center established or affiliated with a UCI investigator and determine whether the Coordinating Center has sufficient mechanisms in place for the protection of research participants when acting as a Coordinating Center.
 3. The UCI IRB must determine that the UCI Coordinating Center has sufficient mechanisms in place to assure that:
 - a. An adequate plan is in place to address project management and data and safety monitoring given the nature of the research.
 - b. IRB approval at the participating sites will be obtained prior to initiation of the research at that site (the UCI investigator is responsible for obtaining each site's IRB approval letter and IRB approved informed consent documentation);
 - c. UCI IRB approval will be obtained before implementing any changes to the UCI IRB-approved study, and IRB approval will be obtained at the participating sites before implementing modifications at the sites.

- d. Participating sites have a mechanism for reporting interim results.
- e. The participating sites have written procedures for assuring prompt reporting to the UCI IRB of any unanticipated problems involving risk to participants or others; any serious or continuing non-compliance; and any suspension or termination of IRB approval for cause.
- f. In addition, each site is responsible for reporting any unanticipated problems involving risk to participants or others; any serious or continuing non-compliance; and any suspension or termination of IRB approval for cause directly to OHRP, the FDA, as applicable.

IX. UCI IRB as the Relying IRB

- A. The Senior Director of Human Research Protections (HRP), the Director of HRP or designee, including the IRB Chair/s or IRB Vice Chair/s, the Associate Vice Chancellor, or the Institutional Official will make all final determinations regarding the UCI IRB Committee's willingness to rely on a non-UCI IRB.
- B. UCI will maintain the responsibility of the Privacy Board for matters relating to UCI HIPAA.
- C. In general, UCI may rely upon the IRB of another institution provided one of the following is true:
 - 1. The IRB is the IRB of an AAHRPP accredited organization, or the organization is actively seeking AAHRPP accreditation.
 - 2. The IRB has current certification from the Consortium for Applied Research Ethics Quality (CARE-Q).
 - 3. The UCI Investigator is a collaborator on human research primarily conducted at another institution and the UCI investigator's role does not include interaction or intervention with subjects.
 - 4. UCI is engaged in human research solely because UCI is the prime awardee. UCI investigators will not interact or intervene with subjects or collect or possess private identifiable information about subjects, nor obtain informed consent.
 - 5. Unless it is an IRB Organization, the institution must maintain an OHRP-approved Federalwide Assurance ("FWA"), regardless of whether it engages in federally funded human subjects research that is subject to the Federal Policy for the Protection of Human Subjects ("Federal Policy").
 - a. **If the reviewing institution is not signed on to the SMART IRB (requiring the above), evidence of the FWA is to be verified by HRP Staff.**
 - 6. An executed Memorandum of Understanding (MOU) will be executed. The MOU will outline the specific provisions and responsibilities for each party entering into the agreement.

X. Department of Defense (DoD) Research

- A. When UCI IRB is relying, the relying IRB will address requirements as per the DoD Instruction [\(DoDi\) 3216.02](#).
- B. **Department of Navy (DoN) Research:**
 - 1. DoN commands and activities may collaborate with each other, other DoD agencies, non-defense federal agencies and non-

federal institutions. An appropriate written agreement shall be established between the collaborators that includes a Statement of Work (SOW) and specific assignment of responsibilities.

- a. The agreement should briefly describe the research, specific roles and responsibilities of each institution, responsibility for scientific and IRB review, recruitment of subjects, and procedures for obtaining informed consent. The agreement also should describe provisions for oversight and ongoing monitoring, reporting requirements, documentation retention and compliance for the entire research project. All collaborators must ensure compliance with all relevant human subject protection regulations at their sites. Collaborating institutions that rely on other institutions' IRBs for human subject protections to avoid duplication of effort must ensure that such reliance does not compromise any standards of requirements.

References:

21 CFR 50.3(c)

45 CFR 46.102 (d, f)

California Health and Safety Codes 102231, 125115-125117

UCI Research Policy for the Protections of Human Subjects in Research

SECNAVINST 3900.39D 8f

DoDi 3216.02

Procedure Number: 4.A

Title: Procedure for Review of UC MOU Multi-campus Research

Procedure:

MOU with other UC Campuses: This procedure describes the process for review of protocols under the UC MOU for multi-campus research studies.

- I. **When the UCI IRB is Relying on Another UC Campus:**
 - A. The UCI investigator notifies the UCI IRB and the UC reviewing IRB of the intent to submit a protocol under the UC MOU via the IRB Application.
 - B. The UCI IRB will determine if reliance upon another UC campus for IRB review is acceptable. Also, the reviewing IRB has to agree to perform the review. The UCI IRB and/or the reviewing IRB will notify the UCI investigator by e-mail or phone if there is a problem.
 - C. UCI will maintain the responsibility of the Privacy Board for matters relating to UCI HIPAA.
 - D. UCI will maintain consent template injury language, as applicable in the UCI consent form/ document.
 - E. The UCI IRB will issue an Administrative Registration letter to the UCI investigator and the Reviewing IRB. The registration period will coincide with the reviewing IRB approval expiration date. The UCI investigator must keep a copy of the registration letter and approval documents for their records.
- II. **When the UCI IRB is Reviewing for Another UC Campus:**
 - A. UCI will require the use of the SMART IRB to facilitate multisite research.
 - B. The UCI IRB will determine if reliance upon another UC campus for IRB review is acceptable. In addition, the reviewing IRB has to agree to rely.
 1. When UCI requests that UC Berkeley rely, HRP Staff will reach out to the UC Berkeley IRB Director to confirm prior to moving forward with the reliance.
 - C. UCI will not serve as the Privacy Board for non-UCI sites.
 - D. The UCI IRB will issue an IRB Approval letter to the UCI investigator.
 - E. The UCI investigator must keep a copy of the registration letter and approval documents for their records.
 - F. **Further, the UCI investigator is responsible for forwarding all UCI IRB approval documents to the non-UCI site.**
- III. **UCI Lead Researcher (LR) Responsibilities**
 - A. UCI Investigator Responsibilities to UC Reviewing Campus: The UCI Investigator must comply with all decisions of the reviewing IRB. This includes following the standards and guidelines of the reviewing IRB for the reporting of any unanticipated problem involving risk to participants or others and other safety information.
 - B. UCI Investigator Responsibilities to the UCI IRB: The UCI Investigator is responsible for advising the UCI IRB of any amendments or continuation of the approved study by submitting copies of such materials to the Office of Research Administration.
 - C. Preserving Efficiencies at UCI: Where efficiencies are in place at UCI to reduce researcher burden, such as the use of the Study Team Tracking Log for the addition and removal of Research Personnel, UCI researchers

may continue to utilize such efficiencies. The UCI Investigator should first confirm such practice would not be in conflict with the requirements of the reviewing IRB, as appropriate.

IV. **Non-UCI LR Responsibilities**

- A. UC Relying Campus Investigator Responsibilities: Investigators should contact their IRBs for details on the acknowledgment process for their campus.

V. **IRB Analyst or Higher Responsibilities**

- A. When a request to rely on another UC IRB is received, prepares materials for IRB review to determine if reliance on another UC IRB is acceptable.
- B. Prepares correspondence requesting revisions from the IRB and approval letters using the appropriate template.
- C. Assures all appropriate database entries are completed.
- D. Assures all relying campuses receive UCI IRB acceptance or approval documentation.

Procedure Number 4.B**Title: Procedure for Review of NCI CIRB Approved Studies****Procedure:**

This procedure describes the process for review of NCI CIRB-approved studies by the UCI IRB Committees.

I. Background

The Central Institutional Review Board (CIRB) Initiative is sponsored by the National Cancer Institute (NCI) in consultation with the Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP). The CIRB provides expert IRB review at the national level before the Cooperative Group distributes the protocol to local investigators. The CIRB is composed of individuals who represent a broad range of oncology disciplines and may include oncology physicians, nurses, patient representatives, pharmacists, ethicists and attorneys. Because UCI has established a formal agreement with the NCI CIRB, investigators who wish to participate in the Cooperative Group Trials reviewed by the NCI CIRB may take advantage of these reviews.

The CIRB currently reviews Cooperative Group Trials from the following cooperative groups: ACOSOG, CALGB, ECOG, GOG, NCCTG, NCIC, NSABP, RTOG, and SWOG, as well as any other studies opened in the Cancer Trials Support Unit.

II. NCI CIRB Review Procedures

- A. The established national cooperative research groups are charged with designing and evaluating protocols related to specific disease types. The cooperative groups forward to the NCI CIRB the protocol, the informed consent document(s), a completed CIRB application and, when appropriate, an investigator drug brochure via the Protocol Information Office at NCI.
- B. The CIRB members meet at least once a month. At the meetings the Board members discuss the protocol and may consult by telephone with the Study Chair to explore any concerns they may have.
- C. The Board takes one of the following actions for each protocol: approve, approve pending modification, table, or disapprove. Any non-approval is followed up with communication with the Study Chair to resolve, wherever possible, outstanding issues identified by the Board.
- D. After approval or disapproval, the Study Chair and Cooperative Group sponsor are formally notified.
- E. For each protocol, the CIRB's primary reviews, minutes, notification letters, and any other correspondence are posted in a section of NCI CIRB for participating institution's IRBs to access.
- F. In addition to conducting initial reviews, the CIRB conducts Continuing Reviews and reviews of Serious Adverse Events (SAEs), Data Safety Monitoring Board (DSMB) reports, protocol amendments, national subject recruiting materials, etc. These actions are also posted on the web site for prompt access by participating institutions.

III. **Lead Researcher (LR) Responsibilities**

- A. The single IRB (sIRB) Application for CIRB studies must be accompanied by the Local IRB Facilitated Review Packet available on the NCI CIRB website.
- B. The sIRB Application for CIRB studies is brief and is designed to capture information about the local context (e.g., study team, recruitment and informed consent processes, reporting of any unanticipated problem involving risk to participants or others and confidentiality of data).
- C. In addition to completing the sIRB Application, the NCI CIRB consent must include specific UCI template language additions.
- D. The following information must be included with the sIRB Application:
 - 1. The Local IRB Facilitated Review Packet from the "Participant side" of the NCI CIRB website.
 - 2. An informed consent document that conforms to the UCI consent template.
- E. LRs must review the CIRB website regularly to keep current with all information including amendments to CIRB-approved studies. UCI requires facilitated review of study amendments.
- F. LRs must track study expiration dates to prevent study approvals from expiring. UCI requires facilitated review of continuing renewals.
- G. LRs must submit any internal (on-site) unanticipated problem involving risk to participants or others to both the UCI IRB and the NCI CIRB.
- H. LRs must submit renewal and modification materials to both UCI and CIRB in a timely manner so that approvals and facilitated reviews may be kept in synch.

IV. **UCI IRB Review Procedures:**

- A. A subcommittee of the IRB will conduct a "facilitated review" of the study submitted by the UCI investigator. The subcommittee is usually the IRB Chair, Vice Chair or another voting member with sufficient oncology expertise. The subcommittee reviews the submission and any other materials available on the CIRB web site (e.g., minutes), so they can determine whether there are local concerns that need to be addressed and whether to accept the CIRB Review.
- B. The subcommittee has the authority to accept the CIRB approval "as is," accept it with minor modifications (see Policy # 11) or they may decide not to accept the CIRB review and require that the investigator submit a protocol for full committee review (see Policy # 14). If the subcommittee does not accept the CIRB review they may still utilize CIRB written materials as resources for full committee review.
- C. The subcommittee has authority to require and approve additions to the informed consent. UCI template language must be added to the informed consent dealing with institutional requirements and IRB policies. *No CIRB approved information may be deleted from the informed consent document.* The IRB may also make minor word substitutions or additions in the informed consent document, particularly to facilitate better comprehension by the local population, as long as the proposed changes do not alter the meaning of the CIRB approved contents. Additional risks may be added to the informed consent document. NOTE: Revisions/changes to the UCI consent form other than those described above require full committee review. In this instance, facilitated review will not be used and the CIRB will not serve as the IRB of record for the protocol at UCI.

- D. Once approved, the UCI IRB sends a CIRB approval notice to the investigator. The date of protocol expiration is set to the expiration date of the CIRB approval. Example: the CIRB study expiration date is April 20, 2007. UCI accepts CIRB approval on June 10, 2007. The UCI approval period for the study would be June 10, 2007 to April 20, 2008.
- E. The UCI HRP office will notify the CIRB Administrative Office each time it accepts the CIRB review of a protocol, by clicking on the "Facilitated Review Acceptance" link within the main menu for each protocol and completing the Facilitated Review Acceptance Form. In order for the CIRB to become the Official IRB of Record for the site for a particular study, this form needs to be completed and submitted online. A separate form must be submitted for each protocol review that is accepted.
- F. The CIRB will use UCI's reply to set up a database both for record keeping and notification purposes. The CIRB will notify the local IRB when there are any actions taken on the protocol, e.g., an SAE report requiring a change in the consent form, an approved protocol amendment, a change in the protocol/informed consent resulting from the Continuing Review, etc.

**University of California, Irvine
Human Research Protections
Standard Operating Policies and Procedures**

Policy Number: 5

Title: IRB Records and Documentation

Date of Last Revision: 01/29/09, 09/26/10, 01/27/11, 06/05/13, 02/24/15, 05/01/16, 02/08/17, 08/01/17, 10/25/17, 12/10/19, 02/17/22, 09/12/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to maintain IRB office records for research activities under its jurisdiction.

- I. The IRB records must be maintained in a manner that contains a complete history of all IRB actions related to review and approval of a protocol, including renewals, amendments and any reportable events (serious or continuing non-compliance, unanticipated problems).
- II. **Document Retention**
 - A. IRB records are stored for 10 years beyond the end of the calendar year in which the study is closed in both onsite and off-site locations. Records are stored electronically and on paper.
 1. IRB paper files for currently active or archived studies are stored off-site at an Iron Mountain Storage Facility.
 2. IRB minutes and rosters are stored off-site at an Iron Mountain Storage Facility with the more recent documents (post-2019) being stored in UCI's electronic IRB database.
 3. Completion of a study occurs when the Lead Researcher submits a closing report or 30 days after IRB approval of the study expires, whichever comes first.
 4. If a study is canceled without participant enrollment, records also are still maintained for 10 years beyond the end of the calendar year in which the study is closed.
- III. **Access to Documents**

The Office of Research (OR) must make all IRB records accessible for inspection and copying at reasonable times and in a reasonable manner by:

 - A. Internal entities authorized to review IRB files including OR and the Office of Internal Audit.
 - B. Authorized representatives of any regulatory oversight agency such as the FDA, OHRP, National Institutes of Health (NIH) and other government sponsors of human research.
 - C. Administrative records (e.g., minutes, member lists, and budgets) are maintained indefinitely.
 - D. Access to UCI's electronic IRB database is limited to appropriate Office of Research, OR staff and UCI partners as needed for business purposes (e.g., School of Medicine). Electronic systems are frequently backed up and have a data recovery and disaster management plan.
 - E. For Department of Defense sponsored research there may be a requirement to submit records to the Department of Defense for archiving.

- IV. **The HRP must prepare and/or maintain all of the following documents:**
- A. IRB Applications - All research applications/protocols reviewed (including studies that never enrolled subjects), including scientific and scholarly evaluations, if any, approved sample informed consent documents, data safety monitoring board/committee reports, progress reports submitted by the Lead Researchers, and reports of any unanticipated problems to participants including reports of injuries to subjects and others, any reports of serious or continuing noncompliance.
 - B. Renewals - Records of continuing review activities.
 - C. Amendment Requests - Records of minor and significant changes to research activities.
 - D. Suspension or termination of IRB approval – Per 45 CFR 46.113: An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head.
 - E. Correspondence with Lead Researchers - Correspondence between the IRB and the Investigators.
 - F. New Findings - Statements of significant new findings developed during the course of the research, which may relate to the participant's willingness to continue participation that will be provided to the participants. This information may be provided in the Re-consent Cover memo. The cover memo will be attached to the revised Consent Form.
 - G. IRB Minutes - The minutes of all IRB Committee meetings.
 - H. IRB Rosters - Changes in membership are updated as per the Health and Human Services (HHS) Registration requirements and maintained electronically.
 - I. IRB Policies and Procedures - The IRB will maintain written policies and procedures that will be reviewed at least every three years.

References:

45 CFR 46.115

UC Records Retention Schedule, Research Administration Records, B.5. - IRB Records including Human Studies Exempted from IRB Review records; Approved 2015-11-20

OHRP: [Update or Renew an IRB Registration Webpage](#)

Procedure Number 5.A

Title: Procedure for IRB Records and Documentation

Procedure:

This procedure outlines the necessary maintenance of IRB office records associated with research activities under the jurisdiction of the UC Irvine (UCI) Institutional Review Board (IRB).

- I. IRB Administration Responsibilities are assumed by the Office of Research Administration. Human Research Protections (HRP) staff prepares and/or maintains adequate documentation of IRB activities, including the following:
 - A. **Protocol File** – The following documentation is retained in the relevant protocol file:
 1. *New Submission* - All available documents related to the submission of a research protocol including but not limited to:
 - a. The Initial Application
 - b. Scientific Evaluations, if any
 - c. Consent and Assent Forms
 - d. Recruitment Advertisements
 - e. the Master Protocol, if applicable
 - f. the Sponsor's Brochure, if applicable
 - g. DHHS-approved sample informed Consent Form, if applicable
 - h. DHHS-approved protocol, if applicable
 2. *Renewal* – records of continuing review activities including but not limited to:
 - a. The Renewal Application
 - b. The most current Consent/Assent Forms
 - c. Data Monitoring reports, if available
 - d. List of unanticipated problems, and any serious or continuing noncompliance submitted to the IRB since initial approval (may need to be generated by the HRP staff via a separate report).
 3. *Amendment Request* - records of requests for revisions to protocol including but not limited to:
 - a. The Amendment Application
 - c. The revised Consent/Assent Forms, if applicable
 - d. Recruitment advertisements, as applicable
 - e. The Sponsor's Amendment, if applicable
 4. *IRB Approval letter* for each of the above IRB activities. The approval letter will document:
 - a. The specific permissible Exempt or Expedited category(ies);
 - b. Determinations required by the regulations for:
 - (1) Waiver or alteration of the consent process;
 - (2) Research involving pregnant women, fetuses, and neonates;
 - (3) Research involving prisoners;
 - (4) Research involving children; and
 - c. The initial and renewal, the frequency (approval period) for the next continuing review.
 5. *Individual Reports of New Information* including reports of noncompliance submitted by the Lead Researcher are maintained in

the protocol file.

6. *IRB/HRP documentation* – All review activity documentation such as materials provided by the HRP staff to the IRB reviewer(s):
 - a. The specific permissible Exempt or Expedited category(ies) are noted in the IRB application, along with the below.
 - b. Determinations required by the regulations and protocol-specific findings supporting those determinations including:
 - (1) Waiver or alteration of the consent process;
 - (2) Research involving pregnant women, fetuses, and neonates;
 - (3) Research involving prisoners;
 - (4) Research involving individuals with impaired decision-making capacity;
 - (5) Research involving children; and
 - c. The frequency (approval period) for the next renewal, as noted in the Reviewer Checklist.
7. *Correspondence* - All correspondence between the IRB, HRP staff and Investigators is maintained. Correspondence related to a research protocol are kept in the protocol within UCI's electronic IRB database.

- B. ***IRB Minutes*** - The minutes of all IRB Committee meetings must be in sufficient detail to demonstrate:
 1. The specific IRB Committee;
 2. The approval of previous meeting minutes;
 3. The review of a summary of exempt and expedited reviews and determinations made by the Subcommittee since the last IRB meeting;
 4. Attendance at the meeting, to include:
 - a. The name of the alternate voting;
 - b. An account in the voting block of all the members present in the room at the time of the vote. This will include documentation of the following:
 1. When a member is present for the discussion and vote or leaves the room/ video meeting;
 2. When a member absents themselves during the vote due to a conflict of interest and
 3. Initial and continued presence of a majority of members, including at least one nonscientist.
 5. IRB Committee Members absent due to conflicting interest are identified and documented on a per protocol basis. Members' absent due to conflicting interest are not counted towards quorum.
 6. For each protocol discussed at the meeting, the minutes should detail:
 - a. The assigned reviewers and their scientific or non-scientific status as indicated on the IRB Committee rosters [e.g. NS (non-scientist), OS (other scientist), and PS (physician scientist), and/or a non-voting member, including the use of any expert consultants and their scientific or nonscientific status and specialty;
 - b. If a consultant is used and attends the meeting in person or by teleconference, a statement that the consultant received all pertinent study material before the meeting, a statement that the

consultant was able to actively and equally participate in all study-related discussions and the key information provided by the consultant.

- c. If a Committee Member is recused from the discussion or vote of a study due to a conflict of interest;
 - d. Actions taken by the IRB Committee;
 - e. Separate deliberations for each action
 - f. Discussion of any controverted issues and their resolutions;
 - g. If discussing a suspension or notification of expiration, issues that arise where treatment may be continued for safety purposes; and
 - h. The vote on these actions including the number of votes “for”, “against,” or “abstain” in order to document the continued existence of a quorum.
7. When a protocol is approved, the minutes reflect that the criteria for approval found in regulations 45 CFR 46.111 and if applicable, 21 CFR 56.111 were discussed and that the protocol was approved based on the criteria.
8. When a protocol is approved, the level of risk (e.g., minimal or greater than minimal) and the approval period (review interval) appropriate to the level of risk are determined.
9. When protocol revisions are requested or a proposal is disapproved, the basis for the revisions or the disapproval is included.
10. For Renewal.
- a. The minutes reflect the IRB Committee’s determination regarding which protocols require continuing review more often than annually, as appropriate to the risk, and the approval period; and
 - b. The minutes reflect the criteria for approval found in regulations 45 CFR 46.111 and if applicable, 21 CFR 56.111 have been discussed and documented.
 - c. The minutes reflect the level of risk (e.g., minimal or greater than minimal) and the approval period, appropriate to the level of risk.
11. For DHHS-Supported Study - When the IRB Committee reviews DHHS-approved informed consent documents for DHHS-supported studies, the minutes reflect the justification of any deletions or substantive modifications of information concerning risks or alternative procedures contained in the DHHS-approved sample informed consent document.
12. Specific IRB Findings. When specific findings on the part of the IRB Committee are required, these findings are fully documented in the minutes and include protocol-specific information justifying each determination. For example:
- a. Alteration or Waiver of Informed Consent. When approving a procedure that alters or waives the requirements of informed consent, the minutes document that the Committee made the determination.
 - b. Waiver of Documentation of Informed Consent. When approving a procedure that waives the requirements for obtaining a signed informed consent document, the minutes document the Committee rationale for this determination.
 - c. Significant/Non-significant risk device. When the sponsor or the investigator claims that the device is not significant risk a

determination of whether the device is non-significant or significant risk and a rationale for the determination is documented.

13. Research Involving Prisoners. When approving research involving prisoners, the minutes will document that the Committee made the seven additional findings and indicate the specific category, which authorizes the research, required in accordance to IRB policy.
 - a. Additionally, the minutes must reference that a majority of the IRB Committee (exclusive of prisoner member/representative) has no association with the prison(s) involved, apart from their membership on the IRB; and
 - b. At least one member of the IRB Committee is a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except where a particular research project is reviewed by more than one IRB, only one IRB need satisfy this requirement.
14. Research Involving Children. When approving research involving children, the minutes will document that the Committee made the findings in accordance with federal regulations and IRB policy.
15. Wards of the State or Other Agency. When reviewing research involving children who are wards of the state or any other agency, institution, or entity, the IRB must determine documents in the minutes that such research is:
 - a. Related to the child's status as wards; or
 - b. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as participants are not wards.
16. Research Involving Pregnant Women, Human Fetuses and Neonates. When approving research involving fetus, pregnant women, neonates the minutes document that the Committee made the findings in accordance with IRB policy.
17. Research Involving Individuals with Impaired Decision Making Capacity. When reviewing research involving individuals who are determined to have impaired decision-making capacity, the IRB must find and document in the minutes that the use of a Surrogate Decision-Maker is appropriate.
18. Alternates. Meeting minutes document when an alternate Committee member replaces a voting Committee member. Alternates should have the same scientific or non-scientific status as the Committee Member (e.g. NS, OS, and PS).
19. Minority Report. IRB Members may file a minority report at their discretion. The report will be included with the minutes.

C. ***Distribution of Minutes***

1. The Administrator develops a draft of the IRB Committee meeting minutes and includes the draft in the full Committee materials for the next convened meeting.
2. The IRB Committee members review and communicate to the Administrator any necessary revisions.
3. The final version of the meeting minutes is maintained electronically. The Institutional Official has access to all final versions of minutes via

a secure folder in FileNet with minutes post 2019 in UCI's electronic IRB database.

- D. **List of IRB Members** - A roster of regular and alternate IRB members identified by:
1. Name;
 2. Earned degrees;
 3. Representative capacity;
 - a. Physician Scientist (PS) , Other Scientist (OS), or Non-Scientist (NS)
 - b. Affiliation with UCI: Affiliated or Non-Affiliated – Individuals considered affiliated with UCI include:
 - (1) Individuals with a current employment or other relationship (e.g., full-time or part-time employee, full-time or part-time student, trainee, member of governing panel or board, or paid or unpaid consultant or agent) with UCI.
 - (2) Individuals with a former employment or other relationship UCI.
 - (3) Individuals who have an immediate family member (spouse, domestic partner or dependent children) with a current employment or other relationship UCI.
 - (4) Individuals who have an immediate family member with a former employment or other relationship UCI.
 - (5) Representatives of a vulnerable population
 4. Indications of experience and expertise sufficient to describe each regular and alternate member's anticipated contribution to the IRB's deliberations; and
 5. Employment or other relationship between each member and UCI (i.e., full-time employee, graduate student, part-time employee, emeritus faculty, unpaid consultant, unpaid IRB member).
 6. All changes in Committee membership are reported to OHRP and FDA on a quarterly basis.
- E. **Policies and Procedures** – HRP Standard Operating Policies and Procedures Manual includes the following information:
1. Policies and procedures for conducting initial and the renewal of research and for reporting findings and actions to the Lead Researcher and the Institution.
 2. Policies and procedures for determining which projects require review more often than annually and which projects need verification from sources other than the Lead Researcher that no material changes have occurred since previous IRB review.
 3. Policies and procedures for ensuring prompt reporting to the IRB of proposed changes in the research and for ensuring that such changes in approved research are not initiated without IRB review and approval except when necessary to eliminate apparent immediate hazard to a subject.
 4. Policies and procedures for ensuring prompt reporting to the IRB, Institutional Officials, the Study Sponsor, and all applicable federal agencies (e.g., OHRP, FDA) of any unanticipated problems involving risks to subjects or to others.

5. Policies and procedures for ensuring prompt reporting to the IRB, appropriate UCI personnel, and of the appropriate Department of Agency head (e.g., OHRP, FDA) of:
 - a. of any serious or continuing non-compliance with these policies and procedures or with the requirements or determinations of the IRB; and
 - b. any suspension or termination of IRB approval.
 - F. **Emergency Use Reports** – All documents related to Emergency Use of a FDA-regulated test article (i.e., investigational drug, biologic, or medical device) is maintained electronically and, beginning in Summer 2022, via UCI's electronic IRB database.
 - G. **Reports of any subject complaints** – All subject complaints are followed up and resolved by the HRP staff and IRB, if necessary. Subject complaint documentation is maintained electronically.
 - H. **Regulatory non-compliance reviews** – All noncompliance reviews are followed up and resolved by the HRP staff and the IRB, if necessary. Noncompliance review documentation is maintained electronically.
 - I. **Attendance records** – the HRP staff maintains attendance lists of IRB training sessions.
- II. **The Human Research Protections (HRP) Team Responsibilities**
- A. The HRP team (Administrator, Senior Analyst, and Analyst) under the direction of the Administrator is responsible for the retention of all research documents and required documentation in the IRB file.
 - B. The HRP team will maintain the collation of all IRB documents into the protocol file following the HRP Administrative Procedures.
 - C. The IRB Administrator will be responsible for electronically retaining the final approved copy of all IRB Committee meeting minutes.

Procedure Number: 5.B**Title: Procedure for Planning and Implementing IRB Committee Meeting Agendas****Procedure:**

This procedure provides guidance on the purpose, development, and implementation of the UC Irvine (UCI) Institutional Review Board (IRB) Committee meeting agendas.

I. IRB Committee Responsibilities

- A. At a convened IRB Committee meeting, the following items will be placed on the agenda for review:
 - 1. New IRB Applications submitted for Review. All newly proposed research involving human participants, excluding those projects that meet one or more of the exemption categories as authorized in 45 CFR 46.104(d) and 21 CFR 56. 104(d) or one or more of the expedited categories as authorized in 45 CFR 46.110;
 - 2. Renewal Applications. Continuing review of all human participants research at intervals appropriate to the degree of risk, but not less than once per year, excluding those projects that meet one or more of the exemption categories as authorized in 45 CFR 46.101(b) and 21 CFR 56. 104(d) or one or more of the expedited categories as authorized in 45 CFR 46.101(b) (8) or (9);
 - 3. Significant Amendments. All major amendments to currently approved human participants research activities that materially affect an assessment of the risk/benefit profile of the study or substantially change the specific aims or design of the study; and
 - 4. Unanticipated Problems Involving Risk to Participants or Others. All unanticipated problems involving risks to participants or others. Factors that help determine the need for review at a convened meeting are:
 - a. The seriousness of the event;
 - b. Whether the event is described in the study protocol and informed consent document;
 - c. Whether the event occurred at a location for which the UCI IRB is the IRB of record; and
 - d. The Investigator's recommendations as to whether the problem was a direct result of a participant's participation in the research study.
 - 5. Expedited Review Determinations. A report documenting approval of research per expedited review procedures for the previous month is provided to the IRB Committee as an item on the next convened IRB Committee meeting agenda.
 - a. This documentation must include a citation to the specific permissible category or categories justifying the expedited review.
 - b. This documentation advises all Committee members of research proposals that have been approved under the expedited review procedure.
 - 6. Noncompliance. The HRP reports promptly to the IRB Committee any serious or continuing noncompliance with the Federal regulations or requirements of the IRB as an item on the next convened IRB Committee meeting agenda.

7. Education. As necessary, education will be placed on the agenda for IRB Committee members, which may include:
 - a. Federal regulations;
 - b. Local policies and procedures;
 - c. Any changes in Federal regulations;
 - d. Any changes in local policies and procedures; or
 - e. Other items as requested by the IRB.
- B. Agendas and review materials will be distributed via an electronic agenda to Committee members one week prior to scheduled Committee meeting, allowing ample time for adequate review and preparation.
- C. Addendums and review materials will be distributed to Committee members via e-mail in a timely manner that allows ample time for adequate review of the addendum item.

II. **IRB Administrator Responsibilities**

- A. It is the responsibility of the Administrator to place all scheduled items for Committee review on the next available agenda. In general, there is a review cap of 25 items per meeting - 10 new IRB applications and 15 other items (i.e., combination of renewal and amendment requests, and may include reports of unanticipated problems involving risk to participants or others).
- B. The Administrator will assure that the agenda includes all relevant sections to be discussed during the Committee meeting.
- C. It is the responsibility of the Administrator to include the reports of all approvals that have occurred since the previous Committee meeting by either expedited means or registered determinations of exempt status with the agenda for notification to the Committee.
- D. When an addendum to a finalized agenda is warranted, the Administrator will assemble materials and assure distribution via e-mail in a timely manner that allows ample time for adequate review of the addendum item. Consideration of the complexity and the scope of the research should be given in determining the appropriate time for adequate review.
- E. If a Committee Member notifies the Administrator that additional time will be required for an adequate review, the Administrator will evaluate the addendum item for prioritization and reassignment of the addendum item.

References:

45 CFR 46
21 CFR 50
21 CFR 56

**University of California, Irvine
Human Research Protections
Standard Operating Policies and Procedures**

Policy Number: 6

Title: IRB Fees for Industry-Supported Applications

**Date of Last Revision: 01/29/09, 09/25/09, 02/03/12, 05/01/16, 08/01/17, 05/03/19,
03/04/22, 09/12/2022, 12/07/2022**

Policy:

- I. The Human Research Protections (HRP) unit in the Office of Research will charge Institutional Review Board (IRB) fees for new clinical research submissions that are partially or fully supported by industry sponsors, including chart review studies.
- II. If UCI defers review to an independent IRB (e.g., WCG, Advarra), HRP charges a fee for administrative review and oversight.
- III. Effective September 1, 2021, NEW clinical research protocols partially or fully supported by industry sponsors will be charged a ONE-TIME fee at the time of UCI or sIRB approval.
 - A. There will be no fee for renewals.
 - B. There will be no fee for amendments.
 - C. There will be no fee for closing reports.
 - D. There will be no fee for unanticipated problems.
 - E. Currently approved protocols will no longer be charged.

This fee will adjust annually to align with HRP expenses. The rate will adjust up or down based on actual expenditures for the current fiscal year, and projected expenses for the following fiscal year. For budgeting purposes, Researchers should assume that the future fee will be at least 3% higher than the current rate.

- IV. IRB applications that are dependent on State, Federal, non-profit foundations, or fully supported by non-Industry Sponsor funds will be excluded from IRB fees.
- V. Under extenuating circumstances, the Associate Vice Chancellor for Research Administration or the Director of Research Protections may waive the assessment of IRB fees with a formal request from the Investigator and appropriate documentation to support such circumstances.
- VI. **It is expected that Investigators incorporate and negotiate applicable IRB fees into the research contract.**
- VII. IRB fees will be assessed as recharges to the account and fund number assigned to the research study. E-mail notification is provided to the investigator and the department business office regarding the amount and date of each charge.
- VIII. The collected IRB fees provide benefits to the campus research enterprise. IRB fees are used to pay for continued education and training opportunities for IRB Staff. IRB fees are used to provide compensation to the IRB Chairs and IRB members. A percentage of select IRB Staff salaries are dependent on IRB fees.

University of California, Irvine
Human Research Protections
Standard Operating Policies and Procedures

Policy Number: 7

Title: Composition of IRB Committees

**Date of Last Revision: 01/29/09; 11/11/10; 05/04/12; 06/01/16; 07/12/16; 03/17/17;
06/20/17, 08/24/17; 12/06/19; 09/12/22; 12/04/23; 08/21/24**

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) that the composition of IRB Committees is in accordance with Federal regulations.

- I. UCI's Federalwide Assurance (FWA) designates four IRB Committees as follows:
 - A. IRB00000393- IRB "A" (Biomedical)
 - B. IRB00000394- IRB "B" (Biomedical)
 - C. IRB00000395- IRB "C" (Social Behavioral)
 - D. IRB00008624- IRB "E" (Regulatory & Institutional Compliance)

UCI has registered through the Department of Health and Human Services and has obtained the following IORG Registration Number: **IORG0000236**

Biomedical research is reviewed by IRB A and IRB B.

Social, behavioral and educational research is reviewed by IRB C.

The purpose of IRB E is to review matters of suspected non-compliance related to human subject research conducted by a UC Irvine student, faculty member or staff. IRB E also reviews unanticipated problem reports that involve matters of potential non-compliance. IRB E will determine if non-compliance has occurred, if the event is "reportable" to federal agencies and whether a corrective action plan is appropriate. IRB E will also review all pending IRB transactions related to a protocol when a significant non-compliance matter is pending resolution. Recommendations from the IRB are provided to the Institutional Official, who has final authority to report the matter to federal agencies. Approved IRB E minutes are included on the IRB A, B, and C agendas.

- II. **Composition** - Each IRB Committee must include at least one member whose primary interests are in a scientific area, one member whose primary interests are in a non-scientific area and one member who is not affiliated with UCI (i.e., not a family member or spouse of an employee, not an active alumnus). At least one non-affiliated member and one non-scientist should be present at convened meetings. The non-scientist and non-affiliated member may be the same individual. Except when an expedited review procedure is used, the IRB will review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. In order for the research to be approved, it shall receive the approval of a majority of those members present at the meeting. In addition, the IRB must have members with sufficient knowledge of the specific scientific discipline(s) relevant to the research that it reviews.

Scientist/Nonscientist - Members are assigned a scientist or non-scientist status based on their training, background, and expertise. Members whose training, background, and occupation would incline them to view scientific activities from the standpoint of someone within a behavioral scientific or biomedical research discipline should be considered a scientist, 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 – whose primary concerns are in the “non-scientific” area, should be considered a nonscientist.

Affiliation - An employee or agent of the organization registering the IRB (or a member of that person’s immediate family) is considered affiliated. Affiliated members include, but are not limited to, individuals who are: part-time employees; current students; members of any governing panel or board of the institution; paid or unpaid consultants; healthcare providers holding credentials to practice at the institution; and volunteers working at the institution on business unrelated to the IRB. An individual that has no affiliation with the organization registering the IRB, other than as an IRB member, is considered unaffiliated with the entity operating the IRB. Unaffiliated members may include people whose only association with the institution is that of a patient, subject, or former student at that institution. Paying unaffiliated members for their services would not make the member “otherwise affiliated” as stated in the regulations or cause the member to have a conflicting interest.

- III. **Roster(s)** - An IRB Membership Roster is generated for each IRB Committee. The Roster contains the list of IRB Members identified by name, earned degrees, representative capacity, scientific status (i.e., PS= Primary Scientist, OS= Other Scientist, NS= Non-Scientist), affiliation status, indications of experience such as board certifications, licenses, etc., sufficient to describe each member’s chief anticipated contributions to IRB deliberations and any employment or other relationship between each member and the institution.
- IV. Likewise, an IRB Membership Roster is generated for the listing of IRB Committee Alternate Members. Alternates formally listed on the IRB roster may vote in place of an absent voting member. Alternates are assigned according to their scientific or non-scientific status, as indicated on the Committee member rosters, and in accordance with the area of expertise required for adequate review. Meeting minutes must document when an alternate member attends a meeting.
 - A. Alternate members serve the same function as other IRB members. Alternate members participate in the review, discussion and vote of protocol transactions when an IRB member cannot attend the convened meeting. Alternates will have access to meeting materials in advance of an IRB meeting.
 - B. Alternate members abide by the same UCI Conflicts of Interest in Human Subjects Research policy as other IRB members.
 - C. A primary member of any IRB registered under the same IORG number may serve as an alternate for any comparably qualified member on any other IRB of that institution or organization. Primary members serving as alternate members do not need to be listed as an alternate on any roster.

- D. When an alternate member substitutes for a primary member at an IRB meeting, the minutes must reflect the alternate member's expertise and that their scientific status is equivalent to that of the primary member the alternate will replace.
 - 1. If both a primary IRB member and their alternate(s) attend the same IRB meeting, the primary member acts as the official voting member of the IRB for review of research protocols, unless the minutes clearly indicate otherwise. A designated alternate IRB member for a primary IRB member may substitute for the primary IRB member for an entire meeting or at any time during a meeting. Substitution during a meeting may occur when the primary member is (a) absent from the room for part of the meeting, or (b) recused from review of certain research protocols because the primary IRB member has a conflicting interest with respect to a specific research protocol. Whenever this occurs, the minutes of the IRB meeting should indicate clearly that the alternate IRB member has replaced the designated primary IRB member.

- V. **Membership Selection** - Selections for IRB Committee member voting positions and Chairpersons for the IRB Committees are made by the Institutional Official (IO) with the assistance of the IRB Chairs and the Senior Director of Human Research Protections, based upon the specific needs of the IRB Committee, (e.g., medical specialty, vulnerable population representative, diversity, non-scientist, non-affiliated, etc.).
 - A. The biomedical IRB Committees are primarily made up of School of Medicine and UCI Medical Center faculty and staff with sufficient scientific expertise and scholarship to review each protocol to determine the study meets the criteria for IRB approval (i.e., 45 CFR 46.111 and if applicable, 21 CFR 56.111).
 - B. The social/behavioral/ educational IRB Committee is made up of faculty and staff from the School of Social Sciences, School of Social Ecology, School of Humanities; the Donald Bren School of Information and Computer Sciences; School of Medicine, School of Education; and School of Business with sufficient scientific expertise and scholarship to determine that each study meets criteria 45 CFR 46.111 and if applicable, 21 CFR 56.111.
 - C. In general, IRB E is comprised of IRB Chairs, IRB Vice-Chairs, senior members from IRB A, B and C, and a non-scientist member.
 - D. Non-affiliated members are drawn from the local Orange County community (e.g., clergy, attorneys, teachers, and advocates for vulnerable subject populations, etc.).
 - E. At least one member who represents the general perspective of participants is present at convened meetings, such as a former or current research participant or a research participant advocate or an individual who otherwise represents the general perspective of research participants. This member may be a non-scientist or non-affiliated member.
 - F. To support American Nurses Credentialing Center Magnet designation, each Biomedical IRB includes at least one UCI nurse as a voting member.
 - G. The IRB Committee requests faculty volunteers and also seeks the

- advice of IRB Committee Chairs, IRB Committee Members, Division Chiefs, Department Chairs, and Deans in making its recommendations.
- H. Decisions for selecting Committee members are made to assure that the IRB Committees retain diversity while maintaining regulations for required individuals to serve on the Committee.
 - I. Community-based participatory research (CBPR) is a form of community engaged research, involving a collaborative approach for participation, shared decision-making, and mutual ownership in all aspects of the research process by communities affected by the issue being studied, researchers, and organizational representatives.
 - 1. When reviewing research that involves (CBPR) the IRB will assure that the committee has IRB members and/or consultants with CBPR expertise to review community-based participatory research project at UCI.
 - 2. Should CBPR research grow at UCI the IRB will:
 - a. Expand the number of community members on the IRB; or
 - b. Engage community consultants as collaborators in the review process; or
 - c. Coordinate with a community-based IRB.
 - J. Committee Chairs and Vice Chairs are selected as highly respected individuals from within the institution, fully capable of managing the IRB and matters brought before it with fairness and impartiality.
 - K. Individuals with potential competing business interests cannot serve on the IRB or be involved in the day-to-day operations of the review process. For example, the Senior Director of Sponsored Projects, the Vice Chancellor for Research or others who are responsible for raising funds or garnering support for research cannot not serve on the IRB or be involved in the daily operations of the review process.
- VI. **Number of Members** - The IRB Committees are required to have a minimum of five members each (on average 12-20 members), with varying backgrounds and expertise to provide complete and thorough review of research activities commonly conducted by the Institution.
- VII. **Qualifications of IRB Members**
- A. The IRB Committee membership must be:
 - 1. Sufficiently qualified through 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; and
 - 2. Able to ascertain the acceptability of proposed research in terms of institutional commitments, regulations, applicable law, and standards of professional conduct and practice;
 - B. Additional Qualities of IRB Committee Members and Chairpersons.
 - 1. Need to be committed to the workload;
 - 2. Understand time commitment;
 - 3. Come to meetings prepared for discussion;
 - 4. Commitment to institutional goals for human research protections;
 - 5. Good communication skills;
 - 6. Willing to contact Lead Researchers to discuss issues and initiate solutions prior to the meeting; and

7. When applicable, have
 - a. Strong clinical expertise; and/or
 - b. Research experience.
 8. The Chair must possess strong leadership skills to effectively organize, influence and expedite IRB meetings, have a strong command of the regulations pertaining to human subjects research, be a tenure track faculty member and have a M.D. for the biomedical committees; or a Ph.D. in a related field for the social-behavioral committee.
- C. The Institutional Official, the Senior Director of Human Research Protections or designee and the IRB Chairs continually assess the composition of the IRB Committees' membership to ensure that each committee is adequately charged in light of the anticipated scope and complexity of UCI's research activities, and the subject populations likely to be involved in the research.
- D. Term of Service.
1. Committee Members
 - a. Committee members are requested to serve a renewable three-year term.
 - b. Committee members are requested to serve as alternate members at the completion of their term.
 2. IRB Chairs
 - a. It is recommended that Chairs serve one year as a Committee member prior to assuming the role of Chair.
 - b. The Chair shall serve a two-year term and shall be considered for re-appointment at the end of each term.
 - c. Chairs may be requested to serve six months or longer as a Committee member at the completion of their term to mentor the newly selected Chair to promote consistency and continuity. In addition, this will provide a resource for the newly selected Chair and Committee members on historical perspectives, rationale for decisions made regarding policy, and meeting facilitation skills.
 - d. Chairs are requested to serve as alternate members at the completion of their term.
- E. Child Representative - An IRB Committee considering a protocol involving children as participants should:
1. Assess its needs for pediatric expertise among the IRB voting membership to assure that it possesses the professional competence necessary to review the specific research activities.
 2. When the IRB reviews research involving children (or other participants vulnerable to coercion or undue influence), the IRB will ensure that one or more individuals who are knowledgeable about and experienced in working with children (or other vulnerable groups as appropriate) are present. To fulfill this requirement, the IRB Committee may invite nonvoting consultants to assist in the review of issues which require expertise beyond, or in addition to, that available among voting IRB members. Should the IRB be unable to obtain expertise in this area, the IRB will defer review until such expertise can be obtained through membership or consultation.
 3. When reviewing proposed research on handicapped children or mentally disabled persons sponsored by the Department of

Education, the UCI IRB must also include a member with expertise with this population.

- F. Prisoner Representative - Federal regulations require that when the IRB Committee will review research involving prisoners, at least one member of the IRB Committee shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity.
- G. Pregnant Women, Human Fetuses and Neonates - The IRB Committee considers all applicable Federal regulations regarding research with this population and may request review by an expert, as needed.
- H. Individuals with Impaired Decision-Making Capacity - The IRB Committee may include, if necessary, at least one member with expertise in the area of individuals with impaired decision-making capacity population when reviewing studies with this population or studies in which the participants may become cognitively impaired through the course of the research.
- I. Economically or Educationally Disadvantaged: The IRB Committee will consider this population as potentially vulnerable to coercion and undue influence and may request review by an expert, as needed.
- J. Expert Consultants - On a case-by-case basis, the IRB Committee may request review by an individual with competence in a scientific or scholarly area not represented by the Committee membership.
 - 1. Before the convened meeting the HRP administrative staff review the agenda to confirm that the Committee has the expertise to review the scheduled research in consultation with the IRB Chair as needed. If it is determined that a consultant is needed to address specific issues that require expertise or qualifications beyond or in addition to the IRB Committee membership, HRP staff will obtain a consultant.
 - 2. Consultants will either participate in the discussion of the protocol in-person, telephone, teleconference, or provide written comments which will be given to the reviewers and IRB Chair to present at the convened meeting. IRB members may obtain copies of the consultants' comments.
 - 3. If the consultant participates in the meeting, the minutes will document the key information provided by the consultant. Written comments will be retained in the protocol file.
 - 4. The consultant will sign a UCI IRB Consultant Standards document to ensure the confidentiality of the review and to assure that no conflicting interest exists with the protocol under review. If a consultant declares a conflicting interest as defined in the UCI Conflicts of Interest in Human Subjects Research policy, the HRP staff and/or IRB Chair will arrange for another consultant. A consultant's conflict of interest is determined on a protocol-by-protocol basis.
 - 5. Consultants are not IRB members, and their presence is not counted towards quorum.

VIII. **Assignment to IRB Committees**

In general, the Lead Researcher's primary school, department, or program determines whether a protocol is reviewed by a biomedical committee or by the social/behavioral/educational committee. For example, School of Medicine protocols will be reviewed by one of the biomedical committees, while School of Social Sciences protocols will be reviewed by the social/behavioral/educational committee.

- A. The social/behavioral/educational committee may review research that involves prospective collection of biological specimens (e.g., blood, saliva, deciduous teeth) and/or collection of data via non-invasive measures (e.g., magnetic resonance imaging, tests of sensory acuity, electrocardiography) that customarily may be considered clinical in nature, as long as the procedures involve no more than minimal risk (e.g., procedures that qualify for Expedited review under Categories 2, 3 or 4 of the Federal regulations [(Federal Register: November 9, 1998 (Volume 63, Number 216))].
- B. Research involving access, creation, use, and/or disclosure of individually identifiable private health information will be reviewed by a biomedical Committee.

IX. **IRB Committee Member and Chair Performance Evaluations**

- A. Committee members and Chairs complete an annual self-evaluation which includes the following:
 - 1. Knowledge and application of the Federal regulations;
 - 2. Knowledge and application of IRB policies and procedures;
 - 3. Participation in Committee meeting discussions;
 - 4. Interaction with Investigators; and
 - 5. Affiliation status.
- B. The self evaluations and other verbal and written feedback from members and Chairs are used to identify areas where additional member education may be required.
- C. IRB Committee Members and Chairs may be replaced on the Committee at the discretion of the Vice Chancellor for Research based upon the Committee needs for specific areas of expertise, or performance issues such as a breach of confidentiality, excessive absences, etc.

References:

45 CFR 26.103(b)(3)

45 CFR 46.107

OHRP Step by Step Instructions on Registering an IRB

21 CFR 56.108(c)

21 CFR 56.115(a)(5)

34 CFR 350 and 356

ICH-GCP: 3.2.1, 3.2.6

AHRQ Publication No. 04–E022-2: *Community-Based Participatory Research: Assessing the Evidence*, July 2004

Clinical and Translational Science Awards Consortium Community Engagement Key Function Committee Task Force on the Principles of Community Engagement [Principles of Community Engagement – Second Edition](#)

Federal Register: November 9, 1998 (Volume 63, Number 216)

NIH: Office of Behavioral and Social Sciences Research [Community-Based Participatory Research](#)

OHRP IRB Guidebook

OHRP Compliance Activities: Common Findings and Guidance, July 10, 2002

University Policy on the Protection of Human Subjects in Research: 18-261

UCI IRB Members Standards – Core Voting Members

UCI IRB Members Standards – Alternate Voting Members

UCI IRB Non-Voting Consultants Standards

Policy Number: 8

Title: Committee Member Compensation and Responsibilities

Date of Last Revision: 01/29/09, 10/23/10, 01/24/11, 09/15/11, 07/06/12, 05/01/13, 01/28/15, 05/01/16, 11/02/16, 06/27/18, 12/10/19, 03/04/22, 09/12/22, 12/04/23, 08/15/24

Policy:

I. Compensation

UC Irvine IRB members and chairpersons serve as volunteers. In recognition of the vital service provided by these individuals to the campus research community and the Human Research Protection Program, the University provides nominal compensation to each individual as outlined below. Compensation is intended to recognize the time invested by the individual in committee activities, offset a possible loss of income to the home department, facilitate recruitment to the committee and encourage attendance. IRB Chairpersons have received compensation for travel expenses and research-related costs from the Office of Research since the 1990's. Compensation to vice chairpersons and members was effective starting January 1, 2008.

A. Coverage

1. *Faculty and Staff Included in a Health Sciences Compensation Plan*

For IRB members, vice chairs and chairs from organizational units where unit members are covered by a compensation plan, funds will be transferred to the member's home department to compensate the unit for the member's time and proportionately relieve the member's earnings obligation. The use of these funds is governed by UCI expense policies, Academic Personnel additional compensation policies, and/or faculty compensation plan policies.

2. *Faculty Not Included in a Health Sciences Compensation Plan*

For IRB members, vice chairs and chairs from organizational units where unit members are not covered by a compensation plan, funds will be transferred to the member's home department. The use of these funds is governed by UCI expense policies, Academic Personnel additional compensation policies, and/or faculty compensation plan policies.

3. *Staff Employees*

For IRB members who hold staff positions, current policy does not allow compensation for committee participation.

4. *Community Members*

For IRB members who are not University employees, compensation will be provided by check.

B. Compensation Process and Rates

1. Funds related to the IRB service of faculty and staff members, including IRB chairpersons will be transferred the member's home department quarterly, in arrears. Checks related to the IRB service of

community members will be issued quarterly, in arrears, directly to the individual member.

2. IRB Committee A & B and IRB Team D (Biomedical) Members

- a. *Committee Vice Chairperson's Rate*
Effective January 2011, IRB vice chairpersons (1 per committee) will receive a monthly research allowance of \$500 per month of appointment.
- b. *Academic Appointee Rate*
IRB members who hold faculty positions will earn \$200 for each full committee meeting attended with engagement in the meeting for 75% of the duration.
- c. *Staff Appointee Rate*
IRB members who hold non-Office of Research staff positions will earn \$200 for each full committee meeting attended with engagement in the meeting for 75% of the duration.
- d. *Community Member Appointee Rate*
IRB members who are unaffiliated with the university will earn \$200 for each full committee meeting attended with engagement in the meeting for 75% of the duration.
- e. *Acting Chair Rate*
When the IRB Chair delegates responsibilities of the IRB Chair to another experienced member of the IRB, in the absence of the IRB Chair and IRB Vice Chair, additional compensation may be provided to the IRB member for that meeting, not to exceed \$350.00 total, per meeting.

3. IRB Committee C (Social, Behavioral & Educational) Members

- a. *Committee Vice Chairperson's Rate*
Effective January 2011, the IRB vice chairperson will receive a monthly research allowance of \$500 per month of appointment.
- b. *Academic Appointee Rate*
IRB members who hold faculty positions will earn \$100 for each full committee meeting attended with engagement in the meeting for 75% of the duration. In addition, members will receive \$50 for each week of subcommittee service (approximately 9 weeks annually) with participation for 75% of the meeting duration.
- c. *Staff Appointee Rate*
IRB members who hold non-Office of Research staff positions will earn \$100 for each full committee meeting attended with engagement in the meeting for 75% of the duration. In addition, members will receive \$50 for each week of subcommittee service (approximately 9 weeks annually) with participation for 75% of the meeting duration.
- d. *Community Member Appointee Rate*
IRB community members will earn \$100 for each full committee meeting attended with engagement in the meeting for 75% of the duration.

4. IRB Committee E (Noncompliance) Members

- a. *Academic Appointee Rate*
Effective January 1, 2020 the IRB Chair will earn \$600 per month and IRB members will earn \$200 for each full

committee meeting attended with engagement in the meeting for 75% of the duration.

b. **Staff Appointee Rate**

IRB members who hold staff positions will earn \$200 for each full committee meeting attended with engagement in the meeting for 75% of the duration.

c. **Community Member Appointee Rate**

IRB members who are unaffiliated with the university will earn \$200 for each full committee meeting attended with engagement in the meeting for 75% of the duration.

5. **IRB Alternate Members**

- a. Alternates called upon to attend meetings will be compensated on a per meeting basis in accordance with their appointment and the provisions of this policy.

6. **Biostatistics, Epidemiology and Research Design (BERD) unit in the Institute for Clinical and Translational Science (ICTS) – IRB Members**

- a. BERD statistician reviewers may serve as IRB members, to maximize the efficiency of their review process, which generally precedes the RB review of an Investigator Initiated Study.
- b. BERD reviewers who hold staff or faculty positions will earn \$300 monthly compensation for their efforts. Compensation is to be issued quarterly.

II. **IRB Member Responsibilities**

- A. UCI IRB has the responsibility to uphold the ethical principles of the *Belmont Report* to all proposed research involving human participants regardless of sponsorship. The ethical principles set forth in the *Belmont Report* are:
1. Respect for Persons: Recognition of the personal dignity and autonomy of individuals and special protection of those persons with diminished autonomy;
 2. Beneficence: Obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risk of harm; and
 3. Justice: Fairness in the distribution of research benefits and burdens.
- B. It is the responsibility of the UCI IRB to:
1. Understand federal regulations, state laws, and University of California (UC)/UCI policies regarding the protection of human subjects in research.
 2. Verify that all protocols reviewed by the IRB Committees conform to Federal regulations, state laws, Department of Defense (DoD) requirements, Department of Justice (DoJ) requirements, Department of Energy (DOE) and UC/UCI policies relevant to the health, welfare, safety, rights, and privileges of human subjects, and to assist investigators in complying with these regulations and policies.
 3. Evaluate each research protocol based on the criteria for IRB approval, including consideration of scientific merit relative to the risk/benefit profile and to the complexity of the study. Research should be scientifically sound and clearly described.
 4. The IRB, in conjunction with the Biostatistics, Epidemiology and Research Design (BERD) unit in the Institute for Clinical and

Translational Science (ICTS) consider scientific review to ensure that risks to subjects are:

- a) Minimized by using procedures that are consistent with sound research design, and which do not unnecessarily expose subjects to risk;
 - b) Reasonable in relation to any anticipated benefits and the importance of the knowledge that may reasonably be expected to result.
 - (1) As applicable, outside groups (e.g., NIH review, Cooperative Group review) and other campus committees/entities (e.g., the Chao Family Comprehensive Cancer Center Protocol Review and Monitoring Committee (PRMC)), Department Chairs, and School Deans) may also review the study's scientific merit relative to the research design and the likelihood of the research achieving its aims.
5. For research conducted within the Bureau of Prisons, the research must have an adequate research design and also contribute to the advancement of knowledge about corrections.
 6. For studies that involve DoD-supported research with human subjects, independent review of the research for scientific merit or scholarship is required prior to IRB review.
 7. Review and approve, require changes to, or withhold approval of proposed human subject research activities.
 8. Conduct continuing review of on-going research activities at least every 365 days. (See Policy #13 for extended three-year IRB approval exception.)
 9. Determine which studies require review more often than annually.
 10. Determine if the proposed use of placebo is acceptable. (See Policy # 43.)
 11. Determine the specific risk category for children, pregnant women, fetuses, fetal tissue, neonates and prisoners as satisfied by the conditions of the applicable subparts. (See Policies # 36, 37 and 38.)
 12. Evaluate available clinical and nonclinical information on an investigational product to determine if the information is adequate to support the proposed clinical trial.
 13. Determine whether an investigational device poses significant or non-significant risk and if, accordingly, an Investigational Device Exemption (IDE) applies. (See Policy # 42.)
 14. Determine if an Investigational New Drug (IND) application is needed for a single agent or a combination of agents. (See Policy # 41.)
 15. Determine if the use of Short Forms, surrogate consent or other alterations to the informed consent process are appropriate. (See Policies # 30, 31 and 39.)
 16. Monitor on-going research, including review of unanticipated problems involving risks to human subjects or others and oversight of investigator compliance with research requirements.
 17. Determine whether additional expertise, not available among IRB members, is required for a protocol review. If the IRB does not have the required expertise, the IRB will follow the policies and procedures to obtain *Expert Consultants* (Note: IRB members are encouraged to directly consult with colleagues for information, provided that

confidentiality of submitted protocols and IRB proceedings is maintained.)

18. Assure that conflicts of interest in protocol review and conduct of research are avoided. Committee Members must declare any conflict of interest before review of any research under IRB jurisdiction. Members with conflicting interests must absent themselves from the meeting during the discussion and vote on the affected research protocol. IRB members with a conflicting interest do not count towards quorum. Members agree to abide by the UCI Conflicts of Interest in Human Subjects Research policy when they sign the UCI IRB Members Standards document upon appointment to the IRB.
19. Report serious or continuing noncompliance, unanticipated problems involving risks to human subjects or others and any suspension or termination of IRB approval to University officials and governmental oversight entities.

III. ***Specific Member Duties***

- A. All IRB members are expected to make every effort to attend Committee meetings. Members are asked to attend at least 75% of full committee meetings and be available for subcommittee service. In the event that an IRB member is unable to attend, sufficient advance notice must be provided to the HRP staff so that alternate arrangements can be made as necessary to achieve quorum.
- B. Duties of IRB Chairperson
 1. Convene IRB meetings
 - a. Assure the members review applications and related documentations consistent with federal criteria for approval of human subjects research and HRP policies and procedures.
 - b. Open debate and request amendments to the motion, if necessary.
 - c. Guide debate and ask for a formal motion.
 - d. Call for a vote (i.e., second, all those in favor, against, abstain).
 - e. State whether motion carries.
 - f. If motion does not carry, reopen discussion and propose new motion.
 2. Review and approve minor modifications in approved research, in accordance with federal regulations.
 3. Review and register exempt research proposals, as requested in accordance with 45 CFR 46.101(b) (1-6), taking into consideration 45 CFR 406.301(a), 45 CFR 46.401(b) and 21 CFR 6.104(d).
 4. *Biomedical Chairpersons* – Advise on emergency use of an investigational test article, in accordance with 21 CFR 50.23(a-c), 21 CFR 56.102(d) and 21 CFR 56.104(c).
 5. Review reportable events and problems including unanticipated problems involving risks to human subjects or others, protocol violations, and subject complaints and determine whether the event constitutes an unanticipated problem involving risks to human subjects or others.
 6. Make decisions in emergency situations to protect subjects and remain in compliance with regulations.
 7. Suspend the conduct of research when subjects are placed at unacceptable risk or, if warranted, when investigators do not comply

with IRB guidelines, Federal regulations, State laws or UC/UCI policies.

8. Relate concerns of IRB members to HRP administration and Institutional Official (IO) regarding issues involving human subject safety and IRB review procedures.
9. Facilitate communication and dissemination of information from the IO and HRP staff to the IRB members and to the research community in general.
10. Act as an advisor to UCI's research community.
11. Sign official approval documentation on behalf of the UCI IRB.
12. Call special meetings, as necessary.
13. Be available for consultation with HRP staff.
14. Attend IRB Working Group meetings with HRP staff.
15. Delegate any of his/her responsibilities as appropriate to other qualified and duly appointed members of the IRB.
16. Lead the full IRB in addressing serious and continuing non-compliance
17. Participate in quality assurance reviews of on-going research, when appropriate.
18. Participate in IRB member education and training sessions.

B. Duties of IRB Vice Chair

1. Perform duties of the IRB Chairperson in his/her absence.
2. Assist the IRB Chairperson as needed.

C. Duties of IRB Members

1. Attend convened meetings so that protocols may be reviewed in accordance with 45 CFR 46.108(b) and 21 CFR 56.108(c).
2. Serve as primary or secondary reviewer or discussant on assigned full committee or expedited protocols.
3. Maintain confidentiality of IRB meeting proceedings and any information contained in protocol reviews.
4. Review IRB applications and other reportable items to ensure they are in compliance with applicable Federal regulations, State laws and/or UC/UCI policies.
5. Disclose any potential conflict of interest to the IRB Chair and HRP staff as soon as it is recognized.
6. Participate in protocol audits for possible noncompliance, as requested.
7. Understand UC/UCI policy and procedures regarding the protection of human participants in research.
8. Participate in IRB member education and training opportunities.

D. Duties of Non-Scientist

1. The duties of IRB members with non-scientific status primarily consist of reviewing the informed consent document and the recruitment materials to ensure that the information provided to the participant or the participant's legally authorized representative is in an understandable language and format. Non-scientists also provide additional expertise relevant to the subject populations they represent (e.g., cognitively impaired participants). IRB members with non-scientific status are not assigned primary and secondary reviewer responsibilities.

- IV. **Reporting of Undue Pressure or Influence upon IRB Members and Human Research Protections Staff**
- A. IRB members and HRP staff are expected to report any exertion of undue pressure or influence/coercion to the Director of Human Research Protections or designee, the Associate Vice Chancellor for Research or the Vice Chancellor for Research to assure that the IRB members and staff can function without outside pressures.
 - B. Reports of undue pressure or influence/coercion can also be made to the designated officials named in the UCI Whistleblower Policy and Procedures.
 - C. Reports of undue pressure or influence/coercion can be made in writing, by phone and in person.
 - D. Appropriate action and follow-up with the individual exercising undue pressure or influence/coercion and the individual's supervisor (e.g., Dean, Department Chair, etc.) will be performed to prevent any further problems from the individual on IRB members and staff.
- V. In an effort to create a transparent process, the IRB roster is available on the Human Research Protections website. Proceedings of IRB meetings are confidential; therefore, investigators should not attempt to contact individual committee members to discuss individual committee deliberations.

References:

21 CFR 50
21 CFR 56
45 CFR 46
OHRP IRB Guidebook
OHRP Compliance Activities: Common Findings and Guidance, July 10, 2002
UC Irvine Administrative Policy & Procedures Sec. 700-06 (Whistleblower Policy)
UCOP Research Integrity – Policy and Procedures for Reporting Improper Governmental Activities and Protection against Retaliation for Reporting Improper Activities, October 2002
DoD: SECNAVINST 3900.39D, para 8c(6)
DoJ: 28 CFR 512.11(a)(2)
ICH-GCP: 2.4, 2.5, 3.2.3, 3.2.4

Procedure Number: 8.A**Title: Procedure for Maintaining Quorum Required for IRB Committee Review****Procedure:**

This procedure provides guidance on the maintenance of quorum that must occur when the UC Irvine (UCI) Institutional Review Board (IRB) Committees review and approve research under its jurisdiction.

I. IRB Committee Responsibilities**A. Quorum**

1. An IRB Committee meeting may convene at an announced meeting and render a vote only under the following conditions:
 - a. Quorum requires a majority of the Committee voting members to be present, defined as more than half of the membership (e.g., 10 voting members requires 6 voting members for quorum; 9 voting members requires 5 voting members for quorum); and
 - b. A minimum of one non-scientist present.
 - c. The Committee member may not send a proxy to vote in their absence either by phone or in person.
2. The IRB Committee meetings will take place with all participating IRB members present in person, via telephone, or via a teleconference call.
3. Each Committee member will receive access to all pertinent materials prior to the meeting.
4. Committee members attending via telephone or teleconference call will actively and equally participate in the discussion of all protocols (e.g., each member can hear and be heard by all other participating members).
5. Only members who participate in the IRB review and discussion should vote/provide their opinion and/or advice.
6. When the IRB Chair calls for a vote, members either raise their hands, or vote via teleconference poll in favor or against the determination or abstain from the vote. A majority vote in favor of the determination constitutes IRB approval.
7. When reviewing research that involves children or prisoners, a committee member, an alternate member or an expert consultant who has special knowledge of these vulnerable populations is required to be present during the review process. If the reviewer providing the expertise with regard to the vulnerable population is not included on the IRB roster as a voting member or alternate, he or she may not vote and may not count towards quorum. Additionally, when reviewing research sponsored by the Department of Education, the Committee must include one person with expertise in dealing with children with physical disabilities or mentally disabled persons when reviewing research on those populations.
8. *Failure of Quorum during a Convened Meeting.* Should quorum fail during the meeting (e.g., those with conflicts of interest being excused, early departures, loss of the non-scientific member), the meeting should be suspended until quorum can be restored or terminated.

- B. Conflict of Interest
 - 1. IRB Committee members must absent themselves from the deliberative discussion and vote during the initial or continuing review of a project in which the member has a conflicting interest, except to provide information requested by the IRB Committee.
 - 2. IRB Committee members should inform the IRB Administrator of any potential conflicts on the agenda prior to the meeting or at the beginning of the meeting and absent themselves from the meeting when the IRB Committee discusses and votes on the research in which they have a conflict of interest, which should be noted in the Committee minutes.

II. The Human Research Protections (HRP) Team Responsibilities

- A. The HRP team (Administrator, Senior Analyst, and Analyst), under the direction of the Administrator, will maintain attendance logs in order to assure that quorum is maintained, despite absences and conflicts of interests, for scheduled IRB Committee meetings.
- B. The team members in attendance at the Committee meeting are responsible for recording accurate quorum notes and assuring that quorum is maintained throughout the meeting.
- C. The HRP team will note any absences due to conflicting interest for each protocol in the IRB Minutes. IRB members with a conflicting interest may not participate in any portion of the review of research activities except to provide information requested by the IRB and must absent themselves from the meeting during the IRB's deliberative discussion and vote on the affected research.
- D. When the IRB Committee reviews research that involves a vulnerable population, the Administrators or Analysts will assure that the IRB Committee Members present, includes someone who is knowledgeable and meets the requirements to review the proposed research, or assist in scheduling a consultant or alternate reviewer to conduct the review.
- E. The HRP team records the votes for each item under IRB Committee review in the "IRB Agenda- Notes Version" worksheet, as well as electronically via Zoom.

Policy Number: 9

Title: IRB Committee Member and Consultant Conflicting Interest

Date of Last Revision: 07/28/06, 10/04/10, 01/21/11, 03/04/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) that all conflicting interests of an IRB committee member and consultant be declared before review of any research under IRB jurisdiction. IRB Committee Members and consultants with a conflicting interest may not participate in any portion of the review of research activities except to provide information requested by the IRB and must absent themselves from the meeting during the IRB's deliberative discussion and vote on the affected research.

A conflict of interest is a situation where an IRB Committee Member's outside financial interest(s) or obligation(s) bias or has the potential to bias the deliberative discussion and vote of the affected research protocol. IRB committee members are those individuals serving as members including Chairs, the IRB, alternates or expert consultants regardless of voting privileges.

IRB committee members and consultants are considered to have a conflicting interest if they or their immediate family member (spouse, domestic partner, or child) have any disclosable financial interest; role in the conduct of or participation in the research; or other individual conflict of interest.

Disclosable Financial Interests are:

1. Ownership interest, stock, stock options, or other financial interest related to the research, unless it meets all four tests:
 - a. Less than \$10,000 when aggregated for the immediate family and
 - b. Publicly traded on a stock exchange and
 - c. Value will not be affected by the outcome of the research and
 - d. Less than 5% interest in any one single entity.
2. Compensation related to the research, including salary, consultant payments, honoraria, royalty payments, dividends, loans, or any other payments or consideration with value, including payments made to the University Health Sciences Compensation Plan, unless it meets both of the following tests:
 - a. Less than \$10,000 in the past year when aggregated for the immediate family and the
 - b. Amount will not be affected by the outcome of the research.
3. Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright or licensing agreement.
4. Board or executive relationship (e.g., director, officer, partner, or trustee) related to the research, regardless of compensation.

References:

38 CFR 16.107(e)
21 CFR 46.103, 107
21 CFR 56.107
21 CFR 54 (as reference)
42 CFR 50 Subpart F
45 CFR Part 94
UCI Policy on Conflicts of Interest in Human Subjects Research

OHRP May 2004 Financial Relationships and Interests in Research Involving Human
Subjects Guidance for Human Subjects Protection
UCOP Academic Conflicts of Interest or Commitment Related to Sponsored Research
UC Irvine Administrative Policies & Procedures Sec. 700-09: Policies on Gifts,
Gratuities, and Conflict of Interest

Procedure Number: 9.A**Title: Procedure for IRB Committee Member and Consultant Conflicting Interest****Procedure:**

This procedure outlines the IRB committee member and consultant responsibilities regarding required disclosure of conflicts of interest when reviewing human subjects research.

I. Individual with Conflict Responsibilities

- A. Each committee member must review this Procedure and corresponding Policy and sign the "UCI IRB Members Standards" document at the initial IRB committee member orientation and annually thereafter.
- B. Each committee member must review and sign a "Conflict of Interest (COI) Disclosure Form for IRB Members" at the initial IRB committee member orientation *and annually thereafter*.
- C. Each consultant must read this Procedure and corresponding Policy and sign the "UCI IRB Members Standards for Consultants" before reviewing a research protocol and disclose any conflicting interest.
- D. Each committee member must indicate on the IRB Reviewer checklist whether or not they have a conflicting interest. Also, those members who have a conflict of interest must inform the IRB Administrator before the Committee meeting or at the beginning of the meeting.
- E. At the beginning of each convened IRB meeting the IRB Chair or designee will ask the members if anyone has a conflicting interest with any of the research protocols on the agenda. IRB members are encouraged to review the IRB Members Conflict of Interest Standards provided at each meeting as part of the Desk Reference materials.
- F. IRB committee members with a conflicting interest may not participate in any portion of the review of research activities except to provide information requested by the IRB and must absent themselves from the meeting during the IRB's deliberative discussion and vote on the affected research.
 - 1. This includes the review of unanticipated problems involving risks to participants or others, as well as the review of potential non-compliance matters.
- G. IRB committee members may absent themselves from the discussion and vote for any reason, if they feel it is necessary to avoid any appearance of a conflicting interest.
- H. IRB members who review Expedited level research in subcommittee must also absent themselves from the review and any deliberative discussion and vote on the affected research.
 - 1. This includes the review of unanticipated problems involving risks to participants or others, as well as the review of potential non-compliance matters.
- I. IRB committee members may absent themselves from the discussion and vote for any reason, if they feel any member of the research team or others has exerted undue influence. Such situations should be reported to the Vice Chancellor for Research or to the designated officials named in the UCI Whistleblower Policy and Procedures.

- II. **The Human Research Protections (HRP) Team Responsibilities**
- A. The HRP team (Administrator, Senior Analyst, and Analyst) and other HRP staff under the direction of the Administrator, identify IRB members with COIs (e.g., IRB members or their immediate family member listed as a study team member) in preparing the agenda for a convened meeting, as well as in preparing for subcommittee.
 - B. Members with an identified COI are not assigned as study reviewers.
 - C. The HRP team lists COI recusals on the IRB agenda to remind members to leave the room, when applicable.
 - D. HRP staff monitors COI recusals during the meeting.
 - E. The HRP team and other HRP staff under the direction of the Administrator, evaluates the annual IRB Member's disclosures of financial interest.
 - F. Administrators maintains a spreadsheet titled, "Member Standards and COI Log" which confirms that the "UCI IRB Members Standards" document, as well as the "Conflict of Interest (COI) Disclosure Form for IRB Members" has been completed and reflects any positive disclosures to be considered per member.
 - G. For a convened meeting, the HRP team records in the minutes each time a member is absent from the Committee discussion and vote due to a COI.

Policy Number: 10

Title: IRB Committees' Relationship to Other University Committees, Departments and Units

Date of Last Revision: 06/10/10, 10/23/10, 08/05/11, 10/25/12, 05/01/13, 09/28/15, 03/07/17, 04/08/20, 07/15/20, 02/23/21, 03/04/22, 08/21/24

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to work in coordination with other Committees, departments and units to provide protections to research participants. The UCI IRB functions independently, but in coordination with other UCI Committees.

- I. **Cannabis Research Review Committee (CRRC) (Office of Research)**
 - A. Proposition 64 enacted in California on November 8, 2016 allows for the use, cultivation, and sale/distribution of marijuana for non-medical purposes among people over the age of 21. However, based on federal law, marijuana is categorized as a Schedule I drug with "no currently accepted medical use" in the United States.
 - B. There is no provision for the legal use of marijuana for research at UC except as established and in compliance with the Drug Enforcement Administration (DEA), Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA) policies and regulations. Marijuana remains prohibited on all University property and at all University events, except for as used in approved academic research.
 - C. As applicable, to ensure compliance with State and Federal regulations, CRRC approval is strongly recommended before clinical research procedures involving cannabis are initiated at UCI.
- II. **Chao Family Comprehensive Cancer Center Protocol Review and Monitoring Committee (PRMC)**
 - A. The PRMC must approve all research protocols which involve cancer (e.g., research involving participants at risk for cancer, participants with cancer and program evaluations, quality of life, and health education research involving cancer).
 - B. The PRMC scientific and scholarly review assures that the research uses procedures consistent with sound research design, the study design can be reasonably expected to answer the proposed question, and the importance of the knowledge expected to result from the research is known.
 - C. PRMC review is required for new and renewal IRB review if the cancer related research is:
 1. Investigator authored research,
 2. Is biomedical/ clinical research including clinical investigations,
 3. Involves greater than minimal risk *and*
 4. Has not received peer review for scientific merit
 - D. For all other research, including research that is minimal risk, industry authored, federally supported or sponsored by other non-profit entities, PRMC review is concurrent to IRB review.
 - E. The UCI IRB reserves the right to require scientific merit review prior to IRB review or prior to approval for any research, including modifications.

III. **Clinical Engineering**

- A. UCI Clinical Engineering must approve the use of medical equipment in an area that operates under the hospital's license and/or equipment used on the hospital's patients and research subjects.
- B. Investigators conducting research which involves the use of equipment as described in above must provide written assurance to the IRB that UCI Clinical Engineering's approval will be obtained prior to the use of such equipment.

IV. **Clinical Research Billing (CRB)**

- A. UCI Health System has established the CRB unit in an effort to fulfill regulatory requirements from the federal Office of the Inspector General, the University of California (UC) Corporate Compliance Program and the Joint Commission on Accreditation of Healthcare Organizations (JCAHO). At UCI, CRB may also be referred to as Research Revenue Integrity (RRI).
- B. The CRB reviews human research studies that involve UCIMC clinical services as part of research or clinical care. This includes services or resources owned/ rented/ operated or provided by the UCI Health System (UCI Medical Center, Gottschalk, Pavilions, clinic and/ or hospital visits.
- C. The CRB is responsible for ensuring proper registration and billing practices for all human subjects receiving clinical care while enrolled in clinical research studies.
- D. The IRB strongly recommends that investigators seek CRB approval prior to IRB approval. Applications received by the IRB without CRB approval will be reviewed by an IRB Committee; however, CRB approval must be in place prior to initiation of the research.

V. **Conflict of Interest Oversight Committee (COIOC) (Office of Research)**

- A. COIOC reviews the outside financial interests of investigators as mandated by State, Federal and University requirements and recommends action to the Vice Chancellor for Research (VCR).
- B. The Committee is charged with ensuring that an investigator's personal interest in, or commitment to, entities outside the University's purview does not compromise or appear to compromise his/her objectivity in performing a research project, in mentoring students involved in a research project or in reporting the results of a research project conducted under the aegis of the UC.
- C. COIOC review and resolution is required prior to IRB review. During the IRB process, any financial interests as defined by Institutional policy must be reported to and reviewed by the COIOC. The informed consent documents must include the appropriate language regarding conflict of interest based on the COIOC's recommendations and the VCR's decision, and IRB review of the investigator's financial interest.
- D. The IRB will review the COIOC management plan including the recommended informed consent language and determine whether additional measures are necessary to protect human subjects involved in the research. For specific details of this process see IRB Policy # 25.

- VI. **Dual Use Research Committee (DURC) (Office of Research)**
- A. Dual Use Research of Concern (DURC), under the United States Government Policy, is life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat, with broad potential consequences, to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security.
 - B. Securing DURC approval is the responsibility of the Lead Researcher.
 - C. If applicable, DURC approval is required before clinical research procedures can be initiated.
- VII. **Epidemiology and Infection Prevention Committee (EIP)**
- A. Research protocols involving the study of devices, biologic products or infectious agent in humans on the UCIMC campus or any UCI-affiliated clinical site (including clinical sites on campus or external affiliated sites) require review by the EIP.
 - B. Securing EIP approval is the responsibility of the Lead Researcher.
 - C. If applicable, EIP approval is required before clinical research procedures can be initiated.
- VIII. **Export Control Review Process (Office of Research)**
- A. The Export Control Review Process is recommended as part of considering the feasibility of study conduct and prior to research initiated in countries subject to Office of Foreign Assets Control (OFAC) sanctions (e.g., Cuba, Iran, North Korea and Syria).
 - B. Securing review (and a license, as necessary) is the responsibility of the Lead Researcher. Research requiring a license cannot be approved by the IRB until a license is obtained
- IX. **Human Stem Cell Research Oversight Committee (hSCRO) (Office of Research)**
- A. hSCRO assures human stem cell activities are:
 - 1. In accord with National Academies and California DHS guidelines, the National Institutes of Health Guidelines on Human Stem Cell Research, and the ethical guidelines (e.g., Belmont Report, Declaration of Helsinki), and
 - 2. In compliance with California statute and California Institute for Regenerative Medicine (CIRM) regulations and applicable campus policies and procedures for human stem cell activities.
 - B. hSCRO considers the ethical and social issues presented by human stem cell activities and reviews the scientific/scholarly merit of human stem cell activities to assure procedures are consistent with sound research design, the study design can be reasonably expected to answer the proposed questions(s), and the importance of the knowledge expected to result is known.
 - D. hSCRO review and approval is required prior to IRB review. IRB applications received by the Office of Research (OR) without hSCRO review and approval will be held pending such approval.
 - E. The scientific/scholarly reviews performed by the hSCRO are provided to the IRB.

X. **Institutional Biosafety Committee (IBC)**

- A. The IBC is a Committee managed by the department of Environmental Health and Safety. IBC review is required by Institutions receiving funding from the NIH for research involving recombinant DNA molecules. It is charged with reviewing and approving research conducted with microorganisms pathogenic to humans, plants, or animals.
- B. The IBC also provides guidance on the proper acquisition, handling, transfer, and disposal of potentially hazardous or regulated biological materials.
- C. The following types of human research protocols must receive UCI IBC review and approval:
 - 1. Any research activity involving materials potentially containing human pathogens (e.g. unfixed human specimens, human blood) must be approved by the UCI IBC before the research can be initiated.
 - 2. Any research activity involving the deliberate transfer of recombinant DNA or RNA, or DNA or RNA derived from recombinant DNA into one or more human research participants must be approved by the UCI IBC before UCI IRB review. IBC comments and approval must be provided to the UCI IRB at the time of IRB review.
 - 3. Any research activity utilizing investigational, live, recombinant, and/or attenuated microorganisms for the purposes of vaccination or infection of one or more human research participants must be approved by the UCI IBC before UCI IRB review. IBC comments and approval must be provided to the UCI IRB at the time of IRB review.
 - 4. Any research activity utilizing a "Select Agent" as defined by the CDC in 42 CFR 72 Appendix A must be approved by the UCI IBC before UCI IRB approval may be granted. The "Select Agent" list may be found on the CDC website.
 - 5. Investigators utilizing recombinant DNA or potentially infectious microorganisms in the course of their research, but not for direct and deliberate transfer into human participants must be approved by the UCI IBC before UCI IRB review. IBC comments and approval must be provided to the UCI IRB at the time of IRB review.

XI. **Investigational Drug Service (IDS)**

- A. The IDS is a division of the UCIMC Pharmacy Department that must be consulted in advance of study initiation concerning the storage, handling, and dispensing of investigational drugs, agents, and biologics to assure compliance with all IDS policies and procedures, institutional, State, Federal (FDA) and Joint Commission on Accreditation of Hospital Organizations (JCAHO) requirements.
- B. In order to promote a commitment to compliance with FDA regulations and Good Clinical Practice (GCP) guidelines, UCI Health policy requires that investigational medications are under the control of Investigational Drug Services (IDS) Pharmacy. This includes the storage, control, and distribution of investigational products (IP). UCI Health personnel who prepare, store, administer, and dispose of IP must comply with all federal, state, and institutional policies, and adhere to the procedures indicated in the UCI Health Management of Investigational Medications policy.
- C. IDS Pharmacy oversight waivers may be granted to off-site locations (not located at the Orange Campus). Investigators who wish to request a waiver of the UCI Health requirement to utilize IDS Pharmacy services for studies involving the use of investigational products must follow the IDS Guideline for Consultation and Waiver process.
- D. The HRP staff provides IDS Pharmacy access to the IRB submission and

management system to review clinical investigations involving investigational product (IP).

- E. Research activities may not begin until IRB approval has been granted and IDS pharmacist has been consulted by the Lead Researcher to review the drug pharmacology, method of administration, dosage range and schedule, indication, the potential adverse effects and interactions with other drugs, as appropriate.
- F. The IRB will hold release of final IRB approval for investigator-initiated trials involving IP pending IDS approval or issuance of a waiver, as documented in the IRB submission and management system.
- G. Storage of Investigational Drugs, Agents, or Biologics
 - 1. It is the responsibility of the Lead Researcher to comply with all Institutional, State and Federal regulations with regard to storage of investigational drugs, agents, or biologics.
 - 2. Investigational drugs, agents, or biologics used in the context of research, may be stored in areas other than the IDS under the direct supervision of the Lead Researcher and in accordance with the sponsor, if applicable.
 - 3. Controlled substances may not be stored outside of the pharmacy department.
 - 4. Investigational agent storage facilities outside of the IDS must be in compliance with Institutional, State, Federal FDA and JCAHO requirements.
- H. Dispensing of Investigational Drugs, Agents, or Biologics
 - 1. Investigational drugs, agents, or biologics administered to inpatients or outpatients should be dispensed by a licensed physician or an IDS pharmacist.
 - 2. If IDS is not utilized for the dispensing of investigational drugs, agents, or biologics, it is the responsibility of the Lead Researcher to assure that dispensing is in accordance with all Institutional, State, Federal, and JCAHO requirements.
 - 3. Nursing staff may administer investigational drugs, agents, or biologics to inpatients at UCIMC or one of its ambulatory clinics.
 - 4. The Pharmacy must prepare and dispense controlled substances for all inpatients and outpatients.

XII. Laser Safety Committee (LSC)

- A. Researchers proposing use of an investigational laser or the use of an FDA approved laser off label should consult with the Laser Safety Committee to determine if review would be appropriate.
- B. Securing LSC approval is the responsibility of the Lead Researcher.
- C. If applicable, LSC approval is required before clinical research procedures can be initiated.

XIII. Office of Research Oversight (ORO)

- A. The ORO in UCI Health Affairs conducts directed and random periodic compliance reviews of IRB-approved studies when the Lead Researcher is Health Affairs personnel (i.e., faculty, staff, or student) and/or the research is conducted at UCI Medical Center (UCIMC).
 - 1. The Health Affairs Compliance Officer provides the Director of Human Research Protections (HRP) or designee with a summary of each compliance review.
- B. The ORO will conduct directed and random periodic compliance reviews of IRB-approved studies at the request of the IRB.
- C. HRP staff provides the ORO quarterly reports of recently approved

protocols and protocols with reported unanticipated problems involving risk to subjects or others within the past quarter.

XIV. Operating Room (OR) / Procedural Services Committee

- A. Any HS research studies that will be conducted in UCIMC surgical units must notify the OR/Procedural Services Committee before study procedures are initiated.
- B. A copy of the protocol must be provided to the OR/Procedural Services Committee.
- C. Notification should be sent via email to the Operating Room Director.
- D. Notification is the responsibility of the Lead Researcher and is required before clinical research procedures can be initiated in the surgical units.

XV. Pathology Clearance

- A. Per HRP Policy 15 and the UCIMC Anatomical Pathology/Surgical Pathology - Procedure Number: S-23, all specimens removed from clinic or the operating room must be sent to UCI Health Pathology for review and documentation by a pathologist.

XVI. Radiation Safety Committee (RSC)

- A. All human research protocols involving use of radioactive materials must be performed under a Radiation Use Authorization (RUA) approved by the Medical Center Radiation Safety Committee.
- B. All human research protocols involving use of radiation-producing equipment must be performed or supervised by physicians holding an appropriate state-issued X-ray Supervisors and Operators Permit or Certificate. *X-ray procedures at the Medical Center that are considered "standard-of-care" do not require a specific RUA.*
- C. To expedite radiation reviews of human research protocols at the Medical Center, the Medical Center Radiation Safety Committee has established a Subcommittee consisting of the Committee Chair, the Medical Center Radiation Safety Officer, and the Radiation Physicist.
- D. All protocols involving radiation exposure to normal subjects, and/or to clinical human subjects when the exposure is not considered standard-of-care, is referred to the Subcommittee for review. If appropriate, the Subcommittee may approve the research, or it may refer the protocol to the full Medical Center Radiation Safety Committee for more extensive review.

Examples of procedures that require RSC approval include, but are not limited to:

- Any radiation exposures to normal subjects
- Any use of an investigational radiation device
- Any use of an investigational radiopharmaceutical or investigational implant/seed
- Any use of an investigational contrast medium with radiation
- Any use of imaging where it is the subject of the investigation, such as special CT sequences to guide a new surgical procedure

Examples of procedures that do not require RSC approval include, when standard-of-care:

- Routine chest X-rays
- Routine X-rays of fractures

- Routine diagnostic nuclear medicine tests
- Radioiodine therapy for hyperthyroidism
- Radiation therapy for cancer

- E. The RSC has the authority to approve, require modification in, or disapprove all research activities that fall within its jurisdiction.
- F. UCI RSC approval is required before IRB review. RSC comments and approval must be provided to the UCI IRB at the time of IRB review.

XVII. Radiation Drug Research Committee (RDRC)

- A. The FDA classifies all radioactive drugs as either new drugs requiring an Investigational New Drug Application (IND) for investigational use (21 CFR 312) or as generally recognized as safe and effective when administered under the conditions specified in the Radiation Drug Research Committee (RDRC) regulations (21 CFR 361.1).
- B. Protocols qualifying for RDRC review must be reviewed and approved by the RDRC before IRB review. RDRC comments and approval must be provided to the UCI IRB at the time of IRB review.

XVIII. Statistical Review (SR) (Office of Research Facilitates Process)

- A. UCI's IRB assumes responsibility for statistical review in conjunction with the Biostatistics, Epidemiology, & Research Design (BERD) unit in the Institute for Clinical and Translational Science (ICTS).
- B. The IRB, in conjunction with BERD is charged with ensuring that UCI investigator authored, biomedical or clinical human subject research studies involving greater than minimal risk that have not received prior scientific or scholarly review *or as required by the IRB* will render a scientific, statistically valid interpretation of the results as defined by the study plan and objectives.
- C. The IRB, in conjunction with BERD will assure that the research uses procedures consistent with sound research design, the study design can be reasonably expected to answer the proposed question, and the importance of the knowledge expected to result from the research is known.
- D. **Statistical Review of Human Subjects Research at UCI falls into one of five categories:**
 1. **For research already subjected to full peer review** (e.g., review by a study section or grant committee): No additional internal statistical review is required. The actual protocol (being submitted to the IRB must have been reviewed in its current form. The IRB may request copies of peer review comments. Peer review of a grant that describes a clinical trial in general terms does not satisfy this criterion. In addition, an industry-sponsored, clinical trial authored by a UCI investigator does not satisfy this criterion for independent peer-review.
 2. **For research that involves cancer:** Patients with cancer, individuals at risk for cancer, or individuals in a study involving a specific cancer focus (e.g., program evaluations, quality of life, and health education) require statistic review by the PRMC. No additional statistical review is required. PRMC clearance is not required for cooperative group studies and protocols which have received prior PRMC exemption from review.

3. **For non-cancer research that is UCI investigator-authored and has not been subject to full peer review:**
 - i. **For biomedical/clinical research involving greater than minimal risk (full board review):** UCI HRP staff will directly coordinate with the BERD unit. If the IRB submission including the methodological or statistical information provided is incomplete, researchers will be required to revise their submission prior to IRB review. An incomplete submission may delay IRB review. Lead Researchers proposing investigator-authored studies are strongly encouraged to seek the consultation of a biostatistician prior to submission of an IRB application. This review will help assure the quality of the IRB submission and reduce the turnaround time for IRB review and approval.
 - ii. **For biomedical/clinical research involving minimal risk (Exempt and Expedited level of review):** A scientific statistical review takes place at the school or departmental level. The Department Chair or Institute Director signs the IRB application attesting that the research is appropriate in design (i.e., the research uses procedures consistent with sound research design, the study design can be reasonably expected to answer the proposed question, and the importance of the knowledge expected to result from the research is known). The IRB reserves the right to require statistical review on a study-by study basis.
 - iii. **For social, behavioral, and educational research (all levels of review):** An appropriate scientific statistical review takes place at the school or departmental level. The Department Chair or Institute Director signs the IRB application attesting that the research is appropriate in design (i.e., the research uses procedures consistent with sound research design, the study design can be reasonably expected to answer the proposed question, and the importance of the knowledge expected to result from the research is known). The IRB reserves the right to require statistical review on a study-by study basis.

XIX. Sponsored Projects Administration (SPA) (Office of Research)

- A. SPA is responsible for reviewing, endorsing and submitting proposals to extramural sponsors for research, training and public service projects.
- B. SPA's institutional responsibilities also include the following:
 1. Negotiating and accepting awards on behalf of The UC Regents;
 2. Drafting, negotiating and executing subcontracts;
 3. Ensuring institutional compliance with Federal and State regulations, sponsor policy and University policy;
 4. Representing the campus and The UC Regents when interacting with sponsors; coordinating pre-award and post-award actions that require either institutional or sponsor prior approval;
 5. Resolving problems related to sponsored projects; and
 6. Reviewing UCI consultant agreements.
- C. Funding for human subjects research (e.g., grant, contract) is not finalized without prior IRB approval.

XX. Other Approvals Not Required Prior to IRB Approval

- A. At times, research may be subject to review and approval of other University Committees or External Review Committees.
- B. The IRB approval letter indicates that UCI IRB approval has been granted, but it is the Lead Researcher's responsibility to obtain approval from any other required committee before initiating the research.

References:

21 CFR 50
21 CFR 56
21 CFR 312
21 CFR 361
21 CFR 812
42 CFR 72, Appendix A
FDA Information Sheets
California Health & Safety Code, Section 125300 (hSCRO)
UCOP – Policy DURC
UCI Health Management of Investigational Medications policy

Policy Number: 11

Title: IRB Committee Determinations/Motion

Date of Last Revision: 11/30/2009, 06/01/2010, 06/05/2013, 08/16/2017, 03/09/2022

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to render motions/determinations according to the Federal regulations.

I. Approved

An approval is granted if the research activity meets the criteria for approval as defined in 45 CFR 46.111 (and 21 CFR 56.111, if applicable) and no changes to the research application are required. Investigators are notified that the official IRB approval letter is available within 10 working days. Actual commencement of the study may have to wait until other (non-IRB) approvals have been obtained.

II. Minor Changes

Minor Changes status is granted if the research activity meets the criteria for approval as defined in 45 CFR 46.111 (and 21 CFR 56.111, if applicable) and the changes required by the full Committee or subcommittee, if research qualifies as expedited, are specific, non-substantive changes or are changes that only require simple concurrence by the Lead Researcher (LR). An official IRB communication will be sent via e-mail to the LR within 10 working days. The specified changes can be reviewed via an expedited procedure (i.e., by the Chair or another member designated by the Chair) without going back to the full committee. The application is approved if, on review, the changes have been made by the Investigator and confirmed by the Chair or their Designee. If any required changes have not been made, or additional changes have been made that were not requested, the Chair or their designee may refer the study for re-review.

III. Tabled for Re-review

A study that lacks sufficient information to conduct an adequate review may be tabled for re-review pending receipt of the requested information. In addition, a study may be tabled for re-review if the study does not meet the criteria for approval as defined in 45 CFR 46.111 (and 21 CFR 56.111, if applicable), the subcommittee requires full Committee review of an expedited submission; or the IRB Committee recommends substantial changes to the IRB Application, informed consent document(s), or other pertinent documents rendering it unable to assess the risk/benefit ratio without the completed changes. An official IRB communication will be sent via e-mail to the LR within 10 working days. A completely revised protocol/consent package must be reviewed by the IRB. Meeting deadlines apply to full committee protocols.

IV. Disapproved

A study that does not meet the criteria for approval as defined in 45 CFR 46.111 (and 21 CFR 56.111, if applicable). Disapproval of a protocol is generally only considered after multiple attempts have been made to resolve the issues (i.e.,

Tabled for Re-review) including, at the discretion of the IRB, discussing the issues with the LR or inviting the LR to the Committee meeting. **A study can only be disapproved by the full IRB Committee.** An official IRB communication will be sent via e-mail to the LR within 10 working days. The memo includes the rationale for the Committee's decision to disapprove and gives the LR an opportunity to respond in writing. If the LR chooses to respond, a completely revised protocol/consent package must be reviewed by the IRB. Meeting deadlines apply to full committee protocols.

V. **Administrative Hold**

The IRB Committee or IRB Chairperson or designated Committee member may request the Investigator place some or all research activities of a currently approved study on hold when more information is needed. The determination may be requested and lifted at the level of review for which the study qualifies.

VI. **Sponsor-Imposed Suspension**

A sponsor-imposed suspension is when the IRB receives written notification that the sponsor has suspended the research study. This will be acknowledged by the IRB Committee, Chairperson or their Designee when the appropriate level of review determines the suspension is appropriate. The IRB may impose additional criteria for suspension, if needed, to protect the participants from potential harm.

VII. **Suspension**

A currently approved study may be suspended when evidence of a possible increase in risk to participants or non-compliance by the Investigator has been determined by the IRB. Suspensions are made by the IRB under full Committee review procedures.

VIII. **Expiration**

A currently approved study is expired when continuing review has not been conducted and approved prior to the study's expiration date. The study expires at midnight of the date specified on the approval letter and the informed consent document. No research activities can occur after the expiration date.

IX. **Termination**

A currently approved study may be terminated if the study is not being conducted in accordance with the IRB policies, is not in compliance with Federal regulations, and/or has been associated with unexpected serious harm to participants. Terminations are made under full Committee review procedures.

Procedure Number: 11.A**Title: Procedure for IRB Committee Determinations/Motion****Procedure:**

This procedure describes the process for the rendering of the IRB Committee determinations/motions following the review of proposed research activities.

I. Lead Researcher (LR) Responsibilities

- A. **Approved:** If approval is granted, the LR may begin the research when he/she receives the approval letter and approved documents from the IRB. The LR will be notified by the HRP staff via e-mail when these documents are available in the IRB submission and management system.
- B. **Minor Modifications:**
 - 1. The LR responds to the Committee requirements outlining the changes and the rationale for any changes not incorporated. Changes not incorporated are referred to the Committee. The LR includes in the response a copy of any revised attachments in their entirety. The changes to the documents are highlighted or underlined.
 - 2. Amendments receiving a minor modification status may not be implemented until a satisfactory response by the LR has been received and final approval has been granted in writing by the IRB.
 - 3. Research activities may not start until all conditions have been met and the IRB Chairperson or their designee has approved the study and the approval documents have been processed.
- C. **Tabled for Re-review:**
 - 1. The Investigator responds to the Committee requirements outlining the changes and the rationale for any changes not incorporated. The Investigator includes in the response a copy of any revised attachments in their entirety.
 - 2. Amendments receiving a “tabled for re-review” status are not implemented until a satisfactory response by the LR has been received and approval has been granted in writing by the IRB.
 - 3. Tabled for re-review studies must go back to the original IRB Committee for review once a response is received.
 - 4. Research activities may not begin until all conditions have been met and the IRB Chairperson or their designee has approved the study and the approval documents have been processed.

II. IRB Committee Responsibilities

The IRB Committee Chairperson or their designee, or the full IRB Committee rendering decisions on reviewed research activities may make the following determinations and/or motions:

- A. **Approved:** Approval may be granted if the research activity meets the criteria for approval as defined in 45 CFR 46.111 and no changes to the research application are recommended.
- B. **Minor Changes:** A “minor changes required” status is stipulated only when the requested changes are clear and specific in nature and do not require clarification by the LR. Clarifications that are minor and will not change the risk to the participant regardless of the response can also be

given a “minor changes” status. Changes not incorporated are referred back to the original Committee. The recommended changes are made to the IRB Application, informed consent documents, or other pertinent documents before IRB approval can be granted.

1. New IRB applications receiving a “minor changes” required status are administratively withdrawn if an adequate response to the Committee requirements has not been received by the IRB within 90 calendar days of the date of the “minor changes” required letter.
 2. Continuing review applications receiving a “minor changes” required status expire on the date of study expiration if an adequate response has not been received by the IRB prior to the study expiration date.
- C. **Tabled for Re-Review:** Tabled for re-review is granted if the study lacks sufficient information to conduct an adequate review at the full Committee review level; the study does not meet the criteria for approval as defined in 45 CFR 46.111; the Committee requires full Committee review of an expedited submission; or if the IRB Committee recommends substantial changes to the IRB Application, informed consent document(s), or other pertinent attachments.
1. New IRB applications receiving a “tabled for re-review” status are administratively withdrawn if an adequate response to the Committee requirements has not been received by the IRB within 90 calendar days of the date of the “tabled for re-review” letter.
 2. Continuing review applications receiving a “tabled for re-review” status expire on the date of study expiration if an adequate response has not been received by the IRB prior to the study expiration date.
 3. The IRB reviewers may contact the Investigator directly or the IRB may invite the Investigator to a Committee meeting to allow the LR the opportunity to address the Committee’s concerns.
- D. **Disapproved:** A study that does not meet the criteria for approval as defined in 45 CFR 46.111. Disapproval of a protocol is only considered after multiple attempts have been made to resolve the issues with the Investigator (i.e., Tabled for Re-review status). A study can only be disapproved under full Committee review procedures.
- E. **Administrative Hold:** The IRB Committee or IRB Chairperson or designated Committee member may request that an Investigator voluntarily place some or all research activities on hold when additional information is needed by the IRB. This request is made and lifted at the level of review for which the study qualifies.
- F. **Sponsor-Imposed Suspensions:** A sponsor-imposed suspension notification is reviewed at the level of review for which the study qualifies. If there are no safety issues (e.g., for interim analysis of data), the IRB does not change the study status. If safety issues exist and the review determines the suspension is appropriate, the IRB changes the study status to sponsor-imposed suspension and identifies the criteria for the suspension. The IRB may impose additional criteria for suspension, if needed, to protect the participants from potential harm. Sponsor-imposed suspensions are lifted at the level of review for which the study qualifies.
- G. **Suspension:** A currently approved study is suspended when evidence of a possible increase in risk to participants or non-compliance by the Investigator has been determined by the IRB. Suspension is conducted at the level of review for which the study qualifies.

- H. **Expired:** A currently approved study must expire if continuing review has not been conducted and approved prior to the study's expiration date.
- I. **Termination:** A currently approved study is terminated if the study is not being conducted in accordance with the IRB policies, is not in compliance with Federal regulations, and/or has been associated unexpected serious harm to participants. Terminations for cause are made under full Committee review procedures.

III. **IRB Analyst or Administrator Responsibilities**

- A. The Analyst or higher captures in the minutes the determinations and motions as presented during the full IRB Committee meetings.
- B. The HRP team under the direction of the Analyst or higher prepares all Committee action items and approval letters corresponding to the Committee's determinations.
- C. Administrative Contacts are copied on all Committee correspondence.
- D. Faculty Sponsors (when applicable) are copied on IRB Tabled for Re-review, Disapproval, Administrative Hold and Suspension and Termination correspondence.
- E. Department Chairs may be copied on IRB tabled for re-review, disapproval, administrative hold and suspension and termination correspondence as determined by the IRB Chair.
- F. School Deans are copied on Suspension and Termination correspondence.
- G. Responses from LR's for motions of "minor changes" required are reviewed and changes are verified. The HRP team will meet with the Chairperson or their Designee for review of the response and final approval. Upon completion, approval documents are processed and a copy is placed in the IRB file. Using the IRB submission and management system, the HRP staff will notify the LR when the Approval Letter and approved documentation are available for downloading.
- H. Responses from the LR for motions of "tabled for re-review" are prepared for full IRB Committee or the subcommittee for further review and determination.
- I. The Analyst or higher and/or HRP staff makes appropriate database entries for motions and responses to Committee actions and review correspondence.

Policy Number: 12

Title: IRB Review of Human Subjects Research - Exempt

Date of Last Revision: 10/12/07, 08/21/10, 11/09/10, 01/24/11, 06/05/13, 05/01/16, 06/01/16, 10/19/17, 02/28/18, 04/02/18, 08/19/19, 09/09/19, 01/21/20, 05/28/20, 03/24/21, 03/11/22, 12/05/22, 12/04/23, 08/15/24

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) that all human subjects research activities under its jurisdiction be reviewed to determine whether the research meets one or more of the exemption categories described in the Federal regulations and complies with UC Irvine's ethical standards.

I. Exempt Eligibility

- A. Research activities involving human subjects may be exempt from the requirement that they receive IRB full or expedited review as per the Office for Human Research Protections (OHRP) and Food and Drug Administration (FDA).
1. **Exempt Self-Determination Tool:** Lead Researchers (and Faculty Sponsors as applicable) and Undergraduate Research Opportunities Program ([UROP](#)) students may use the Exempt Self-Determination Tool through the electronic IRB submission and management system to confirm exempt categories 1-4.
 2. When using the Exempt Self-Determination Tool, the following exceptions apply;
 - a. Exemptions 2iii, and 3iC. (limited IRB review is required)
 - b. Exempt Categories 5-8
 - c. The research is regulated by the FDA
 - d. The research is supported by the Department of Justice (DOJ)
 - e. The research is supported by the Department of Energy (DOE)
 - f. The research does not involve the following:
 - i. The use or disclosure of UC/UCI records (e.g., medical, student, employment when the [California Information Practices Act \(CIPA\)](#) is applicable)
 - ii. The creation, access to use or disclosure of [UCI protected health information \(PHI\)](#)^{**1}
 - iii. A targeted recruitment of children
 - iv. A targeted recruitment of adults (age 18 or older) who may not be legally/mentally/cognitively competent to consent
 - v. A targeted recruitment of prisoners (may include parolees)
 - vi. A targeted recruitment of American Indian/Alaska Native tribes
 - vii. A targeted recruitment of undocumented people
 - viii. International Research
 - ix. A request for UCI to serve as IRB of Record for non-UCI individuals engaged in human subjects research.
Note: To initiate a request for UCI to serve in this capacity, the LR must have a dual affiliation with the non-UCI entity and IRB review is required to formalize the reliance process.

¹ Use is any sharing, employment, application, utilization, examination, or analysis within the entity. Disclosure is any release, transfer, provision of access to (*including the observation of*), or divulging outside of entity.

- x. A study team member has a Disclosable Financial Interest

3. **IRB Confirmation of Exemption:** Lead Researchers (and Faculty Sponsors as applicable) may receive exempt confirmation by IRB Chairperson, designated IRB subcommittee, or HRP Staff Reviewer using the following mechanism;

- a. An IRB Application for Exemption
 - i. Investigators must submit a completed IRB application to conduct Exempt human subjects research that otherwise does not qualify for UROP review or completion of the Exempt Self-Determination Tool.
 - ii. Exempt confirmation may be granted for no more than three (3) years. A renewal application may be submitted to continue the research.

B. **2018 Common Rule Exempt Categories:** For research that falls under the 2018 Common Rule (i.e., new studies approved on or after January 21, 2019 or for continuing studies approved before January 21, 2019 receiving a new or renewal of a federal award (See Policy # 18)), research may be granted exempt status if all research activities involve procedures listed in one or more of the specific categories under **45 CFR 46.104(d)**:

- 1. **45 CFR 46.104(d)(1):** 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. **45 CFR 46.104(d)(2):** Research that includes only **interactions involving educational tests** (cognitive, diagnostic, aptitude, achievement), **survey procedures, interview procedures, or observation² of public behavior** (including visual or auditory recording) **if at least one of the following criteria are 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 human subjects can readily be ascertained**, directly or through identifiers linked to the subjects, **and an IRB conducts a limited review to make the determination required by 45 CFR 46.111(a)(7)**

Note: For Category 2iii, any disclosure of the human subjects' responses outside the research *would* reasonably place the subjects at risk of criminal or civil liability or be damaging to the

² Children may be included if procedures include educational tests or observation of public behavior only and the researcher does not participate in the activities being observed.

subjects' financial standing, employability, educational advancement, or reputation.

3. **45 CFR 46.104(d)(3i):** 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:**

- a. 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;
- b. Any **disclosure** of the 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**
- c. 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 subject, **and an IRB conducts a limited IRB review to make the determination required by 45 CFR 46.111(a)(7)**

Note: For Category 3iC, any disclosure of the human subjects' responses outside the research *would* reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation.

- ii. For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, 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.
- iii. 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.

4. **45 CFR 46.104(d)(4): 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**;

Note: Category 4i applies to secondary research use of archives in a public library, for example, or to government or other institutional records where public access is provided on request, or from a commercial entity if the information is provided to members of the public on request or if the only requirement for obtaining the information is paying a user fee, registering or signing in as a visitor to an archive. It would also apply if a

- commercial entity made identifiable biospecimens publicly available to anyone on request or for a fee.
- ii. Information, which may include information about the biospecimens, is recorded by the investigator in such a manner that the **identity of 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**
 Note: Category 4iii is allowable when a UCI healthcare workforce member uses identifiable health information for research purposes and the information obtained for research will not be disclosed outside of the covered entity (i.e., not outside of UCI Health). **IMPORTANT!** Disclosure beyond UCI Health for research purposes does not meet category 4iii and the project should be submitted as Expedited Category 5.
 - 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 section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.
5. **45 CFR 46.104(d)(5): 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 Web site 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. **45 CFR 46.104(d)(6): 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 Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U. S. Department of Agriculture.
7. **45 CFR 46.104(d)(7): Storage or maintenance for secondary research for which broad consent is required:** Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determinations required by §46.111(a)(8).
Note: UCI will not adopt Category 7. UCI's interpretation of Broad consent is that it is a system-wide program that allows institutions to track via a central system biospecimens and data for which individuals provide their broad consent, or decline, as well as the terms of the broad consent to determine which future research uses remain within scope. This interpretation aligns with the Health and Human Services (HHS) Secretary's Advisory Committee on Human Research Protections (SACHRP) interpretation. Consequently, UCI is taking the same position as all UC's, Children's Hospital Orange County, Harvard, and Johns Hopkins and is not implementing Category 7, because UCI currently lacks a system-wide program for collecting broad consent.
8. **CFR 46.104(d)(8): Secondary research for which broad consent is required:** Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:
 - i. **Broad consent** for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens **was obtained** in accordance with 45 CFR 46.116(a)(1) through (4), (a)(6), and (d);
 - ii. **Documentation of informed consent or waiver of documentation of consent was obtained** in accordance with 45 CFR 46.117;
 - iii. An **IRB conducts a limited IRB review** and makes the determination required by 45 CFR 46.111(a)(7) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph (d)(8)(i) of this section; **and**
 - iv. The investigator **does not include returning individual research results** to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual results.**Note: UCI will consider Category 8 on a case-by-case basis.** Researchers interested in Category 8 should contact HRP Staff for more information OR consider Expedited Review under Category 5.

- C. **Pre - 2018 Common Rule Exempt Categories:** For research that does not fall under the 2018 Common Rule (i.e., continuing studies approved before January 21, 2019 that are not receiving a new or renewal of a federal award (See Policy # 18)), research may be granted exempt status if all research activities involve procedures listed in one or more of the specific categories under **45 CFR 46.101(b)**:

1. **45 CFR 46.101(b)(1)**³: Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:
 - i. Research on regular and special education instructional strategies; or
 - ii. Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
2. **45 CFR 46.101(b)(2)**⁴: Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
 - i. Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
 - ii. Any disclosure of the human subjects' responses outside of the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.
3. **45 CFR 46.101(b)(3)**: Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under 45 CFR 46.101(b)(2) if:
 - i. The human subjects are elected or appointed public officials or candidates for public office; or
 - ii. Federal statutes require without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
4. **45 CFR 46.101(b)(4)**: Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or the information is recorded by the Investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
 - a. To qualify for this exemption, data, documents, records, or specimens must have been collected before submission of the IRB application.

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The study procedures should not:

- Entail a significant deviation in time or effort from those educational practices already existent in the study site; or
- Involve an increase in the level of risk or discomfort beyond normal, routine educational practices.
- Note: The school or other institution grants written approval for the research to be conducted.

4

If the research involves children as participants, the research must be limited to educational tests (cognitive, diagnostic, aptitude, achievement), and observation of public behavior when the investigator(s) do not participate in the activities being observed. Audio/video recordings and photographs may be permissible in this category.

- b. Under this exemption, an investigator (with proper institutional authorization) may inspect private, identifiable records, but may only record information in a non-identifiable manner. The data must be permanently and completely de-linked at the time of extraction. A code may be used to organize data as it is collected. However, the code may not be a means of re-linking the data set to the original data source. Investigators are required to provide a data abstraction sheet to the IRB.
5. **45 CFR 46.101(b)(5):** Research and demonstration projects, which are conducted by or subject to the approval of Federal Department or Agency heads, and which are designed to study, evaluate, or otherwise examine:

Public benefit or service programs; this exemption is for federally supported projects and is most appropriately invoked with authorization or concurrence by the funding agency. The following criteria must be satisfied to invoke the exemption for research and demonstration projects examining (i) "public benefit or service programs:"

- The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services under the Older Americans Act);
 - The research or demonstration project must be conducted pursuant to specific Federal statutory authority;
 - There must be no statutory requirements that the project be reviewed by an IRB; or
 - The project must not involve significant physical invasions or intrusions upon the privacy of participants.
- ii. Procedures for obtaining benefits or services under those programs;
 - iii. Possible changes in or alternatives to those programs or procedures; or
 - iv. Possible changes in methods or levels of payment for benefits or services under those programs.

Note: This exemption is for projects conducted by or subject to approval of Federal agencies and requires authorization or concurrence by the funding agency.

6. **45 CFR 46.101(b)(6) and 21 CFR 56.104(d):** Taste and food quality evaluation and consumer acceptance studies;
- a. If wholesome foods without additives are consumed; or
 - b. 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 Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

- II. **2018 Common Rule Exempt Categories:** Exceptions to exempt research:
- A. These categories do not apply to research involving prisoners unless they are incidentally included.
 - B. Exempt categories 1-4 do not apply to FDA regulated research.
 - C. None of these exemption categories apply to research involving derivation and use of human embryonic stem cells or human embryonic germ cells, including somatic cell nuclear transplantation.
 - D. Observational research involving sensitive aspects of subjects' behavior, or in settings where subjects have a reasonable expectation of privacy, does not qualify for exemption from IRB review.
 - E. Under FDA regulations at 21 CFR 56.104(c), the emergency use of test articles is exempt from IRB requirements. However, OHRP at 45 CFR 46 does not address emergency use of test articles. Emergency use constitutes emergency medical care, the patient is not considered to be a research subject; therefore, prior IRB review and approval is not required. Such emergency care may not be claimed as research, nor may the outcome of such care be included in any report of a research activity.
- III. **Pre - 2018 Common Rule Exempt Categories:** Exceptions to exempt research:
- A. These categories do not apply to research involving prisoners.
 - B. Exempt categories 1-4 do not apply to FDA regulated research.
 - C. None of these exemption categories apply to research involving derivation and use of human embryonic stem cells or human embryonic germ cells, including somatic cell nuclear transplantation.
 - D. Observational research involving sensitive aspects of subjects' behavior, or in settings where subjects have a reasonable expectation of privacy, does not qualify for exemption from IRB review.
 - E. Under FDA regulations at 21 CFR 56.104(c), the emergency use of test articles is exempt from IRB requirements. However, OHRP at 45 CFR 46 does not address emergency use of test articles. Emergency use constitutes emergency medical care, the patient is not considered to be a research subject; therefore, prior IRB review and approval is not required. Such emergency care may not be claimed as research, nor may the outcome of such care be included in any report of a research activity.
- IV. All research conducted under exempt review is subject to all applicable UCI institutional and IRB policies and procedures.
- V. Exempt research activities are subject to the same subject protections and ethical standards as outlined in The Belmont Report.
- VI. Single IRB review requirements **do not apply** to exempt research.
- VII. The full Committee is advised of research proposals/activities that have been registered under the exempt review procedure. As a means of notifying the Committee and allowing for comments regarding a review conducted utilizing exempt review procedures, a report documenting registration of exempt research for the previous month is provided to the IRB Committee as a standing item on the IRB Committee meeting agenda.
- VIII. Modifications to Exempt protocols initially confirmed by the IRB are reviewed and approved by IRB Chairperson, designated IRB subcommittee, or HRP Staff Reviewer. If the amendment affects the status of the protocol review level, the designated HRP Staff Reviewer or IRB Chair will determine the appropriate review level (i.e., Expedited or full Committee review).

- IX. Use of the Exempt Self Determination Form by UROP undergraduate students are managed in accordance with the UROP program.

References:

OHRP 45 CFR 46

45 CFR 46.104(d)

45 CFR 46.101(b)

45 CFR 46.101(i)(footnote 1)

45 CFR 46.102(i)

45 CFR 46.201(b)

45 CFR 46.401(b)

21 CFR 56.104(c) and (d)

OHRP, *Exemption for Research and Demonstration Projects on Public Benefit and Service Programs*. <http://archive.hhs.gov/ohrp/humansubjects/guidance/exmpt-pb.htm>

OHRP, *Exempt Research and Research That May Undergo Expedited Review*, May 5, 1995.
<http://www.hhs.gov/ohrp/policy/hsdc95-02.html>

OHRP Compliance Activities: Common Findings and Guidance -7/10/2002

[NOT-OD-16-094](#)

45 CFR 46.114

Procedure Number: 12.A**Title: Procedure for IRB Review of Human Subjects Research – Exempt****Procedure:**

This procedure provides guidance in accordance with regulations to review and approve human subjects research in an exempt category.

I. Lead Researcher (LR) Responsibilities

- A. Where exempt self-determination is allowed, the Lead Researcher (including the UROP undergraduate student) (and Faculty Sponsor as applicable) complete the Exempt Self Determination Tool, available via the electronic IRB submission and management system.
- B. For exempt research that requires UCI IRB review, the IRB Application is completed in its entirety and electronically submitted to the HRP staff for processing. The Department Chair or the Organized Lead Unit Director logs into electronic IRB submission and management system to confirm their “approval” of the submission. (See IRB Policy 1.)
- C. The Consent form(s) is written using the template consent document, as applicable.
- D. When research requires UCI IRB review, the Investigator replies to all requests for revisions and/or clarifications requested by the HRP Staff Reviewer or IRB reviewer, when applicable.
- E. Once IRB confirmed as exempt, any proposed and necessary changes which require an amendment are submitted to the IRB via the electronic IRB submission and management system. (*See Policy # 17.) The Investigator must receive written IRB approval before implementing any changes to the research study.
- F. All unanticipated problems to participants or others or possible non- compliance are submitted to the IRB using the New Information Report in the electronic IRB submission and management system.

II. Reviewer Responsibilities

- A. The Reviewer reviews the IRB Application and validates or declines the researcher’s claim for review under the exempt category.
- B. The Reviewer reviews the proposed research, consents, and applicable documents to determine if the research meets the ethical standards of the Belmont Report. The Reviewer documents the exempt determination through the electronic IRB submission and management system.
- C. When the research involves interaction with subjects, a determination is made by the Reviewer whether some type of consent process is appropriate. The Reviewer documents the consent process in the electronic IRB submission and management system and the Exempt confirmation or registration letter. The Reviewer will ensure that the consent document provided to subjects contains such information as:
 - 1. a statement that the activity involves research;
 - 2. a description of the procedures;
 - 3. a statement that participation is voluntary;
 - 4. a statement that there are adequate provisions to protect the privacy and confidentiality of the subjects; and
 - 5. the name and contact information for the researcher.
- D. If the Reviewer disagrees with the proposed level of risk, the appropriate level of review is determined (i.e., Expedited). An IRB Chair will be consulted if the appropriate level of review is full Committee.

- E. If the Reviewer confirms the exemption, the Reviewer first completes a brief checklist in the IRB submission and management system and then a letter of Exempt Registration is generated.
- F. When revisions are requested prior to initial registration, the modified documents are re-reviewed and, if acceptable, exempt registration is granted.
- G. If proposed changes to an exempt study are submitted for review and approval, and the IRB requires a prospective review of such changes, the Reviewer will review and approve, as applicable.
- H. If needed, the IRB Chair or designated IRB subcommittee member is available to assist the Reviewer in determining if the study meets exemption criteria. If the Reviewer has a conflict of interest, another experienced Reviewer will conduct the review.
- I. HRP Staff Reviewers are delegated the authority to register IRB applications and approve amendments related to research activities deemed exempt from the federal regulations regarding the protection of human subjects under 45 CFR 46.101 (b). Exempt studies are accepted on a rolling basis and are administratively reviewed weekly by an HRP Staff Reviewer.
- J. Exempt Research receives a three-year registration with the UCI IRB. An abbreviated version of the renewal may be submitted to continue the research. The abbreviated renewal prompts the LR to confirm currently registered information about the research, as well as the status of enrollment. Finally, the LR can upload any relevant documents that the study team may want reviewed as part of the Exempt renewal.
- K. Delegation is provided in the HRP Staff Reviewer Delegation of Authority document maintained on the HRP WIKI page – and signed by the IRB Chairs for A, B, C, and Vice- Chair for Team D.
 - 1. An HRP Staff Reviewer is defined as follows:
 - a. **Tier 1:** Administrator or above, CIP certified and appointed as IRB members or alternate members. Exceptions are noted as applicable.
 - b. **Tier 2:** Analysts or above, CIP certified. Those without current CIP have been designated by an IRB Chair, Director or Assistant Director of Human Research Protections to have the appropriate experience to review minimal risk protocols. Exceptions are noted as applicable.
 - 2. An HRP Staff Reviewer may review and approve exempt protocols **with the following exceptions:**
 - a. Only an IRB Member or Tier 1 may review:
 - i. Protocols involving limited IRB review
 - ii. New or changes to waiver of HIPAA
 - iii. Involves California Information Practices Act
 - b. Only an IRB Member may review:
 - i. New of changes to disclosure of financial interest
 - ii. Potential noncompliance or unanticipated problem reported during last approval period
 - c. HRP Staff Reviewers may review and approve modifications related to exempt protocols in accordance with HRP Policy # 17

III. **Human Research Protections (HRP) Team Responsibilities**

- A. Conducts a pre-review to determine whether the application includes all information required and requests additional information, if needed, from the LR, to assist the Reviewer in making a determination.
- B. The HRP team will also review the proposed research to determine if it meets the ethical standards of the Belmont Report.
- C. Requests for information will be sent via to the LR via the electronic IRB submission and management system.
- D. When consultants to the IRB are utilized, obtain a signed Consultant's standards

document which includes a description of Disclosable Conflict of Interest and a statement of confidentiality.

- E. Assembles and prepares for distribution of review materials.
- F. Draft correspondence from the Reviewer and approval letters using the appropriate template which includes a citation to the specific permissible category or categories justifying the expedited review.
- G. New approvals, amendments and renewals are processed according to corresponding IRB policies and procedures.
- H. Appropriate database entries in the electronic IRB submission and management system are completed.
- I. Approved documents are processed.

Policy Number: 13

Title: IRB Review of Human Subjects Research – Expedited

Date of Last Revision: 08/10/05; 10/05/10; 05/04/12; 05/29/13; 06/05/13; 01/09/15, 06/01/16, 09/07/17, 01/25/18, 10/16/18, 01/31/19, 03/23/22, 12/05/22, 12/04/23

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) that all human subjects research activities under its jurisdiction be reviewed to determine whether the research meets one or more of the expedited categories described in the Federal regulations.

I. Expedited Eligibility

- A. Federal regulations (45 CFR 46.110 and 21 CFR 56.110) allow the IRB to review certain applications on an expedited basis if they meet specified criteria (i.e., research activities that present no more than minimal risk to human subjects).
- B. Approved expedited protocols may be approved for a 1-year or 3-year approval period. (See Section I below.)
- C. Additionally, the standard requirements for informed consent (or its waiver or alteration) apply to all IRB approvals regardless of the type of review - expedited or full Committee.
- D. Minimal risk is defined by the federal regulations as “...*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.*” As written, the definition of minimal risk in federal regulations provides an ambiguous standard by which risks involved in a research study are compared to those encountered in daily life. The ambiguity lies with whether the definition applies to those risks found in the daily lives of *healthy individuals* or in the daily lives of the *potential research participants*. The UCI IRB, wanting to afford greater protection to human research participants, has adopted an absolute standard of minimal risk; therefore, UCI’s working definition of minimal risks includes the phrase, “*in daily lives of the general population.*”
- E. An expedited review consists of a review of research involving human subjects by the appropriate IRB Committee Chair, designated IRB subcommittee, or HRP Staff Reviewer. In reviewing the research, the reviewer(s) may exercise all of the authorities of the full Committee except that the reviewer(s) may not disapprove the research.
Disapproval is only determined by the full IRB Committee.
Additionally, the reviewer(s) may refer the application to the full Committee for review as warranted.
- F. General Restrictions on Expedited Review
 - 1. Expedited review procedures may not be used for initial review of research involving intervention or interaction with prisoners.
 - 2. Expedited review procedures may not be used for classified research.
 - 3. Expedited review procedures may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects’ financial

standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

- G. Appropriate Use of Expedited Review Procedures for Initial Review of Research: The IRB may use an expedited procedure to conduct initial review of research provided all research activities do not fall under any of the general restrictions, present no more than minimal risk to human subjects, and involve procedures listed in one or more of the following categories:
1. **45 CFR 46.110(F)(1)/21 CFR 56.110(F)(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 increase the risks or decrease 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;
 - (1) An investigational device exemption application (21 CFR Part 812) is not required; or
 - (2) The medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
 2. **45 CFR 46.110(F)(2)/21 CFR 56.110(F)(2)**: Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
 - a. From healthy, non-pregnant 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, when 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 are considered. For these participants, 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. Children are defined in the federal regulations 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" [See 45 CFR 46.402(a)].
 3. **45 CFR 46.110(F)(3)/21 CFR 56.110(F)(3)**: Prospective collection of biological specimens for research purposes by noninvasive means. For example:
 - 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 gumbase 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 scrapping or swab, skin swab, or mouth washings; and/or
 - j. Sputum collected after saline mist nebulization.
4. **45 CFR 46.110(F)(4)/21 CFR 56.110(F)(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. 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 include:
- 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. **45 CFR 46.110(F)(5)/21 CFR 56.110(F)(5)**: Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis). **NOTE**: Some research in this category may meet exemption under 45 CFR 46.101(b)(4); this listing refers only to research that is not exempt.
- a. **Retrospective chart review - evaluates patient data that is existing at the time the protocol is initially approved by the IRB**. This type of chart review uses information that has usually been collected for reasons other than research, such as administrative data and medical records. Therefore, the outcome of interest has already occurred by the time the study is started.
 - b. **Prospective Chart Review** – evaluates patient data that **does not yet exist** at the time the protocol is approved by the IRB for initial review. The protocols are designed before any information is collected. Study subjects are identified and followed forward to see if the outcome of interest happens over time.
6. **45 CFR 46.110(F)(6)/21 CFR 56.110(F)(6)**: Collection of data from voice, video, digital, or image recordings made for research purposes.
7. **45 CFR 46.110(F)(7)/21 CFR 56.110(F)(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 meet exemption under 45 CFR 46.101(b)(2); this listing refers only to research that is not exempt.

- H. Appropriate Use of Expedited Review Procedures for Continuing Review of Research: The IRB may use an expedited procedure to conduct continuing review of research provided all research activities do not fall under any of the general restrictions, present no more than minimal risk to human subjects, and involve procedures listed in one or more of the following categories:
1. Research procedures that meet the criteria for initial review of research by an expedited procedure; or
 2. **45 CFR 46.110(F)(8)/21 CFR 56.110(F)(8)**: Continuing review of research previously approved by a full IRB Committee as follows:
 - a. Where the research is permanently closed to the enrollment of new subjects; all subjects have completed all research-related interventions; and the research remains active only for long-term follow-up of subjects; or
 - b. Where no subjects have ever been enrolled (at UCI performance sites) and no additional risks have been identified; or
 - c. Where the remaining research activities are limited to data analysis; or
 3. **45 CFR 46.110(F)(9)/21 CFR 56.110(F)(9)**: Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories (2) through (8) do not apply but the IRB has determined and documented at a convened full IRB Committee meeting that the research involves no greater than minimal risk and no additional risks have been identified.
- I. Extended 3 Year IRB Approval
1. **2018 Common Rule Eligible:**
 - a. **For research that falls under the 2018 Common Rule** (i.e., new studies approved on or after January 21, 2019, or for continuing studies approved before January 21, 2019 receiving a new or renewal of a federal award) the UCI IRB allows for an extended 3-year IRB approval.
 - i. Exceptions include FDA regulated studies or as per the IRB Chair or their designee's discretion. Reasons for requiring a 1-year approval should be specified in the electronic IRB submission and management system.

2. **Prior to the 2018 Common Rule Eligible:**

- a. UCI's Federalwide Assurance (FWA# 00004071) allows some flexibility in applying human subjects federal regulations to non-federally supported research. Research that involves **no more than minimal risk to participants** (as defined by [45 CFR 46.102](#)) or research that is **not subject to federal oversight** is eligible for a 3-year approval.
 - i. Exceptions include any research subject to Federal oversight, including projects that receive federal support, projects implemented at the direction of federal agencies, or otherwise subject to federal oversight are excluded from this policy. Examples of Federal oversight include: Federal sponsorship, directly or indirectly, including federal training and program project grants, student projects when the faculty sponsor uses federal funding for the student's project, Federal no-cost extensions, studies seeking or obtaining Certificates of Confidentiality (which are granted by NIH) and studies where the UCI IRB is serving as the IRB of record for an institution that applies the federal standards to all research regardless of source of funding.
3. The UCI IRB reserves the right to make exceptions to this policy, and inclusion/exclusion of any research project under this procedure will be at the IRB's discretion.
4. If the UCI IRB determines that the study is eligible for the Extended 3-Year IRB Approval, the determination will be inserted on the UCI IRB approval letter. Further the IRB approval period will be set of a period of 3 years. Studies that are granted an extended approval period will continue to have the same post-approval submission requirements. LR must continue to be responsible for submitting:
 - a. Amendments to the study, which must receive IRB approval before they are implemented;
 - b. Reports of Unanticipated Problems, new and/ or continuing non-compliance and other safety information meeting HRPP reporting criteria;
 - c. A renewal at least 4-6 weeks prior to the study's expiration date, if the study is still active; and
 - d. A closeout report when the study is complete.
5. If the study becomes ineligible for an extended approval period because of new federal funding or other changes, the lead researcher is responsible for notifying the IRB of this change via the submission of a formal modification to the study protocol. Further, an application for renewal must be submitted to the IRB for renewal so that the study can be re-reviewed and re-set on a 1-year (no more than 365 days) approval cycle.

J. Collecting Human Blood in a Non-Clinical Setting

All researchers conducting the collection of human blood samples in a non-clinical / nontherapeutic setting for research purposes must abide by the following minimal standards. For researchers who cannot meet the following standards, the UCI Institute for Clinical and Translational Science nursing staff provide blood collection services for a fee.

- a. **Training and Competency:** It is the responsibility of the Lead Researcher (LR) to ensure that all personnel listed on an IRB application have the appropriate training and experience to perform their assigned duties. Collection of blood for research purposes must be performed by California licensed physicians, nurses or clinical lab scientists, or other licensed professionals where phlebotomy is in their scope of practice, or by certified phlebotomists able to provide documentation of competency.
- b. **Risk to Subjects:** The blood collection procedure in non-clinical setting must present no more than minimal risk to human subjects. Collection can be by finger stick, ear stick, or venipuncture from healthy, non-pregnant adults who weighs at least 110 pounds. The amounts drawn may not exceed 100 ml (~ 7 tablespoons) in an 8-week period and collection may not occur more frequently than 2 times per week.
- c. **Adverse Event Management Plan:** The LR must provide a safety management plan explaining how the research team will prevent and manage an adverse event (e.g., fainting, vasovagal response) including an emergency situation (cardiac arrest). Consideration should be made to ensuring that subjects are afforded a controlled environment.
- d. When the institutional requirement in an emergency is to call 911, the expectation is that at least two research team members are California licensed physicians or nurses, or individuals who hold current CPR certification through the American Red Cross or American Heart Association and that these members must be present at the time of the blood draw.
- e. **Environmental Health And Safety (EH&S) Employee Safety Requirements:**
 - i. UCI employees handling human material must complete the Bloodborne Pathogens Training course [via the UCLC](#) within 7 days of their assignment; before collecting blood. The Bloodborne Pathogens Training must be completed annually.
 - ii. The LR must ensure that a [Bloodborne Pathogens Exposure Control Plan \(ECP\)](#) has been completed and reviewed by all applicable employees. The ECP must be on file and a hard copy or electronic copy must be readily available.
 - iii. The employee must be offered the Hepatitis B vaccine or titer.
 - iv. [Universal precautions](#) must be used to prevent contact with blood or other potentially infectious materials (OPIM) at all times which includes utilizing engineering and work place practices and wearing appropriate personal protective equipment to limit exposure.

- v. All incidents/exposures must promptly be reported to the LR and the [EH&S](#) incident reporting system.
 - vi. **EH&S Institutional Biosafety Review (IBC)**
Registration: Collection of blood for analysis in a UCI laboratory requires IBC registration. It is the responsibility of the LR to register the research with IBC prior to the initiation of the research procedures. See the [EH&S IBC web page](#) for more information.
- K. Expanded Category of Minimal Risk Research Procedures – Skin Punch Biopsy for Children and Adults
- a. **Applies to research that is not federally funded, not subject to FDA regulations.**
 - b. Category “13” allows for a skin punch biopsy of no greater than 2 mm for both children (minors under the age of 18) and adults.
 - c. Placement of biopsy must be on the upper inner arm, upper inner thigh, or lower back/upper buttock below the pant line. The location must be agreed upon by the parent or legally authorized representative, the child subject or adult subject, in consultation with the lead researcher.
 - d. The biopsy must be no greater than 2 mm.
 - e. A biopsy greater than 2 mm requires full committee review for both children and adults.
 - f. Additional Considerations for Children:
 - i. If the child is not affected by the condition under study, he/she must be age 7 and above to allow for assent. Parental permission is required.
 - ii. Greater than 2 mm skin biopsies on non-affected (healthy) children will require an additional review process (in addition to full committee review).
 - iii. If the child is affected by the condition under study, there is no age restriction. Parental permission is required.
 - g. Additional guidance for researchers (the following text may also be included in the IRB submission when describing the procedure):
 - i. Use of EMLA or similar topical numbing cream should be used at least 2 hours in advance of the procedure for minors. Then, after selecting a biopsy site on the upper inner arm, upper inner thigh, or lower back/upper buttock the area will be cleansed with an antiseptic solution. Lidocaine or other local anesthetic will then be infiltrated into the biopsy area by injection to provide local anesthesia. A single 2 mm piece of skin will be removed via punch biopsy. A sterile gauze pad will be placed over the site to control bleeding, and the site will be bandaged. The biopsy site may be closed with a stitch if desired. The parents will be provided with post-biopsy care instructions.
 - ii. If multiple 2 mm skin punch biopsies are proposed, the IRB will consider whether the procedures in totality rise to a level greater than minimal risk on a case-by-case basis.

- L. Single-Patient Expanded Access Use: For an expanded access (compassionate) use of an investigational drug outside of a controlled clinical trial for a patient (with an IND), prospective IRB Chairperson approval is allowable through an expedited review process. (See Policy # 41.)

II. **Required Review**

- A. Applications for expedited research are accepted on a rolling basis. The appropriately experienced IRB Committee Chair, designated IRB subcommittee, or HRP Staff Reviewer is required to review and approve research meeting expedited criteria.
- B. An experienced IRB member means a voting member or alternate voting member who has received training relative to the expedited review categories, and possesses the scientific expertise needed to review the proposed research. However, a Reviewer may request a second reviewer or refer the research to the full IRB Committee for further determination.
- C. The Reviewer may also request review of the research by an expert consultant for issues which require expertise beyond, or in addition to, that available on the Committee.
- D. When research is Department of Navy (DoN) sponsored, U.S. Navy-wide survey research requires additional Navy Survey Review and Approval. In addition to UCI IRB approval, the Navy Survey approval manager may require IRB approval by the DoN prior to granting approval.
- E. Research materials submitted include sufficient detail for the Reviewer to determine that the study meets criteria 45 CFR 46.111 and 21 CFR 56.111, if applicable, for approval:
 - 1. Risks to subjects are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and 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 Reviewer 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 Reviewer 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 that fall within the purview of its responsibility;
 - 3. Selection of subjects is equitable considering 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 vulnerable populations and the potential need for additional protections, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons;
 - 4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by the Federal and State regulations and Institutional policies and procedures including the IRB;

5. Informed Consent will be appropriately documented, in accordance with, and to the extent required by the Federal regulations and Institutional policies and procedures including the IRB;
 6. When appropriate, the research plan makes adequate provisions 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; and
 8. There are adequate provisions to protect the rights and welfare of vulnerable populations from coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. The Reviewer must determine that additional safeguards have been included in the study to protect the rights and welfare of these subjects.
- F. **Materials to be Reviewed** - The following materials are provided to the Reviewer(s) for expedited review:
1. The IRB Application is completed in its entirety and electronically submitted to the HRP staff for processing. The Department Chair or the Organized Lead Unit Director logs into electronic IRB submission and management system to confirm their "approval" of the submission. (See IRB Policy 1.),
 2. Sponsor and/or Master protocol, if applicable,
 3. Proposed informed consent document(s) including "Experimental Subjects Bill of Rights", as appropriate and/or Study Information sheet and/or informed consent script as appropriate;
 4. Copies of surveys, questionnaires, or videotapes
 5. Copies of letters of assurance or cooperation with research sites
 6. Investigator's brochure (if one exists)
 7. Advertising intended to be seen or heard by potential subjects, including e-mail solicitations
 8. DHHS-approved sample informed consent form, if applicable
 9. DHHS-approved protocol, if applicable
 10. DHHS grant application – human subjects section, if applicable and considered to be in a fundable range
- G. The Reviewer determines a review interval for the research as appropriate to the degree of risk, but not greater than one year from the last date of IRB approval. The IRB may review a protocol more often than annually when the following circumstances apply:
1. Studies conducted by researchers who have been determined to be in serious non-compliance in the past two years; and
 2. Other situations where the IRB believes that more frequent continuing review is required.
- H. 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 the research must occur on or before the date when IRB approval expires.
- I. Approval Period for Expedited Research is assigned as follows:
1. For expedited research, the approval period starts on the date of the approval. The expiration date would be 365 days from the approval date, minus one. (For example, if the IRB approves the research on April 12, 2005 for one year, the approval period is April 12, 2005-April 11, 2006.)
 2. In all cases the expiration date (the last day the research is approved) is the last day of the approval period. Research may be conducted on

the expiration date, but not after the expiration date without continuing approval. (For example, if the approval period is April 12, 2005-April 11, 2006, the expiration date is April 11, 2006.)

- J. Standard requirements for informed consent or its waiver or alteration apply to all studies meeting criteria for approval under the expedited criteria.
- K. The full Committee is advised of research proposals/activities that have been approved under the expedited review procedure, including initial reviews, continuing reviews and reviews of modifications to previously approved research. As a means of notifying the Committee and allowing for comments regarding a review conducted utilizing expedited review procedures, a report documenting approval of research per expedited review procedures for the previous month is provided to the IRB Committee as a standing item on the IRB Committee meeting agenda.
- L. All research activities approved by expedited review are conducted in accordance with all applicable UCI IRB policies and procedures.
- M. Research cannot be disapproved by the Chair or his/her designee; only the full Committee can disapprove research.**

References:

45 CFR 46.110

21 CFR 56.110

21 CFR 56.102(i)

45 CFR 46.102(i)

DHHS Federal Register Notice: November 9, 1998 (Volume 63, Number 216),

“Categories of

Research That May Be Reviewed by the Institutional Review Board (IRB) Through an Expedited

Review Procedure.” <http://www.hhs.gov/ohrp/policy/63fr60364.html>

OHRP Guidance on the Use of Expedited Review Procedures, August 11, 2003.

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

OHRP Guidance on Continuing Review, January 15, 2007.

<http://www.hhs.gov/ohrp/policy/contrev0107.html>

FDA Information Sheets: *IRB Continuing Review After Clinical Investigation Approval*, February 2012.

<http://www.fda.gov/oc/ohrt/irbs/review.html>

DoD: SECNAVINST 3900.39D, para. 6e

OPNAVINST 5300.8C

Procedure Number: 13.A**Title: Procedure for IRB Review of Human Subjects Research – Expedited**

Procedure: This procedure provides guidance for the review of human subjects research activities that qualify for expedited review under the Federal regulations.

I. Lead Researcher (LR) Responsibilities

- A. The IRB Application is completed in its entirety and electronically submitted to the HRP staff for processing. The Department Chair or the Organized Lead Unit Director logs into electronic IRB submission and management system to confirm their “approval” of the submission. (See IRB Policy 1.)
- B. The Consent form(s) is written using the UCI template consent document.
- C. The Investigator replies to all questions or requests for revisions requested by the pre-reviewers or reviewers, when applicable, and provides an explanation if the requested revisions are not made.
- D. If an Investigator disagrees with any IRB comments and/or requests for revisions, the investigator should provide written justification for his/her position for review by the original IRB committee.
- E. Once IRB approved, any proposed changes to IRB approved documents are submitted to the IRB using an Amendment in the electronic IRB submission and management system. The Investigator must receive written IRB approval before implementing any changes to the research study.
- F. All unanticipated problems to participants or others or possible non-compliance are submitted to the IRB using the New Information Report in the electronic IRB submission and management system.

II. IRB Committee Responsibilities

- A. Review of New Protocols and Continuing Review of Protocols
 - 1. Applications for new expedited research are accepted on a rolling basis and are reviewed weekly by the appropriately experienced IRB Committee Chair, designated IRB subcommittee, or an HRP Staff Reviewer.
 - 2. In considering a new expedited protocol, an experienced Reviewer means an IRB voting member or alternate voting member who has received training relative to the expedited review categories, and possesses the scientific expertise needed to review the proposed research.
 - 3. Applications for continuing review of expedited research protocols are reviewed weekly by the appropriately experienced IRB Committee Chair, designated IRB subcommittee, or an HRP Staff Reviewer.
 - 4. Delegation is provided in the HRP Staff Reviewer Delegation of Authority document maintained on the HRP WIKI page – and signed by the IRB Chairs for A, B, C, and Vice- Chair for Team D.

5. An HRP Staff Reviewer is defined as follows:
 - a. **Tier 1:** Administrator or above, CIP certified and appointed as IRB members or alternate members. Exceptions are noted as applicable.
 - b. **Tier 2:** Analysts or above, CIP certified. Those without current CIP have been designated by an IRB Chair, Senior Director or Director of Human Research Protections to have the appropriate experience to review minimal risk protocols.
6. An HRP Staff Reviewer (**Tier 1** or **Tier 2**) may review and approve expedited protocols **with the following exceptions:**
 - a. Only an IRB member or Tier 1 May Review:
 - i. Inclusion of vulnerable populations
 - ii. New or changes to waiver of HIPAA
 - iii. Protocol involves the California Information Practices Act
 - iv. Expedited Categories 8a, 8c
 - b. Only an IRB Member may review:
 - i. FDA regulated research
 - ii. New or changes to disclosure of financial interest
 - iii. New or changes to inclusion of prisoners
 - iv. Expedited categories 1, 8b, 9, 13
 - v. *Note: For greater than minimal risk research*
 - (a) *Change in Lead Researcher or Faculty Sponsor or a Co-Researcher*
 - (b) *Changes to existing eligibility criteria or the addition of a new subject population*
 - (c) *Adding any new procedures*
 - (d) *Adding questions about sensitive behavior or health status*
 - (e) *Changes to consent process*
 - (f) *Changes to compensation plan*
7. The Reviewer(s) is required to review and approve research meeting expedited criteria. Research may involve/ represent one or more approvable categories of research.
8. The Reviewer(s) assigned will have expertise in the area of the research adequate to the scope and complexity of the research.
9. If a Reviewer has a conflict of interest, the Reviewer will be recused from the review.
10. A Reviewer may request a second reviewer, request review by an expert consultant to the IRB, or refer the study to full IRB Committee for determination.
11. The determination of disapproval can only be made at full Committee.
12. The Reviewer(s) reviews the IRB Application and validates or declines the researcher's claim for review under the expedited category. When declined, the Reviewer(s) refers the study to full Committee.
13. The Reviewer(s) assesses the protocol for both scientific and scholarly merit in relationship to the level of risk.
14. The Reviewer(s) reviews the proposed research, consents, and applicable documents to determine whether the study meets criteria 45 CFR 46.111 and if applicable, FDA 21 CFR 56.111 for approval. This is documented on the final version of the IRB Application approved by the IRB.

15. When revisions are requested, the modified documents are re-reviewed and, if acceptable, approval is granted.

16. HRP staff prepares the IRB Approval Letter.

B. Review of Minor Modifications

1. Minor modification requests are accepted on a rolling basis and are reviewed weekly by appropriately experienced IRB Committee Chair, designated IRB subcommittee, or an HRP Staff Reviewer.
2. An experienced Reviewer is an appropriately experienced IRB Committee Chair, designated IRB subcommittee, or an HRP Staff Reviewer who has received training relative to the expedited review categories and HRP SOPPs, and possesses the scientific expertise needed to review the research. HRP Staff Reviewers are delegated the authority to approve modifications related to expedited level research activities.
3. HRP Staff Reviewers may review and approve modifications related in accordance with HRP Policy # 17.
4. The Reviewer(s) is required to review and approve modifications meeting expedited criteria.
5. The Reviewer(s) assigned will have expertise in the area of the research adequate to the scope and complexity of the research. If the Reviewer has a conflict of interest, they will be recused from the review. A Reviewer may request a second reviewer, request review by an expert consultant to the IRB, or refer the study to full IRB Committee for determination. However, the determination of disapproval can only be made at full Committee.
6. The Reviewer(s) reviews the submitted materials and validates or declines the researcher's claim for review under expedited review criteria. When declined, the Reviewer(s) refers the study to full Committee.
7. The Reviewer(s) assesses the protocol for both scientific and scholarly merit in relationship to the level of risk.
8. The Reviewer(s) reviews the proposed research, consents, and applicable documents to determine whether the study meets criteria 45 CFR 46.111 and FDA 21 CFR 56.111 as applicable for approval. This is documented on the final version of the IRB Application approved by the IRB.
9. The Reviewer(s) determines the review interval appropriate to the degree of risk, but not less than once per year.
10. The Reviewer(s) may request that the study be approved, minor modifications required, tabled for re-review by subcommittee, tabled for review by full Committee, or request administrative hold.
11. When revisions are requested, the modified documents are re-reviewed and, if acceptable, approval is granted and documented in the electronic IRB submission and management system.
12. HRP staff prepares the IRB Approval Letter.

III. Human Research Protections (HRP) Team Responsibilities

- A. Conducts a pre-review to determine whether the application includes all information required and requests additional information, if needed, from the LR, to assist the Reviewer in making a determination.

- B. Requests for information will be sent via to the LR via the electronic IRB submission and management system.
- C. When consultants to the IRB are utilized, obtain a signed Consultant's standards document which includes a description of Disclosable Conflict of Interest and a statement of confidentiality.
- D. Assembles and prepares for distribution of review materials.
- E. Draft correspondence from the Reviewer and approval letters using the appropriate template which includes a citation to the specific permissible category or categories justifying the expedited review.
- F. New approvals, amendments and renewals are processed according to corresponding IRB policies and procedures.
- G. Appropriate database entries in in the electronic IRB submission and management system are completed.
- H. Approved documents are processed.

Policy Number: 14

Title: IRB Review of Human Subjects Research – Full Committee

Date of Last Revision: 08/10/05, 10/05/10, 01/24/11, 05/04/12, 06/05/13, 05/01/16, 08/16/17, 02/26/20, 03/10/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) that all human subjects research activities under its jurisdiction be reviewed according to the criteria described in the Federal regulations.

I. Full Committee Eligibility

- A. An Investigator may suggest a particular type of review, but the final determination is made by the IRB.
- B. The IRB at a convened meeting must review studies not qualifying for IRB review under the exempt or expedited review procedures.
- C. The IRB has the authority to approve, require amendment to, or disapprove all research activities that fall within its jurisdiction.

II. IRB Quorum Required for Full Committee Review

- A. The IRB Committee may only review proposed research at a convened meeting where a quorum is present.
- B. A majority of the voting members of the IRB Committee are present, including at least one member whose primary interests are in nonscientific areas. IRB meetings are not convened if a nonscientist is not present.
- C. A non-affiliated member is present at convened meetings. The non-scientist and non-affiliated member may be the same individual.
- D. No official actions take place at a meeting where a majority of the voting members are not present.
- E. Should quorum be lost during a meeting, the IRB cannot take votes until the quorum is restored.
- F. Wherever possible, IRB Committee meetings take place with all participating IRB members physically present. However, circumstances sometimes warrant conducting IRB meetings with a member present by telephone conference call (e.g., member has expertise but is unexpectedly unable to attend meeting). OHRP recognizes that “convened” IRB meetings can be conducted via teleconference, provided that each participating IRB member:
 - 1. Has received all pertinent material prior to the meeting to allow adequate time for review and the request of additional information, if needed.
 - 2. Can actively and equally participate in the discussion of the protocol (i.e., each member can hear and be heard by all other participating members).
 - 3. The minutes of such meetings clearly document that these two conditions have been satisfied in addition to the usual regulatory requirements (e.g., attendance; initial and continued presence of a majority of members, including at least one nonscientist member; actions taken by the IRB; the vote on such actions; discussion and resolution of controverted issues).

- G. No IRB member may participate in the review of research (e.g., new submissions, renewals, amendments, unanticipated problems, or potential noncompliance issues) in which the member has a conflict of interest. If a conflict exists, the Committee member can provide information requested by the IRB Committee but cannot be present for the discussion and the vote.
- H. The IRB will defer a protocol to another meeting, if at least one person (i.e., IRB member or consultant) with appropriate scientific or scholarly expertise is not available to conduct an in-depth review of the protocol.
- I. When the convened IRB reviews research involving prisoners, the prisoner representative is present.

III. **Required Review**

- A. Substantive review of protocols takes place at convened meetings. Applications undergoing review are individually presented and discussed at a convened meeting of the IRB Committee.
- B. In conducting the full IRB Committee review, the majority of the Committee must agree that materials are in sufficient detail to determine the study meets criteria 45 CFR 46.111 and if applicable, 21 CFR 56.111 for approval:
 - 1. Risks to subjects are minimized by (a) using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (b) 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 Committee 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 Committee 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 that fall within the purview of its responsibility;
 - 3. Selection of subjects is equitable considering 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 vulnerable populations and the potential need for additional protections, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons;
 - 4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by Federal and State regulations and Institutional policies and procedures including the IRB;
 - 5. Informed Consent will be appropriately documented, in accordance with, and to the extent required by the Federal and State regulations and Institutional policies and procedures including the IRB;
 - 6. When appropriate, the research plan makes adequate provisions 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;

8. There are adequate provisions to protect the rights and welfare of vulnerable populations from coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. The IRB Committee must determine if additional safeguards need to be included in the study to protect the rights and welfare of these subjects; and
 9. When appropriate, the Informed Consent Document should include the additional elements of informed consent.
- C. The full IRB Committee determines a review interval for the research as appropriate to the degree of risk, but not greater than one year from the last date of IRB approval. The following factors are taken into consideration when determining the appropriate review interval, but are not limited to:
1. Research with procedures that pose risk and have never been tested in humans before;
 2. Phase I research studies;
 3. Involvement of recombinant DNA or other types of gene transfer protocols;
 4. Research that involves procedures where there is a high likelihood of serious harm or death;
 5. Studies conducted by researchers who have been determined to be in serious non-compliance in the past two years; and
 6. Other situations where the IRB believes that more frequent continuing review is required.
- D. The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval. Therefore, renewal and re-approval of the research must occur on or before the date when IRB approval expires. The study expires at midnight of the date specified on the approval letter and the informed consent document.
- E. Approval Period for Full Committee Research:
1. For research reviewed and approved by at the full Committee at a convened IRB meeting, the approval period starts on the date of the convened meeting. The expiration date (the last day the research is approved) is the last day of the approval period. For example, if the IRB approves the research for one year at a convened meeting held on April 12, 2005, the approval period is April 12, 2005-April 11, 2006.
 2. For research that was determined by the full Committee to require minor modifications, the approval period begins on the date a Reviewer, usually the IRB Chair, verifies that the investigator has made the revisions requested by the full Committee. (For example, if the IRB determines that minor modifications are required at a convened meeting held on April 12, 2005 and approval is for a one year period, when an IRB Chair verifies the changes and approves the research on April 27, 2005, the approval period is April 27, 2005-April 11, 2006.)
 3. In all cases the expiration date (the last day the research is approved) is the last day of the approval period. Research may be conducted on the expiration date, but may not be conducted after the expiration date without continuing approval. (For example, if the approval period is April 27, 2005-April 11, 2006, the expiration date is April 11, 2006. Research must end at midnight on April 11, 2006 unless the Investigator receives continuing approval of the research.)

- F. Standard requirements for informed consent or its waiver or alteration apply to all studies meeting the criteria for approval by the full IRB Committee.
- G. All research approved by the full IRB Committee is conducted in accordance with all applicable UCI policies and procedures.
- H. The decisions and requirements for modifications by the IRB Committee are promptly conveyed to the Investigator electronically by HRP Staff. Written notification from the IRB of a decision to disapprove a protocol, the correspondence is accompanied by the IRB Committee's reasons for the decision and may include an invitation for reply by the Investigator, either in person or in writing.

References:

45 CFR 46

21 CFR 50 and 56

ICH-GCP: 3.2.2, 3.2.3., 3.3.3, 3.3.4.

Procedure Number: 14.A**Title: Procedure for IRB Review of Human Subjects Research – Full Committee**

Procedure: This procedure provides guidance for the review of human subjects research activities that qualify for full IRB Committee review under the Federal regulations.

I. Lead Researcher (LR) Responsibilities

- A. The IRB Application is completed in its entirety and electronically submitted to the HRP staff for processing. The Department Chair or the Organized Lead Unit Director logs into electronic IRB submission and management system to confirm their “approval” of the submission. (See IRB Policy 1.)
- B. The Consent form(s) is written using the template consent document.
- C. The Investigator replies to all questions or requests for revisions requested by the pre-reviewers or reviewers, when applicable, and provides an explanation if the requested revisions are not made.
- D. If an Investigator disagrees with any IRB comments and/or requests for revisions, the investigator should provide written justification for his/her position for review by the original IRB committee.
- E. Ancillary Partner review and clearance will be provided in the electronic IRB submission and management system (e.g., Radiation Safety Committee (RSC)),
- F. Once IRB approved, any proposed changes to IRB approved documents are submitted to the IRB using an Amendment in the electronic IRB submission and management system. The Investigator must receive written IRB approval before implementing any changes to the research study.
- G. All unanticipated problems to participants or others or possible non-compliance are submitted to the IRB using the New Information Report in the electronic IRB submission and management system.

II. IRB Committee Responsibilities

- A. Research that involves greater than minimal risk must be reviewed by the full IRB Committee at a scheduled convened meeting. Each UCI IRB Committee meets once a month. IRB Applications for full Committee review are accepted per posted submission deadlines.
- B. The assigned IRB Committee receives a copy of the IRB Application prior to the scheduled meeting (usually seven days in advance) to allow adequate time for review and the request of additional information, if needed (e.g., supporting documentation from the Investigator, literature search, etc.)
- C. IRB members and consultants with a conflict of interest are asked to disclose at the beginning of the meeting and must absent themselves from the meeting room during the discussion and vote on the research in which they have a conflicting interest. IRB Committee Members and consultants are considered to have a conflicting interest if they or his or her immediate family member have any:
 - 1. Disclosable financial interest; (See IRB Policy 9.)
 - 2. Role in the conduct of or participation in the research; or
 - 3. Other individual conflict of interest that could impede or discourage objective decision-making on behalf of human subjects.

- D. Each new study submitted as posing greater than minimal risk is assigned a Primary and Secondary Reviewer. The reviewers assigned will have expertise in the area of the research adequate to the scope and complexity of the research. The Reviewers conduct an in-depth review of all pertinent documentation.
1. The Primary Reviewer is to present the study in summary form to the full IRB Committee highlighting any controverted issues and recommending modifications, if applicable.
 2. The Secondary Reviewer is prepared to provide any additional information not presented by the Primary Reviewer highlighting any controverted issues and recommending modifications, if applicable.
 3. If the Committee does not have a member available with expertise adequate to the scope and complexity of the research, a consultant with expertise in the area of research will be asked to review the study and provide written recommendations or may be asked to attend the Committee meeting. The consultant may not count toward the quorum or vote. If the Committee is unable to secure adequate expertise the protocol is held over for another convened meeting.
 4. The Reviewers will assess the protocol for both scientific and scholarly merit in relationship to the level of risk.
 5. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, economically or educationally disadvantaged persons, the IRB Committee determines if additional safeguards need to be included in the study to protect the rights and welfare of these subjects (See IRB Policies 36-40). This is documented on the final version of the IRB Application approved by the IRB.
 6. All Committee members are given the opportunity to review, ask questions of the reviewers, and request modifications in the proposal.
 7. The Committee reviews the proposed research, consents, and applicable documents to determine whether the study meets criteria 45 CFR 46.111 and 21 CFR 56.111 if applicable, for approval. This is documented on the final version of the IRB Application approved by the IRB.
 8. The Committee determines the review interval appropriate to the degree of risk, but not less than once per year.
 9. Typically, although not required, the Primary Reviewer makes the motion regarding the status of the study in accordance with applicable UCI IRB policies and procedures.
- E. Non-scientists: The primary duties of IRB members with non-scientific status consist of reviewing the informed consent document and the recruitment materials of new IRB Applications to ensure that the information provided to the participant or the participant's legally authorized representative is in an understandable language and format. Non-scientists also provide additional expertise relevant to the subject populations they represent (e.g., cognitively impaired participants). Non-scientists may also represent the general perspective of research participants. IRB members with non-scientific status are not assigned primary and secondary reviewer responsibilities.

III. IRB Administrator Responsibilities

- A. The Administrator conducts a pre-review for studies submitted requesting full Committee review. **If the Administrator determines that the study meets criteria for exempt or expedited review, the IRB Chair is consulted for confirmation.**
- B. The Administrator requests any additional documents needed for the review, as well as any pre-review changes. This is documented in the electronic IRB submission and management system.
- C. The Administrator places the new study on the next available Committee agenda and assigns the reviewers.
 - 1. In general, the IRB agenda is limited to 25 items to allow for adequate discussion of each item.
- D. The Administrator assigns reviewers with expertise in the area of the research adequate to the scope and complexity of the research. If the Committee does not have at least one member available with expertise adequate to the scope and complexity of the research, the Administrator assists in arranging review by a consultant with the required expertise.
- E. The Administrator may be asked to arrange for the consultant to attend the Committee meeting. The consultant may not count toward the quorum or vote.
- F. The Administrator gathers the following documents for all Committee Members to review in the electronic IRB submission and management system:
 - 1. A completed IRB Application which includes an Investigator's Assurance statement and disclosure of Investigator's financial interests, confirmed upon submission of the IRB Application,
 - 2. Sponsor's Master protocol, if applicable
 - 3. Proposed informed consent document(s) and/or Study Information sheet and/or script as appropriate;
 - 4. Copies of surveys, questionnaires, or videotapes;
 - 5. Copies of letters of assurance or cooperation with research sites;
 - 6. Investigator's brochure, if applicable
 - 7. Advertising intended to be seen or heard by potential subjects, including e-mail solicitations.
 - 8. DHHS-approved sample informed consent form, if applicable
 - 9. DHHS-approved protocol, if applicable
 - 10. DHHS grant application – human subjects section, if applicable and considered to be in a fundable range
- G. The Administrator and the HRP team monitor quorum status throughout the meeting.
- H. In addition, HRP staff takes notes of discussions of controverted issues, all IRB recommendations, determinations, motions, and votes for each study reviewed during the Committee meeting in accordance with applicable UCI IRB policies and procedures. The minutes of the IRB Committee meeting clearly reflect the determinations regarding risk and approval period (review interval). If a member has a conflicting interest, it is noted in the minutes that a conflict exists and the Committee member was absent during the discussion and vote for that specific research study.
- I. Requests for revisions from reviewers, and approval letters are drafted using the appropriate template.
- J. Amendments, unanticipated problems involving risks to human subjects or others, and renewals are completed per corresponding policies and procedures.

- K. Appropriate electronic IRB submission and management system entries are completed.
- L. Confirmation of applicable Ancillary Partner clearance is noted.
- M. Approved documents are processed and released.

Procedure Number 14.B**Title: Procedure for Initial Application Materials to be Reviewed by the Full IRB Committee****Procedure:**

This procedure outlines the initial application materials to be reviewed by the full IRB Committee in order to make preliminary or final determinations on the approval of the proposed research activities.

I. Lead Researcher (LR) Responsibilities

- A. The following materials are to be provided by the LR in order for the IRB Committee to obtain information in sufficient detail to make the preliminary or final determinations required by the Federal regulations for research approval:
 - 1. A completed IRB application packet which includes:
 - a) A completed IRB Application which includes an Investigator's Assurance statement and disclosure of Investigator's financial interests, confirmed upon submission of the IRB Application. The Department Chair or the Organized Lead Unit Director logs into electronic IRB submission and management system to confirm their "approval" of the submission. (See IRB Policy 1.)
 - 2. Sponsor's protocol and Investigator's brochure, if applicable;
 - 3. Proposed Informed consent documents and/or information sheets and/or scripts, as appropriate;
 - 4. Copies of research instruments (e.g., surveys, questionnaires, videotapes);
 - 5. Copies of letters of cooperation or IRB approval letters for each research site, if applicable;
 - 6. All advertising materials intended to be seen or heard by potential participants, (e.g., email solicitations, TV/radio spots, flyers/brochures).
 - 7. DHHS-approved sample informed consent form, if applicable
 - 8. DHHS-approved protocol, if applicable
 - 9. DHHS grant application – human subjects section, if applicable and considered to be in a fundable range
- B. Investigators will provide the IRB reviewers/staff with additional information as requested.

II. IRB Committee Responsibilities

- A. The materials listed in the Lead Researcher's section of this policy will be distributed to all Committee members via electronic agenda and reviewed by the Primary and Secondary Reviewers for presentation at the full IRB Committee meeting. The materials will be received by members sufficiently in advance (usually seven days) of the meeting date to allow review of the material and the request of additional information, if needed.
- B. If NIH-supported, the IRB Committee must receive and review a copy of the NIH-approved sample informed consent document (ICD) and the full NIH-approved Investigator's protocol as a condition for review and approval of the local ICD. In addition, if any deletions or substantive modification of information concerning risks or alternative procedures

contained in the sample ICD, they must be approved by the IRB Committee.

- C. If a DHHS grant application exists, an IRB member should review the human subjects section of the application, to ensure that the research described in the IRB application is consistent with the grant application. The grant application does not need to be reviewed by every IRB member.

III. **The Human Research Protections (HRP) Team Responsibilities**

- A. The HRP team (Administrator, Sr. Analyst, and Analyst) under the direction of the Administrator will verify that all of the required documents as described in the Lead Researcher's section of this policy have been submitted.
- B. The HRP team will verify that appropriate clearances have been obtained, as applicable (e.g., Department Chair, Ancillary Partners).
- C. Additional requests will be sent via to the LR via the electronic IRB submission and management system.
- D. The HRP team prepares the agenda per applicable procedures.
- E. If study is NIH-supported, any deletion or substantive modification of information concerning risks or alternative procedures contained in the sample ICD must be approved by the IRB Committee and reflected in the IRB Committee minutes.

Policy Number: 15

Title: Research with Human Specimens and Data: Establishment of Specimen/Data Repositories

Date of Last Revision: 5/13/2009, 12/08/10, 06/05/13, 07/31/20, 03/11/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to review and approve the prospective collection of human specimens/data, the use of existing identifiable specimens/data and the establishment of specimen/data repositories for research purposes.

I. IRB Oversight

- A. The UCI IRB is responsible for overseeing the prospective collection and subsequent use, storage, and re-use of all identifiable human specimens/data generated within, transferred to, or transferred from UCI for research purposes.
 - 1. The IRB must review and approve all collection, use, storage, and re-use of identifiable human specimens/data for research purposes.
 - 2. The IRB does not oversee the storage or management of specimens/data collected and stored as part of routine clinical care or hospital procedures.
 - 3. The IRB does not oversee the use or management of specimens/data sent to a UCI Investigator/employee for specialized analysis as part of a contractual agreement.
 - 4. The IRB does not oversee the storage or management of de-identified (stripped of all 18 HIPAA identifiers) specimens/data.
- B. The use of human participants' specimens/data for research can be classified into the following categories:
 - 1. Specimens/data to be collected prospectively for pre-defined research purposes only in connection with a single IRB approved proposal. In most cases, this type of collection would not be appropriate for a "research repository."
 - 2. Specimens/data to be collected prospectively or retrospectively (previously stored), for undefined future research purposes that will be shared, used again, or stored for research purposes beyond the scope of the Researcher's originally approved IRB application. IRB approval to establish a research specimen/data repository is required.
 - 3. Specimens/data to be collected prospectively to add additional samples to an existing specimen/data repository approved by the IRB must seek IRB approval to do so.
- C. Extraction of identifiable or coded specimens/data from a repository will require IRB approval under a specific study protocol.
- D. When specimens/data are included in a repository then extracted as de-identified (stripped of all 18 HIPAA identifiers) for research purposes, the research may meet the definition of "non-human subjects research." (See Policy # 16.)
- E. When specimens/data are included in a repository then extracted as coded specimens, if the recipient of the specimens does not have access

to the key code, the research may meet the definition of “non-human subjects research.” (See Policy # 16.)

F. Examples of Human Participant Specimens for Research:

1. Bodily human materials such as: cells, mucosal and skin; blood; urine; amniotic fluid; excreta and external secretions (including sweat); saliva; sputum; placenta tissue; organs; hair; nail clippings; teeth; dental plaque and calculus; if obtained through “intervention or interaction with an individual” or if “identifiable”; and/or
2. Residual diagnostic human specimens, including specimens obtained for clinical patient care that otherwise discarded if not used for research.

G. Examples of Human Participant Data for Research:

1. Private information such as clinical notes and medical information identifiable to a specific individual, whether or not the information collected is for the research study in question. This also includes private information provided for specific purposes by an individual, which the individual can reasonably expect will not be made public;
2. Data obtained from voice, video, digital or image recordings; and/or
3. Data obtained from surveys, interviews, oral histories, focus groups, program evaluations, quality assurance methodologies, etc.

II. **Establishment of Repositories**

- A. A repository may be established within or outside UCI. There is no single “repository” site or mechanism within UCI.
- B. Repositories may be proposed, built, and maintained by individuals (e.g., Investigators), groups, programs, departments, or institutes. A single Investigator or a group of Investigators may wish to pool research specimens/data from multiple research studies into a single specimen bank or database that could be accessed by the group and others for further use.
- C. Examples of outside repositories that a UCI Investigator may wish to utilize include the National Institutes of Health (NIH), Center for Disease Control (CDC), and National Surgical Adjuvant Breast and Bowel Project (NSABP) laboratories, as well as laboratories managed by colleagues at other academic institutions.

III. **Other Conditions in which an Investigator Should Consider the Establishment of a Repository**

- A. A clinical database created for research intent to collect, maintain and potentially distribute or share the data with other Investigators must prospectively establish a repository prior to the collection of data. The research repository is established through submission and receipt of IRB approval.
- B. Likewise, databases maintained by physicians/Investigators for record keeping of individual patients for research intent must have prospective IRB approval to do so. If data contained in the database will be accessed for multiple projects or by multiple Investigators, IRB approval should be obtained.

IV. **Informed Consent Requirements for the Establishment and Use of a Repository**

- A. Informed consent is required from the participant or his/her legally authorized representative prior to the collection of specimens/data to be deposited and stored in a repository, unless a waiver of informed consent has been granted by the IRB.
- B. The Investigator is required to obtain written informed consent from each participant prior to accessing the repository for his/her proposed research activity when the extracted data will contain personal identifiers. However, the Investigator may in some situations be able to demonstrate that it is truly not practicable to obtain informed consent from individuals who provided the data in years past and request that the IRB grant a waiver of the informed consent.
- C. The Office for Human Research Protections (OHRP) recommends that a Certificate of Confidentiality be sought for repositories, especially for the banking of genetic samples/information (See IRB Policy # 24.). OHRP also recommends inclusion of language in the informed consent document that explains the protections provided by the Genetic Information Nondiscrimination Act of 2008 (GINA).
- D. The Investigator may withdraw data from a repository without any identifiers; in which case, the study may qualify as “non-human research” or meet criteria for exemption from IRB approval and informed consent requirements. However, only the IRB may determine which activities qualify for exempt review.

V. **Medical Center and IRB Policies for Control of All Human Tissue - UCIMC Anatomical Pathology/Surgical Pathology - Procedure Number: S-23** requires that all specimens removed from clinic or the operating room must be sent to pathology for review and documentation by a pathologist, with the exception of specimens specifically listed as exempt (see Section V.D.).

- A. Of non-exempt specimens, only remnants are to be used for research. A remnant is defined as tissue not needed for diagnosis. Only a faculty pathologist may make the determination of whether or not a specimen is to be released for research.
- B. Under no circumstances will tissue bypass pathology from the clinics or the operating room to a research lab.
- C. A pathologist is the only physician authorized to release tissue for research. The determination cannot be made by surgeons or other physicians. The pathologist may determine in some cases that no tissue may be released for research.
- D. Exempt categories are defined as:
 - 1. Specimen that by nature or condition do not permit meaningful examination, such as a cataract, orthopedic appliance, newborn foreskin, bone from degenerative joints, bunions, spinal procedures, or portion of and removed only to enhance operative exposure; menisci, articular cartilage and blood clots.
 - 2. Therapeutic radioactive sources, the removal of which shall be guided by radiation safety monitoring requirements.
 - 3. Traumatically injured members that have been amputated and for which examination for either medical or legal reasons is not deemed necessary.
 - 4. Foreign bodies (for example, bullets) that for legal reasons are given

- directly in the chain of custody to law enforcement representatives.
5. Placentas that are grossly normal as determined by the delivering gynecologist and have been removed in the course of operative and nonoperative obstetrics.
 6. Tonsil and adenoids of patients under age 17.
 7. Stones of visceral organs.
 8. Palmar fibromatoses repair procedures tissue.
- E. Categories 1 and 5 may be exempted from the requirement to be examined by a Pathologist, if special requests are made by surgeon or patient. These specimens require gross examination only. Gross examination includes gross description only. No tissue is submitted for processing. UCI IRB requires documentation from a pathologist granting the special request.
- F. All Investigators who propose to perform research with human tissue must comply with this UCIMC procedure.
- G. IRB policy requires IRB review of all research utilizing participant identifiable specimens or private data, regardless of whether the research is retrospective or prospective (See IRB Policy # 2.).

References:

45 CFR 46

OHRP: Issues to Consider in the Research Use of Stored Data or Tissues, November 1997.

OHRP Guidance on Research Involving Coded Private Information or Biological Specimens,
August 10, 2004.

Genetic Information Nondiscrimination Act of 2008 (GINA)

UCI Department of Pathology and Laboratory Medicine: Anatomical Pathology/Surgical Pathology - Procedure Number: S-23

Procedure Number 15.A

Title: Procedure for Establishment of Specimen/Data Repositories and Extraction of Specimens/Data for Research

Procedure:

This procedure outlines the process for establishing a research specimen/data repository and extracting specimens/data for use in research.

I. Lead Researcher (LR) Responsibilities

- A. LRs who plan to collect specimens/data prospectively for pre-defined research purposes only in connection with a single IRB approved project should submit an IRB Application to the IRB.
- B. LRs who plan to collect specimens/data prospectively or retrospectively (previously stored), for undefined future research purposes that will be shared, used again, or stored for research purposes beyond the scope of the Investigator's originally approved IRB application should submit an IRB Application to the IRB.
- C. LRs who plan to prospectively add to existing specimen/data collections, that have not been established as IRB approved "research repositories", should submit an IRB Application to the IRB.
- D. Informed Consent Documents (ICDs) or requests for a waiver of consent should be completed according to IRB policies and procedures.
- E. Investigators that wish to share samples with other Investigators within or outside UCIMC must set up an IRB-approved Specimen/Data Repository as above.
- F. The Investigator should apply for a Certificate of Confidentiality, when applicable.
- G. The repository should not release specimens/data to an Investigator without receiving written documentation of IRB determination/approval for research using the specimens/data.
- H. The Investigator will comply with all IRB policies and procedures applicable to the collection, use, storage, and re-use of all human specimens/data that are generated within, transferred to, or transferred from UCI for research purposes.

II. IRB Committee Responsibilities

- A. The IRB will determine whether or not the specimens/data can be identified with the participant and whether specimens/data were collected retrospectively or will be collected prospectively.
- B. The IRB will assess the repository to assure that adequate measures have been taken to protect the confidentiality of participants. This review will include:
 - 1. The type of specimens or data to be banked;
 - 2. Whether the specimens/data are identified or coded;
 - 3. Who will have access to the codes that link patient identifying information to the sources of the tissue specimens and what physical and/or IT encryption procedures will be employed to minimize the chance of identifying information being released.
 - 4. What procedures are in place to "de-identify" the specimens/data;
 - 5. Will the collection of specimens/data require interaction with human subjects;

6. Are the specimens/data “on the shelf” at the time the proposal is initiated;
 7. Will informed consent be required;
 8. Who will manage the repository;
 9. How and where the specimens/data will be stored and released; and
 10. What will happen to the specimens/data should the subject withdraw informed consent, or the Investigator should leave UCI.
- C. If a UCI Investigator plans to send any specimens/data to an outside repository for storage that can be traced back to a participant, the UCI IRB may:
1. Request the identification of the Repository as well as a copy of its IRB approval;
 2. Request an external “Data Use Agreement” between the outside Repository and the UCI Investigator; and/or
 3. Request a Certificate of Confidentiality be obtained by the Investigator to assure participant confidentiality if there is not an IRB overseeing an outside repository, or when genetic information or tissue samples are involved.
- D. The IRB will review the informed consent documents to verify the inclusion of the essential elements of consent. In addition, the IRB will review the informed consent document(s) for a description of the storage, use, and release of the specimens/data that will be submitted to the repository.
1. When the repository contains genetic specimens/data, the IRB will verify that the UCI IRB specimen template language has been included within the informed consent documents along with inclusion of language that explains the protections provided by the GINA.
 2. Subjects should be provided the right to withdraw their consent and have their tissue removed from the repository if the specimens are identifiable.
 3. If not already NIH supported, and a Certificate of Confidentiality is applicable, the IRB will recommend that the Investigator apply for a Certificate of Confidentiality. In addition, the IRB will verify receipt of a Certificate of Confidentiality and that a description of this protection is included in the informed consent documents, as well as any Investigator plans for voluntary disclosure.
- E. The IRB may review requests for repositories through expedited review procedures when identifiers are used in the storage and/or release of the specimens/data for research purposes and the research meets a specific review category as outlined in 45 CFR 46.110 (f). If the request for a repository does not meet a specific category as outlined in 45 CFR 46.110 (f), the IRB must review the request by the full Committee.
- F. The IRB may determine that the use of de-identified specimens in storage that will be released for use in research does not qualify as human subjects research.
- G. All reviews will be conducted under the appropriate UCI IRB policies and procedures applicable to the level of review.

III. **IRB Analyst or Higher Responsibilities**

- H. The Analyst will pre-review the IRB Application to assure that it meets the requirements under IRB policies and procedures.
- I. The Analyst will verify that a description of the conditions under which the specimens/data will be stored, utilized and released are adequate, or

request clarification from the Investigator.

- J. Correspondence requesting any pre-review changes may be sent to the LR by the Analyst.
- K. Appropriate database entries in in the electronic IRB submission and management system are completed.
- L. Approved documents are processed.

**University of California, Irvine
Human Research Protections
Standard Operating Policies and Procedures**

Policy Number: 16

Title: Human Subject Research/ Non-Human Subject Research Determination

Date of Last Revision: 06/16/08, 05/15/10, 06/01/10, 10/15/13, 01/28/15, 05/03/21, 03/11/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to assist in determining whether an activity meets the definition of human subject research.

I. Non-Human Subject Research Determinations

- A. An investigator may self-determine that an activity does not represent human subject research.
- B. The electronic IRB submission and management system allows for the investigator to self-determine whether the activity either:
 - 1. Meets the DHHS regulatory definitions of “research” that involves “humans subjects,”
 - 2. Meets the FDA regulatory definition of “clinical investigation,”
 - 3. Is DOE funded or DOE laboratory managed and involves intentional modification of an individual’s or a group of individuals’ environment. For example, by installation of devices in homes and/or through the introduction of gases/ chemicals to trace airflow in occupied residential, commercial or public settings. Generalizable also includes studies in human occupied homes or offices that manipulate the environment to achieve research aims or test new materials. Further, collection of an occupants’ views of appliances, materials or devices installed in their homes via survey would constitute “Human Subject Research.”
 - a) Generalizable should be interpreted in terms of contributing to knowledge within the specific field of study.
- C. The investigator must submit the determination of non-human subject research in order to receive written confirmation which is provided via email from the electronic IRB submission and management system.
- D. If the activity does not represent human subject research the activity does not require IRB approval and oversight.
- E. HRP Staff will monitor the electronic IRB submission and management system by performing quarterly assurance to confirm that the activity qualifies as non-human subject research.

II. Non-Research Activities

- A. Activities are not research if they do not involve a systematic approach involving a predetermined method or a plan for studying a specific topic, answering a specific question, testing a specific hypothesis, or developing theory. A systematic approach incorporates collection of data, either quantitative or qualitative, or specimens; and analysis.
 - 1. Examples of activities that would not normally be considered systematic investigations include, but are not limited to:

- a. Training activities (e.g., individuals being trained to perform a certain technique or therapy such as art therapy, psychoanalysis, oral history techniques); and
 - b. Classroom activities involving human participants or human participant data where the objective of the activity is to teach proficiency in performing certain tasks or using specific tools or methods.
 - c. Case reports or case series of three or less individuals.
- 2. Examples of systematic investigations include, but are not limited to:
 - a. Observational studies;
 - b. Interviews (including those that are open-ended) or survey studies;
 - c. Group comparison studies;
 - d. Test development;
 - e. Program evaluation; or
 - f. Clinical investigations.
- B. Activities are not research if they do not intend to contribute to generalizable knowledge or to draw general conclusions (i.e., knowledge gained from a study may be applied to populations beyond the specific study population), inform policy, or generalize findings.
 - 1. Examples of activities that are typically not generalizable include:
 - a. Biographies and service or course evaluations, unless they can be generalized to other individuals;
 - b. Oral history activities in general which are solely designed to create a record of specific historic events;
 - c. Data collection for internal department, school, or other University administrative purposes (e.g., teaching evaluations, “customer service” surveys);
 - d. Classroom activities designed specifically for education or teaching purposes, where the data is collected from and about human subjects a part of a class exercise or assignment that is not intended for use outside of the classroom;
 - e. Quality Improvement activities designed to continuously improve the quality or performance of a department or program or health care; and
 - f. A Case Report or a write up of up to three patients. The Case Report or write up must specifically describe medical care (i.e., not research related care) and outcomes from treatment provided solely as part of the patient’s clinical care.
 - 2. Thesis or dissertation projects conducted to meet the requirements of a graduate degree are usually considered generalizable and therefore, require IRB review and approval.
 - 3. Refer to the 2018 revised Common Rule for examples of what does not meet the definition of ‘research.’

III. Non-Human Subject

- A. Activities **do not involve** humans as participants if they **do not involve** the following definition:
 - 1. *Human subject* means 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.
- B. Examples of activities that would not normally involve human subjects if the research is about things or expertise, rather than “about whom” (i.e., questions are not about the individual providing the information).
- C. Information is considered “not identifiable” if it does not include the following:
 - 1. Name;
 - 2. Any geographic subdivisions smaller than a state, including street address, city, country, precinct, ZIP code, and their equivalent geocodes, except for the initial three digits of a ZIP code;
 - 3. All elements of dates (except year) directly related to an individual (e.g., date of birth, admission);
 - 4. Telephone numbers;
 - 5. Fax numbers;
 - 6. Electronic mail addresses;
 - 7. Social security numbers;
 - 8. Medical record numbers;
 - 9. Health plan beneficiary numbers;
 - 10. Account numbers;
 - 11. Certificate/license numbers;
 - 12. Vehicle identifiers and serial numbers, including license plate numbers;
 - 13. Device identifiers and serial numbers;
 - 14. Web Universal Resource Locators (URLs);
 - 15. Internet Protocol (IP) address numbers;
 - 16. Biometric identifiers, including finger and voiceprints;
 - 17. Full-face photographic images and any comparable images; and
 - 18. Any other unique identifying number, characteristic, or code.
- D. Specimens/data that are received by the Investigator as de-identified (i.e., stripped of all HIPAA identifiers as noted above).
- E. When the Investigator receives private information or specimens with no code or link that would allow an Investigator to establish identity, this would not involve human subjects. For example, a publicly available, unidentifiable, non-linked dataset qualifies as not involving human subjects.
- F. The Investigator may receive coded private information or specimens and qualify for non-human subject if the following conditions are met:
 - 1. The code is not derived or related to the HIPAA identifiers that must be stripped from the PHI (e.g., patient MR# + last 4 digits of individuals Social Security Number);
 - 2. The private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; **and**

3. The Investigator cannot readily ascertain the identity of the individuals to whom the coded private information or specimens pertain, because:
 - a. The key to decipher the code is destroyed before the research begins;
 - b. The Investigator and the holder of the key enter into an agreement prohibiting the release of the key to the Investigator under any circumstances, until the individuals are deceased;
 - c. The private information is received from an IRB-approved repository or data management center that includes written operating procedures that prohibit the release of the key to the Investigator under any circumstances, until the individuals are deceased; or
 - d. There are other legal requirements prohibiting the release of the key to the Investigator until the individuals are deceased.
- G. An activity only involving analysis of a Limited Data Set (LDS) (a set of data that lacks 16 of the 18 identifiers itemized by the privacy rule) provided by a third party would not involve human subjects. An LDS may contain dates and certain geographic information associated with an individual that would be absent of identifiable information. Information provided by a third party may include the following:
 - a. 5-digit zip code (4-digit extension is not allowed)
 - b. Full dates of birth or death
 - c. Full date(s) of service (admission and discharge)
 - d. Geographic subdivision (other than street address)
- H. A cadaver is not considered to be a human subject.
- I. Notable exception to non-human subject: In-vitro Device (IVD) studies using human tissue specimens while exempt from most provisions of 21 CFR part 812(c)(3), qualify as clinical investigations and are therefore subject to FDA 21 CFR parts 50 and 56, even if the clinical investigation involves de-identified, leftover tissue specimens.

IV. **Amendments**

Changes that might disqualify the activity from its “Non-Human Subject Research” status should be reported to the IRB for review and verification prior to implementation.

- V. All “Non-Human Subject Research” is subject to applicable institutional policies and procedures.

References:

45 CFR 46
 21 CFR 50
 21 CFR 56
 21 CFR 812
 32 CFR 219 (DoD)
 28 CFR 512 (DOJ)
 OHRP Guidance on Research Involving Coded Private Information or Biological Specimens,
 August 10, 2004
[DOE Human Subjects Protection Program](#)

[HRP Policy # 2](#)

Procedure Number: 16.A

**Title: Procedure Human Subject Research/Non-Human Subject Research
Determination**

Procedure:

This procedure provides guidance for the determination of non-human subject or non-research projects.

I. Investigator Responsibilities

- A. Investigators should review the non-human subject research confirmation module in the electronic IRB submission and management system. The portal is located on the HRPP website. To receive an email of confirmation, the Investigator must submit the non-human subject confirmation module.
- B. Investigators must inform the HRP staff, or the IRB of any proposed changes might disqualify an activity from its “non-human subject research” status.

II. HRP Staff

- A. Under the EQUIP program or as requested by HRP Senior Management, the IRB Chair or designee, HRP Staff will monitor the electronic IRB submission and management system by performing quarterly assurance to confirm that the sampled activities qualify as non-human subject research.
- B. Where activities do not qualify as non-human subject research, HRP Staff will provide follow up in accordance with HRP Policy.

University of California, Irvine
Human Research Protections
Standard Operating Policies and Procedures

Policy Number: 17

Title: Amendments to Previously Approved or Registered Research

Date of Last Revision: 08/10/05; 08/23/10; 05/01/13, 06/05/13, 04/23/15, 07/21/15, 08/05/15, 03/05/16, 05/01/16, 10/1/18, 11/13/19, 04/29/20, 08/27/20, 02/23/22, 03/23/22, 09/13/22, 12/05/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to review all requests for amendments to previously approved research projects to determine if a change in the risk/benefit ratio of the study has occurred.

Research activities in which the only involvement of human subjects will be in one or more of the categories specified under 45 CFR 46.104 (d) are exempt from the requirements of the basic Health and Human Services Policy for the Protection of Human Research Subjects (Subpart A). As such, for research confirmed as exempt by the UCI IRB, minor changes may be made without prospective IRB review and approval.

In addition, for specific types of research self-confirmed via the Exempt Self Determination Tool in the electronic IRB submission and management system, changes may also be made without prospective IRB review and approval.

- I. Amendments: For previously IRB approved or IRB confirmed research all planned changes in the conduct of a study and/or changes to the informed consent document must be approved by the IRB prior to initiation. Exceptions for exempt research are noted below in Section F.
- II. In addition, the addition and removal of research personnel is no longer required to be submitted to the IRB as an amendment unless the role of the research personnel mandates accordingly. See Section G below.
 - A. The Investigator may make an amendment to research activities to avoid an immediate hazard to the participant but must report this to the IRB via the New Information reporting process, as applicable (See Policy # 19).
 - B. Investigators must submit the amendment request along with revisions to the research protocol and any proposed changes to the consent document or other documents to the IRB.
 - C. Amendments to the previously approved research must meet the regulatory criteria for approval when one or more regulatory criteria are affected.
 - D. Full Committee Review: Amendments that do not meet the criteria for expedited review must be reviewed by the Full Committee at a convened meeting. **Table 1 provides examples of types of amendments that may qualify for full committee review.** The decision to send an amendment request to the full committee is based on the impact to the risk / benefit ratio and is made with IRB Chair's discretion, based on their expertise.

- E. Expedited Review: Amendments that meet the criteria for expedited review will be reviewed by a Chair, designated IRB subcommittee, or an HRP Staff Reviewer according to the expedited review procedures. **Table 1 provides examples of types of amendments that may qualify for an expedited review process.**
- F. Exempt Protocols: Research activities in which the only involvement of human subjects will be in one or more of the categories specified under 45 CFR 46.104 (d) are exempt from the requirements of the basic Health and Human Services Policy for the Protection of Human Research Subjects (Subpart A). Minor changes may be made without prospective IRB review and approval.
1. **Examples of minor changes to exempt research: Do NOT submit an amendment to the UCI IRB when:**
 - a. Making editorial or administrative revisions to consent documents or other study documents
 - b. Adding non-sensitive questions to a survey or interview or revising current questions
 - c. Adding a new recruitment material that follows IRB guidelines
 - d. Increasing or decreasing the number of participants - unless adding a new population as noted below**
 - e. Making study team/personnel changes - except a change in Lead Researcher (LR)
 2. **Examples of significant changes to exempt research: DO submit an amendment to the UCI IRB when:**
 - a. Adding a new population as follows:
 - i. A targeted recruitment of children
 - ii. A targeted recruitment of adults (age 18 or older) who may not be legally/mentally/cognitively competent to consent
 - iii. A targeted recruitment of prisoners
 - iv. A targeted recruitment of American Indian/Alaska Native tribes
 - v. A targeted recruitment of undocumented people
 - b. Adding non-UCI personnel engaged in research: a) intervening or interacting with the participants and/or b) having access to participant identifiable private information for research purposes.
 - c. Adding an international research site
 - d. Adding questions about sensitive aspects of the participants' behavior such as illegal conduct, drug use, sexual behavior or use of alcohol – to a survey or interview
 - e. For a change in study LR
 - f. To disclose a new financial interest
 - g. When adding Department of Justice (DOJ) funding
 - h. For any change that makes the study no longer eligible for Certification of Exemption (study will require expedited or full committee review)
 3. For research self-confirmed via the Exempt Self Determination Tool, changes that do not impact the level of review (such that the study no longer meets the exempt self-determination categories) may be made without prospective IRB review and approval.

- G. Research Personnel: Only list those research personnel in the IRB Application who may be involved in the following tasks. The Lead Researcher is required to maintain the Study Team log or something similar to track Research Personnel independently. Prior to engaging in human subject research, all Research Personnel must complete the applicable CITI human subject training course, including HIPAA if research involves PHI.

Research Personnel Heat Map

Role of Research Personnel ¹	Minimal Risk Protocol	Greater Than Minimal Risk Protocol
Access to subject identifiable data including Protected Health Information (PHI) for screening/ determining eligibility	<p>List only the Lead Researcher (LR) and Co-Researcher(s) in the UCI IRB Application. The LR is required to <u>maintain a Study Team log</u> or something similar to track Research Personnel independently.</p>	
Recruiting subjects directly via phone, email or in person		
Access to subject identifiable data which may include PHI for data collection purposes		
Involvement in the informed consent process (i.e., explaining the study to prospective subject)		
Performing research procedures that involve greater than minimal risk		
Involvement in the interpretation of study data		
Finalization of the informed consent process (i.e., able to sign off as the individual obtaining consent)	<p>List the LR, Co-Researcher(s) and Research Personnel in the UCI IRB Application.</p>	
Has a <u>disclosable financial conflict of interest</u>		

When using the Research Personnel Heat Map, the assumption is that Research Personnel are *engaged in human subject research* as per the [OHRP Engagement in Human Subject Research](#) document.

III. Types of Amendments

A. Minor Amendments:

- Minor amendments may be reviewed by experienced IRB Committee Chair, designated IRB subcommittee, or an HRP Staff Reviewer.
- Delegation is provided in the HRP Staff Reviewer Delegation of Authority document maintained on the HRP WIKI page – and signed by the IRB Chairs for A, B, C, and Vice- Chair for Team D.
- An HRP Staff Reviewer is defined as follows:
 - Tier 1:** Administrator or above, CIP certified and appointed as IRB members or alternate members. Exceptions are noted as applicable.
 - Tier 2:** Analysts or above, CIP certified. Those without current CIP have been designated by an IRB Chair, Director or Assistant Director of Human Research Protections to have the appropriate experience to review minimal risk protocols. Exceptions are noted as applicable.
- An HRP Staff Reviewer (**Tier 1** or **Tier 2**) may review amendments **except under the following conditions:**
 - Authority examples and exceptions are summarized below and further delineated in Table 1b.
 - IRB Committee Chair or Designated IRB Subcommittee Must Review:

- i. Changes that are exceptions as noted in Policies #12 and #13
 - ii. For protocols approved as involving greater than minimal risk:
 - iii. Changes involving vulnerable populations
 - 1. Changes involving FDA-regulated research activities
 - 2. Adding new procedures
 - 3. Adding a new study site
 - 4. Adding questions about *sensitive aspects of the subjects' behavior and health status (e.g., Hepatitis/HIV status, illegal behavior, abuse, alcohol/drug use, sexual behavior, or use of alcohol – to a survey or interview*
 - 5. Disclosure of a new financial interest
 - 6. Change in LR or FS or a member of the study team who holds a critical role in the study
 - 7. Addition of newly-identified risk
 - 8. Changes to consent process
 - 9. Changes to compensation plan
- 5. Examples of Acceptable Amendments to be reviewed by designated reviewers:
 - a. Adding or removing research personnel (See Policy # 17, Section II. G. above)
 - b. Fixing typographical errors or minor word changes to study documents
 - c. Revisions to or adding data collection instruments
 - d. Adding new recruitment materials
 - e. Increasing or decreasing the number of subjects
- 6. For protocols approved as involving greater than minimal risk, proposed changes:
 - a. Do not increase risk to subjects;
 - b. Constitute a minor change to previously approved research; and
 - c. Involve procedures that fall within Exempt categories 1 – 6 or Expedited categories 1 - 7.
 - d. Authority examples and exceptions are summarized in Table 1b below.

B. Major Amendments:

When a proposed change in a research study does not constitute a minor amendment, the IRB must review and approve changes at a convened meeting (See Procedure # 14.A).

- C. The IRB will determine that any significant new findings that arise from the review process that might be related to participants willingness to continue participation are provided to participants.

- D. **Special Composition Requirements for Vulnerable Populations**
 When a study requires review by the full IRB Committee, it must meet special composition requirements (See IRB Procedures # 36.A, 37.A, 38.A, 39.A, and 40.A) when conducting reviews of amendments.

E. **Re-consent/Notification of Participants**

The IRB will render a determination of whether the changes to the research activities constitute significant new findings that might relate to participants' willingness to continue participation. The IRB will also assess how currently enrolled participants will be informed of the new findings (e.g., change in the ICDs) and, if and how participants who have completed research interventions should be notified.

References:

21 CFR 56.110(b)(2)

45 CFR 46.110(b)(2)

Procedure Number 17.A**Title: Procedure for Amendments to Previously Approved or Registered Research****Procedure:**

This procedure provides guidance for submission, review and approval of amendments to previously approved or registered research projects.

I. Lead Researcher (LR) Responsibilities

- A. The LR will complete the electronic amendment application and explain the requested change along with a justification for the change. All revisions must be incorporated into any applicable, corresponding documents such as the informed consent document (ICD). Changes to the documents should be underlined or highlighted.
- B. If, in the LR's opinion, the risk/benefit ratio has changed, such that it constitutes a significant change that might affect a subject's willingness to participate, the LR should provide a revised ICD to re-consent currently enrolled participants. The IRB Committee may also request re-consenting of the participants.
- C. Except as outlined in the current Policy # 17, Section 1E, any proposed or anticipated changes in UCI confirmed exempt research must also be submitted to the IRB for approval prior to initiation of the change. The research will then be evaluated for appropriate IRB review.
- D. When the LR makes changes to avoid an immediate hazard to the participant, the LR completes an electronic New Information Report. The Investigator is required to submit the form to the IRB in accordance with IRB Policy # 19.

II. IRB Committee Responsibilities

- A. The IRB Chairperson, designated IRB subcommittee, or HRP staff Reviewer may review and approve research that meets the definition of a minor amendment (see Procedure # 13.A).
- B. When a proposed change in a research study represents a significant amendment, the full IRB Committee must review and approve the changes. Only one Reviewer is required for review of significant amendments. The Reviewer and Committee members will receive via access to the electronic IRB submission and management system:
 - 1. The Amendment,
 - 2. All revised documentation highlighted or underlined including the revised informed consent document, if applicable,
 - 3. The Sponsor Protocol, if applicable,
 - 4. The last approved Investigator's Brochure, if applicable,
 - 5. Any additional pertinent material (e.g., questionnaires, advertisements, Data Safety Monitoring Board Reports (DSMB) reports, DHHS-grant application, etc.),
 - 6. Regulatory resources such as the criteria for IRB approval.
- C. The IRB Committee must determine whether the regulatory criteria for approval are met when the amendment impacts one or more regulatory criteria.
- D. The IRB will determine that any significant new findings that arise from the review process and that might be related to participants' willingness to continue participation are provided to participants. When considering notification regarding significant new findings that arise from the review process, the IRB must take into account the prospective participants, participants enrolled in the study and, if applicable, participants who have completed the research.

III. Human Research Protections (HRP) Team Responsibilities

- A. Conducts a pre-review to determine whether the application includes all information required and requests additional information, if needed, from the LR, to assist the Reviewer in making a determination.
- B. Determine if the amendment reflects a significant or minor change.
- C. Changes meeting the criteria for minor amendments are reviewed and approved by the IRB Chairperson, designated IRB subcommittee, or an HRP Staff Reviewer.
- D. Changes meeting the criteria for a significant amendment are prepared for full IRB Committee review, placing the study on the next available Committee agenda, and preparation of materials for the Reviewer and Committee members.
- E. Requests for information will be sent via to the LR via the electronic IRB submission and management system.
- F. When consultants to the IRB are utilized, obtain a signed Consultant's standards document which includes a description of Disclosable Conflict of Interest and a statement of confidentiality.
- G. Assembles and prepares for distribution of review materials.
- H. Draft correspondence from the Reviewer and approval letters using the appropriate template which includes a citation to the specific permissible category or categories justifying the expedited review.
- I. Amendments are processed according to corresponding IRB policies and procedures.
- J. Appropriate database entries in the electronic IRB submission and management system are completed.
- K. Approved documents are processed.

I. Table 1a – Review of amendments submitted for expedited studies (and exempt when applicable)

Amendment Type	Reviewed by ____ (or above)	Example	Exceptions
Minor Change	HRP STAFF REVIEWER: Tier 2	Adding or removing research team personnel (See Policy # 17, Section II. G. above)	
Minor Change	HRP STAFF REVIEWER: Tier 2	Minor non-administrative wording changes in the approved consent form, recruitment materials, or other documents. For example, minor changes to <i>time commitment</i> , and <i>location</i> .	
Minor Change	HRP STAFF REVIEWER: Tier 2	Changing study documents such as surveys, questionnaires or brochures including removing questions or components of a survey/questionnaire, addition of questions or components to a survey/questionnaire that are similar in nature to existing components.	When vulnerable populations are targeted enrollees the amendment must be reviewed by the Tier 1 or IRB MEMBER .
Minor Change	HRP STAFF REVIEWER: Tier 2	Adding new recruitment materials.	
Minor Change	HRP STAFF REVIEWER: Tier 2	Increasing or decreasing maximum or target sample size.	
Minor Change	HRP STAFF REVIEWER: Tier 2	Adding study sites (which may require a Federal Wide Assurance (FWA) and appropriate IRB approval) or the removal of study sites.	
Minor Change	HRP STAFF REVIEWER: Tier 2	Decreasing the number or volume of biological sample collections, provided that such a change does not affect the collection of information related to safety evaluations.	
Minor Change	HRP STAFF REVIEWER: Tier 2	New study documents to be distributed to or seen by subjects that include information or questions that are substantively different from materials already approved by the IRB.	
Minor Change	IRB MEMBER	New or revised financial conflict of interest management plans.	
Minor Change	IRB MEMBER	An increase in risk to subjects not previously disclosed as part of the IRB approved study materials	

Amendment Type	Reviewed by — (or above)	Example	Exceptions
Major Change	HRP STAFF REVIEWER: Tier 2	Changing study documents such as surveys, questionnaires or brochures including removing questions or components of a survey/questionnaire where the new questions would reasonably place subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing if the answers became known outside of the study context.	

II. Table 1b – Review of amendments submitted for greater than minimal risk studies

Amendment Type	Reviewed by ____ (or above)	Example	Exceptions
Minor Change	HRP STAFF REVIEWER: Tier 2	Minor non-administrative wording changes in the approved consent form, recruitment materials, or other documents. For example, minor changes to <i>time commitment</i> .	Addition of new study sites must be reviewed by the IRB MEMBER .
Minor Change	HRP STAFF REVIEWER: Tier 2	Changing study documents such as surveys, questionnaires or brochures including removing questions or components of a survey/questionnaire, addition of questions or components to a survey/questionnaire that are similar in nature to existing components.	When vulnerable populations are targeted enrollees, the amendment must be reviewed by the IRB MEMBER .
Minor Change	HRP STAFF REVIEWER: Tier 1	Adding or removing research team personnel (See Policy # 17, Section II. G. above)	Change in LR or FS or a member of the study team who holds a critical role in the study (e.g., removal of a co-researcher who is performing a critical study assessment, etc.) must be reviewed by an IRB MEMBER (expedited).
Minor Change	IRB MEMBER	Adding new recruitment materials.	
Minor Change	IRB MEMBER	Increasing or decreasing maximum or target sample size.	
Minor Change	IRB MEMBER	Adding study sites (which may require a Federal Wide Assurance (FWA) and appropriate IRB approval) or the removal of study sites.	
Minor Change	IRB MEMBER	Minor changes specifically requested by the Conflict of Interest Oversight Committee (COIOC); Institutional Biosafety Committee (IBC); or other University Committees with jurisdiction over the research.	
Minor Change	IRB MEMBER	Changes in inclusion/exclusion criteria.	

Amendment Type	Reviewed by ____ (or above)	Example	Exceptions
Minor Change	IRB MEMBER	Altering the dosage form (e.g., tablet to capsule or oral liquid) of an administered drug, provided the dose and route of administration remain constant.	
Minor Change	IRB MEMBER	Decreasing the number or volume of biological sample collections, provided that such a change does not affect the collection of information related to safety evaluations.	
Minor Change	IRB MEMBER	Decreasing the length of hospitalization or number of study visits, provided that such a decrease does not affect the collection of information related to safety evaluations.	
Major Change	IRB MEMBER	New study documents to be distributed to or seen by subjects that include information or questions that are substantively different from materials already approved by the IRB.	
Major Change	IRB MEMBER	New or revised financial conflict of interest management plans.	
Major Change	IRB MEMBER	An increase in risk to subjects not previously disclosed as part of the IRB approved study materials.	
Major Change	IRB MEMBER	Changing study documents such as surveys, questionnaires or brochures including removing questions or components of a survey/questionnaire where the new questions would reasonably place subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing if the answers became known outside of the study context.	
Major Change	IRB MEMBER	Add Relying Sites.	

Policy Number: 18

Title: IRB Continuing Review and Calculating the Expiration Date

Date of Last Revision: 08/07/07, 01/29/09, 08/30/10, 06/05/13, 04/21/15, 09/01/15, 03/03/16, 06/01/16, 02/28/18, 03/08/18, 01/24/19, 03/26/22, 09/13/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) that research activities be periodically reviewed at intervals appropriate to the degree of risk.

I. Types of Review

A. Review by Full Committee

1. Research protocols initially reviewed by the full convened IRB Committee are reviewed by the full Committee at continuing review unless the study has been modified such that it can be reclassified as eligible for expedited review, as defined in the Federal regulations (See IRB Policy # 13).
2. Research activities that previously met criteria for exempt or expedited review may change such that full Committee review would be required. This change in review criteria is prompted at the time of continuing review or review of a modification.
3. When conducting continuing review at a full IRB Committee, only one Reviewer is required. The Renewal Application including a description of any amendments previously approved by the IRB, informed consent documents, and any monitoring or audit reports conducted since the last review are evaluated by the assigned Reviewer. The full, convened IRB Committee discusses the protocol and makes a determination with a recorded vote (Per Policy # 8).

B. Expedited Review

1. When conducting research under an expedited review procedure, the IRB Committee Chair or designated IRB subcommittee or HRP Staff Reviewer conducts the review on behalf of the full IRB Committee.
2. Research protocols that were originally reviewed using expedited review procedures may receive continuing review on an expedited basis, unless previously met criteria has changed since the last IRB review and approval.
3. Abbreviated Renewal: Research protocols that are eligible for an extended IRB approval (e.g., no more than minimal risk, not subject to federal oversight and not subject to the UCI Conflict of Interest Oversight Committee (COIOC)) review will undergo an abbreviated version of the Renewal Application. The abbreviated Renewal prompts the LR to confirm currently registered information about the research, as well as the status of enrollment. The LR can upload any relevant documents that the study team may want reviewed.
4. Research protocols that were originally reviewed by the full, convened IRB Committee but currently meet the following criteria may receive expedited review by the IRB Committee Chair or designated IRB subcommittee (excluding an HRP Staff Reviewer):

- a. The research is permanently closed to the enrollment of new participants; and
 - b. All participants have completed all research-related interventions; and
 - c. The research remains active only for long-term follow-up of participants; or
 - d. No participants have ever been enrolled at UCI and no additional risks have been identified; or
 - e. The remaining research activities are limited to data analysis.
- C. Exempt Research Activities
- 1. Exempt confirmation may be granted for no more than three (3) years. An abbreviated version of the Renewal may be submitted to continue the research.

II. **IRB Continuing Review Criteria**

- A. A continuing review process must be substantive and meaningful. The approval criteria for continuing review (including the abbreviated Renewal) are the same as that for initial review (See IRB Policies # 13 and 14 for details). Therefore, it is the responsibility of the IRB to determine that:
 - 1. Risks to subjects continue to be minimized and reasonable in relation to the anticipated benefits;
 - 2. Selection of subjects continues to be equitable;
 - 3. Informed consent continues to be appropriately obtained and documented;
 - 4. There are significant new findings that might relate to participants' willingness to continue participation and whether they were/should be provided to participants;
 - 5. Adequate provisions for monitoring the data collected to ensure the safety of the subjects is provided, when appropriate;
 - 6. Adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data, is provided, when appropriate; and
 - 7. Appropriate safeguards for vulnerable populations are provided.
- B. The IRB will determine the need for verification from outside sources on a case-by-case basis and according to the following criteria:
 - 1. Complex protocols involving unusual levels or types of risks to participants;
 - 2. Protocols conducted by Lead Researchers who previously have failed to comply with Federal regulations or the requirements or determinations of the IRB; and/or
 - 3. Protocols where concern about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports or from other sources.
- C. To allow adequate time for IRB review and to avoid any unnecessary delays, the Lead Researcher (LR) submits an electronic Renewal Application to the IRB preferably 60 days for full Committee and 30-45 days for Expedited or Exempt prior to the IRB expiration date. The Renewal includes a status report on the progress of the research, including confirmation of or an explanation relating to the following:
 - 1. The current status of enrollment;

2. No changes have been made without prospective UCI IRB review and approval;
3. There have been no Unanticipated Problems or subject complaints that require reporting to the UCI IRB;
4. ClinicalTrials.gov registration status, as applicable;
5. The maximum number of participants approved by the UCI IRB to be consented for the life of the study;
6. The total number of participants consented since the previous IRB continuing approval;
7. The total number of participants consented to participate to date (this figure includes any withdrawals by participant, LR or sponsor or screen failures – including the reasons for withdrawal);
8. The total number of participants consented to participate to date breakdown by gender (if collected) and by age group (e.g., adults, minors);
9. A detailed description of the progress of the study, including a brief summary of any interim findings or trends, and plans for the next approval period;
10. There is no new information relating to the circumstances of consent that may raise concern for subjects;
11. All new findings that have developed since the last continuing review have been provided to subjects, as appropriate and applicable;
12. The research team is using the most recently IRB approved consent documents;
13. All signed consent documents are on file and available for inspection;
14. Specificity if any subjects were enrolled using a non-English consent document, including the language in which the subject was consented;
15. Any internal and/or external audits;
16. Any recent relevant literature;
17. Specificity if there has been a change in risk / benefit assessment;
18. Any Data and Safety Monitoring reports;
19. Current version of Investigator's Brochure;
20. Specificity if there has been a change in the financial interests of researchers;
21. Any other relevant information, especially that may impact the risk/benefit ratio (including multi-center reports or other progress reports);
22. In addition, the LR may provide the following documentation as applicable:
 - a. Most recent Data Safety Monitoring Board report and/or most recent group-wide progress report, if available.
 - b. *DHHS-funded studies only* – latest version of the DHHS grant application.
23. HRP staff will ensure the following are available for IRB review:
 - a. The current IRB Application;
 - b. The current IRB approved informed consent documents;
 - c. Any Unanticipated Problems involving risks to participants or others that occurred over the last approval period.
24. Informed Consent Documents (ICDs) - Review of the currently approved ICD must ensure that the information is still accurate and

complete. Any significant new findings that may relate to the participant's willingness to continue participation should be provided to the participant in an updated ICD. Review of currently approved or proposed ICDs occur during the scheduled continuing review of research by the IRB but may be done more frequently if new information becomes available.

- D. For minimal risk studies that are not subject to FDA or DOJ regulations and currently have IRB approval for 3 years or more, the renewal includes confirmation of or an explanation relating to the following:
 - 1. Current status of subject enrollments
 - 2. There have been no Unanticipated Problems or subject complaints that require reporting to the UCI IRB;
 - 3. If there have been any subject complaints that require reporting
 - 4. A confirmation that the research team is using the most recently approved version of the consent/assent document and that it contains the most accurate, up-to-date information about the research
- E. Amendments to Protocol may be submitted at Time of Continuing Review
Amendments or revisions to a research protocol may be submitted at the time of continuing review. The Amendment and Renewal Application are reviewed together and receive one IRB determination. As such, the LR should use discretion to ensure that the changes to the IRB Application are minimal in that they do not impact the continuing review process.

III. **IRB Approval of Continuing Review**

- A. The IRB conducts continuing review of all research proposals at intervals appropriate to the degree of risk.
 - 1. Full Committee Review. Research that meets the criteria for full Committee review is reviewed within one year of the date of the full, convened IRB meeting at which the research was approved (or required specific minor modifications).
 - 2. Expedited Review. Research that meets the criteria for expedited or exempt review is reviewed within one year of the date that approval was granted by the IRB Chair or designated IRB subcommittee – with the following exception.
 - a) Extended 3 Year IRB Approval: (See Policy # 13.)
 - 3. Exempt Review: (See Policy # 12.)
- B. Research may be restricted, amended, or halted altogether based on continuing review by the IRB Committee. A determination of “minor revisions required” or “tabled for re-review” is given to all studies in which the IRB requests changes to current documents during Continuing Review. IRB approval is not granted until all requested changes to previously approved documents are completed by the Investigator, or by the HRP administrative staff, and reviewed and approved by the IRB. This does not extend the expiration period.
- C. Based on the IRB continuing review, previously imposed restrictions may be relaxed or additional restrictions may be imposed.

IV. **Expiration of IRB Approval**

- A. There is no grace period extending the conduct of the research beyond the expiration date of IRB approval. The study expires at midnight of the date specified on the approval letter and the informed consent document.

- B. If the IRB does not re-approve the research by the specified expiration date, study activities must cease, pending re-approval of the research by the IRB.
- C. Once notified of the expiration, if the Investigator feels that stopping ongoing research-related interventions or interactions would jeopardize the rights or welfare of current subjects, the Investigator must immediately submit to the IRB Chair or IRB Vice-Chair or their designee(s) a request to continue to treat active subjects. The request must include an explanation of how discontinuing the research subjects from the protocol would cause harm.
- D. The IRB Chair or IRB Vice-Chair or their designee(s) review the request and allows individual subjects to continue participating in the research interventions or interactions only when the IRB determines that it is in their best interests. However any information collected during the lapse in approval may not be used for research.
- E. Enrollment of new subjects cannot occur after the expiration date.

References:

45 CFR 46.109(e)

45 CFR 46.110

OHRP Guidance on Continuing Review, July 11, 2002

21 CFR 56.109

21 CFR 50.25(b)(5)

Procedure Number 18.A**Title: Procedure for IRB Continuing Review****Procedure:**

This procedure outlines the requirements for continuing review of previously approved human subjects research by the UC Irvine (UCI) Institutional Review Board (IRB).

I. Lead Researcher (LR) Responsibilities

- A. The LR completes the Renewal Application.
 - 1. The Investigator verifies all information contained within the Renewal, submitting corrections as needed.
 - 2. The LR completes and electronically submits the Renewal Application and all applicable documentation preferably 60 days for full Committee and 30-45 days for Expedited prior to the IRB expiration date to allow adequate time for IRB review and to avoid any unnecessary delays or lapse in approval.
- B. Continuing review of ongoing research is required until the criteria for study closure apply. (See Policy # 20.) The study may be closed via the Renewal Application.
- C. If a study expires, the LR will cease all research activities as instructed in the expiration notice. The LR should immediately submit a Renewal Application with the required documentation to continue the research or notify the IRB of study closure.
- D. If stopping ongoing research-related interventions or interactions would jeopardize the rights or welfare of current subjects, the Investigator must immediately submit to the IRB Chair or Vice-Chair a request to continue to treat active subjects. The request must include an explanation of how discontinuing the research subjects from the protocol would cause harm.

II. IRB Committee Responsibilities

- A. Review Criteria
 - 1. All continuing review determinations are completed using the criteria found in 45 CFR 46.111 and 21 CFR 56.111 for approval of research. The Primary Reviewer documents the review of criteria via the final version of the IRB Application, approved by the IRB.
 - 2. Research activities initially reviewed by the full IRB Committee are again reviewed by the full IRB Committee (See IRB Policy # 14 and IRB Procedure 14.A), unless:
 - a. The study has been modified and is now eligible for expedited review as defined in the regulations (e.g., change in risk to minimal); or
 - b. The study meets one of the following expedited review criteria:
 - (1) The research is permanently closed to the enrollment of new participants; and
 - (2) All participants have completed all research-related interventions; and
 - (3) The research remains active only for long-term follow-up of participants; or
 - (4) No participants have ever been enrolled at any site and no

additional risks have been identified; or

(5) The remaining research activities are limited to data analysis.

3. Research activities that were originally reviewed using expedited criteria may receive continuing review on an expedited basis unless the research activities no longer meet the expedited criteria for review and approval.
4. Research activities that had previously met criteria for expedited review may change with the review and approval of modifications, such that full IRB Committee review would be required at the time of continuing review (e.g., risk has changed to be greater than minimal).
5. In addition to the completed Renewal Application and applicable attachments submitted by the Investigator, the Reviewer and Committee Members receive a copy of the current IRB approved Application, current IRB approved Informed Consent documents, any supporting documentation such as a Sponsor's Protocol, Investigator's brochure, and copies of any monitoring reports conducted since the last review. All members have access to the protocol file and relevant minutes.
6. Review of the currently approved consent document must assure that the information is still accurate and complete. Any significant new findings that may relate to the participant's willingness to continue participation is provided to the participant in an updated consent document. Review of currently approved or proposed consent documents must occur during the scheduled continuing review of research by the IRB but may be done more frequently if new information becomes available.

B. Continuing Review Approval Period

1. The IRB Committee approval period for Continuing Review is the same as initial Committee Review provided that the continuing review occurs annually.
2. For research reviewed and approved by the full Committee at a convened meeting, the approval period starts on the date of the convened meeting. The expiration date (the last day the research is approved) is the last day of the approval period. (For example, if the IRB approves the research on April 12, 2005 for one year, the approval period is April 12, 2005-April 11, 2006.)
3. For research that was determined by the full Committee to require minor modifications, the approval period begins on the date a Reviewer, usually the IRB Chair, verifies that the investigator has made the revisions requested by the full Committee. (For example, if the IRB determines that minor modifications are required on April 12, 2005 and approval is for one year period if a reviewer verifies the changes on April 27, 2005, the approval period is April 27, 2005-April 11, 2006.)
4. In all cases the expiration date (the last day the research is approved) is the last day of the approval period. Research may be conducted on the expiration date but may not be conducted after the expiration date without re-approval. (For example, if the approval period is April 27, 2005-April 11, 2006, the expiration date is April 11, 2006. Research must stop at midnight April 11, 2006 unless the Investigator received re-approval of the research.)

5. Expedited Review: Minimal risk protocols may be approved for a 3- or 1-year period. (See Policy # 13.)
- C. If the IRB determines that it needs verification from sources other than the Investigator that no material changes have occurred since the previous IRB review, the IRB may request an independent assessment of information or data provided in the renewal application.
1. The scope and extent of such an independent assessment is determined on a case-by-case basis.
 2. Sources for such outside information could include:
 - a. Compliance review from the HRP EQUIP team or designee;
 - b. Corroboration from School Deans, Department Chairs, Sponsors, other Clinical Research Organizations, and other IRBs at collaborating institutions;
 - c. Copies of FDA audits;
 - d. Literature searches conducted by clinical librarians;
 - e. Reports from subjects or study staff; or
 - f. Directed audit at the direction of the IRB Committee or the HRP Executive Director or designee.
 3. Determining Appropriate Interval for Continuing Review - Appropriate continuing review intervals are addressed with each review conducted by the IRB. The following factors are taken into consideration when determining the appropriate review interval, but are not limited to:
 - a. Involvement of vulnerable populations;
 - b. Research conducted internationally;
 - c. Involvement of recombinant DNA or other types of gene transfer protocols;
 - d. Research for which participants would be exposed to additional risks, e.g. breach of confidentiality, phase I studies, disproportionate number or severity of unanticipated problems;
 - e. Previous Investigator Holds or Suspensions of the research due to compliance, record-keeping, or other concerns; and/or
 - f. Recommendations from other Institutional committees.
- D. Expired Study
1. The IRB Chair and/or IRB Committee addresses on a case-by case basis, those instances where discontinuing intervention and interaction because of study expiration would seriously jeopardize the safety or well-being of an individual (e.g., discontinuing therapy may cause more harm to the participant or they may receive the same therapy off study).
- E. Calculating the "Date of IRB Expiration"
1. Approval at a convened IRB Committee meeting - The date of expiration is calculated from the date of the convened IRB Committee meeting. For example, if the committee meeting date is 2/01/2005, then the "Date of IRB Expiration" is 1/31/2006 (one year minus one day) for a 12-month review interval.
 2. Minor revisions required at a convened IRB Committee meeting - The date of expiration is calculated from the date of the convened IRB Committee meeting. It is not calculated from the date the Chairperson or his or her designee verifies and grants final approval. For example, if the committee approves pending changes on 2/01/2005 and the LR's response is reviewed by the Chair on 3/1/2005, then the "Date of

IRB Expiration” is 1/31/2006 for a 12-month review interval (one year minus one day) and 7/31/2006 for a 6 month review interval (six months minus one day).

3. Expedited review - Since there is no convened meeting in an expedited review, the “Date of IRB Expiration” will be calculated based on the review interval determined by the Chair or designee using the date that the initial IRB application or most recent Continuing Review Application was approved by the Chair or designee. For example, if the Chair requires minor revisions on 2/01/2005 and the LR’s response is reviewed by the Chair on 3/1/2005, then the “Date of IRB Expiration” is 2/28/2006 for a 12-month review interval (one year minus one day).
4. Amendments - The approval date of an amendment does not affect the calculation of the expiration date unless the Committee decreases the review interval.
5. HRP Staff will not stamp the date of IRB expiration on the Informed Consent Documents. (See Policy # 34.)

III. HRP Staff Reviewers

- A. HRP Staff Reviewers are delegated the authority to conduct continuing review of minimal risk research protocols. Expedited continuing review applications are accepted on a rolling basis and are administratively reviewed by an HRP Staff Reviewer in consideration of the expiration date.
- B. Delegation is provided in the HRP Staff Reviewer Delegation of Authority document maintained on the HRP WIKI page – and signed by the IRB Chairs for A, B and C, as well as the Director of Research Protections.
 1. An HRP Staff Reviewer is defined as follows:
 - a) **HRP STAFF REVIEWER:**
 - (1) **Tier 1:** Administrator or above, CIP or CCRP certified and appointed as IRB members or alternate members may review and approve transactions related to exempt and expedited level protocols. Exceptions are noted as applicable.
 2. **An HRP Staff Reviewer (Tier 1) may review and approve expedited Renewal Applications except under the following conditions:**
 - a. Category 1: Clinical studies of drugs and medical devices
 - b. Category 9: Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified
 - c. Other FDA-regulated protocols (e.g., Humanitarian Use Device protocols)
 - d. Protocol involving serious or continuing noncompliance or Unanticipated Problem reported during last approval period
 - e. Increase in risk/decrease in benefit reported during last approval period
 - f. Review required more frequently than annually

- g. Renewals with a positive disclosure of financial interest

IV. **IRB Analyst or Higher Responsibilities**

- A. Assuring Continuing Review Completion
 - 1. The electronic IRB submission and management system automatically sends the LR and Administrative Contact (AC) a reminder notice 90 days prior to the expiration date of the study for full committee studies and 60 days prior to the expiration date of the study for expedited studies.
 - 2. When the Renewal Application IRB approval is not received prior to the study expiration date, the LR and AC receives notice of study expiration.
- B. The Analyst performs a pre-review of the documents submitted for completeness and to verify the type of continuing review in which the study is eligible.
- C. The Analyst provides the following for review via the electronic IRB submission and management system:
 - 1. A copy of the current, IRB approved Application;
 - 2. A copy of the current, IRB approved informed consent documents;
 - 3. A report of all reportable events/problems provided by the LR since initial IRB approval.
 - 4. A summary of any unanticipated problems involving risks to participants or others that occurred over the last approval period.
- D. The Analyst proceeds with preparing the continuing review documents accordingly.
 - 1. Studies requiring expedited continuing review are provided to the Chairperson or designated IRB subcommittee members or a HRP Staff Reviewer for review and approval.
 - 2. Studies requiring full IRB Committee review are assigned a Reviewer and placed on the next available Committee agenda.
- E. Letters requesting reviewer revisions and approval letters are drafted using the appropriate template.
- F. Appropriate database entries are completed.

V. **IRB Analyst Responsibilities**

- A. Upon notification of submission of the Renewal Application, the Analyst assures submission of the proper documents / information (e.g. a completed Renewal Application, etc.)
- B. Once the Renewal Application is approved, the Analyst:
 - 1. Drafts the IRB Approval letter using the appropriate template,
 - 2. Stamps the informed consent documents, and all approved documents, as necessary.
 - 3. Notifies the LR and AC via email when the approval documents are available via the electronic IRB submission and management system.
 - 4. Completes the appropriate database entries.

References:

IRB Policy 13, "IRB Review of Human Subjects Research – Expedited"

IRB Procedure 13.A, "Procedure for IRB Review of Human Subjects Research – Expedited"

IRB Policy 14, "IRB Review of Human Subjects Research - Full Committee"

IRB Procedure 14.A, "Procedure for IRB Review of Human Subjects Research - Full Committee"

Policy Number: 19

Title: Reporting Unanticipated Problems Involving Risk to Participants or Others

Date of Last Revision: 03/09/07, 11/27/10, 08/31/15, 05/01/16, 09/01/17, 09/20/18, 11/20/19, 01/02/20, 03/26/22, 09/14/22, 03/13/23

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to require reporting of unanticipated problems involving risk to participants or others. Additional reporting requirements are as follows:

I. Unanticipated Problems

- A. The phrase “unanticipated problems involving risks to subjects or others” is found but not defined in the HHS regulations at 45 CFR part 46. The Office for Human Research Protections (OHRP) considers unanticipated problems, in general, to include any incident, experience, or outcome that meets all of the following criteria:
 - 1. **Unexpected** (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
 - 2. **Related or possibly related to participation in the research** (in this guidance document, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); **and**
 - 3. **Suggests that the research places subjects or others at a greater risk of harm** (including physical, psychological, economic, or social harm) **than was previously known or recognized.**
- B. Food and Drug Administration (FDA) guidance is consistent with OHRP. The FDA states that an adverse event observed during the conduct of a study should be considered an unanticipated problem involving risk to human subjects, and reported to the IRB, only if it were unexpected, serious and would have implications for the conduct of the study.

II. Reporting of Unanticipated Problems

- A. **All unanticipated problems must be reported to the UCI IRB as follows:**
 - 1. **Where the event occurred at UCI for a single-site study.**
 - 2. **Where UCI is the IRB of record for a multi-site study, and the unanticipated problem occurred at a site relying on UCI IRB;**
 - 3. **Where the event occurred at a UCI site, but UCI is *not* the IRB of record and is relying on a non-UCI IRB.**
- B. UCI considers both OHRP and FDA guidance when assessing whether an event constitutes an unanticipated problem.
- C. Unanticipated problems must be submitted to the IRB via Reportable Events promptly - within 5 business days upon the Lead Researcher's (LRs) knowledge of the event.

- D. In cases where the LR initially determined that an adverse event was not reportable, but either the Sponsor and/or Data Safety Monitoring Board (DSMB) upgrades the event to an unanticipated problem, a Reportable Event must be submitted within 5 business days of the LR learning of the Sponsor and/or DSMB's assessment of the event.
- E. In certain cases, the reports of serious and/or continuing non-compliance that are Unanticipated Problems may come from sources other than via reportable events such as phone call or an email from a participant, a family member, the IRB committee member, Whistleblower Office, UCI Health Affairs Compliance Officer etc. In such case the goals of the IRB, in general is to investigate and manage issues of potential noncompliance for subject safety, developing corrective and preventative action plans and reporting the serious or continuing noncompliance. (See policy #52.)
- F. Where an external IRB is the IRB of record, all unanticipated problems that occur at UCI must be reported to the UCI IRB. UCI will work in partnership with the reviewing IRB to investigate the matter for the purpose of (continued) human subject protection.

III. **Mechanism to Report: UP Reporting System**

- A. Reportable Events is a web-based module. It is accessible via the OR/HRP website 24 hours per day, seven days per week.
- B. The LR provides the following information:
 - 1. A description of the unanticipated problem;
 - 2. The date the event/problem occurred;
 - 3. The date the LR became aware of the event/problems;
 - 4. Identification of the drug, biologic, medical device, treatment or intervention;
 - 5. Explanation of the treatment provided to the participant;
 - 6. Outcome or anticipated outcome; and
 - 7. Status of the individual's participation in the study.
- C. The LR also attaches any associated materials such as redacted medical record notations or safety reports to the Reportable Events form.
- D. When IRB-approved documents (e.g., IRB Application; informed consent document) must be revised, the Investigator is required to submit an electronic Amendment request.
- E. If an unanticipated problem is unresolved at the time of initial reporting, a follow-up report must be submitted if the event or problem is not resolved as expected or if the event/problem results in a chronic condition or death.
- F. The LR is responsible for the accurate documentation, investigation, recordkeeping and follow-up of events or problems, including Safety Reports (SRs) received by the FDA or by a drug/device manufacturer.

IV. **Confirmation of an Unanticipated Problem**

- A. The IRB Chair or, if necessary, the full Committee, will review the Reportable Event to confirm whether the event/problem represents an unanticipated problem involving risk to participants or others.
 - 1. Where UCI is not the IRB of record, and the event occurred at UCI, the IRB Chair or, if necessary, the full Committee reserves the right to (also) review the UP report to ensure the protection of human subjects.

- B. Unanticipated problems involving risk to participants or others will be referred to the convened IRB Committee for further action.
 - C. The LR has the option to place some or all research activities on hold pending review by the convened IRB and/or until additional information can be provided to the Chair or the IRB to determine if a change in the risk-benefit profile has occurred or a change in the rights or welfare of the participants has occurred.
 - D. The IRB Chair or designee can determine that participants are at immediate risk of harm and there is insufficient time to wait for review by the convened IRB Committee, the Chair or designee may immediately place the study on "suspension". (See HRP Policy # 51.)
 - E. All IRB confirmations of unanticipated problems involving risks to participants or others must be reported to the LR, institutional officials, OHRP and the FDA (if applicable) as per federal regulations and per current policy.
- V. **Events/Problems that are not reportable to the UCI IRB**
- A. For protocols where UCI IRB serves as the IRB of record the following events/problems are not reportable to the UCI IRB:
 1. Protocol deviations that do not constitute an unanticipated problem involving risk to participants or others.
 2. Internal adverse events that do not constitute an unanticipated problem involving risk to participants or others.
 3. Safety reports that do not constitute an unanticipated problem involving risk to participants or others.
 4. Data safety monitoring reports that do not constitute an unanticipated problem involving risk to participants or others.
 5. Any other event or occurrence that, in the LR's assessment does not constitute an unanticipated problem involving risk to participants or others.
- VI. **All protocol deviations, internal adverse events, or safety reports whether reportable to the IRB or not as a possible unanticipated problem are to be maintained by the LR.**
- VII. **Other Reporting Requirements for the LR at Continuing Review**
- A. The IRB have access to all reported unanticipated problems during the last approval period as part of the continuing review process.
 - B. Independent safety monitoring reports or DSMB reports must be reviewed by the LR and submitted to the IRB at the time of continuing review.
- VIII. **Additional Reporting Requirements for Human Gene Transfer Research**
- A. Investigators involved in IRB-approved human gene transfer (a.k.a. "gene therapy") protocols have additional reporting responsibilities.
 1. In addition to submitting a Reportable Event to the UCI IRB, the LR must complete and submit an Office of Biotechnology Activities' (OBA) SAE report form when a subject on a gene transfer protocol experiences a hospitalization or a death. The form must be submitted to the UCI IRB, the UCI Institutional Biosafety Committee (IBC), NIH Office of Biotechnology Activities (OBA), OHRP, and FDA.

2. Failure to report SAEs related to gene transfer to the federal authorities can result in sanctions for the individual researcher and for the institution.

IX. Unanticipated Problems related to a Humanitarian Use Device (HUD)

- A. Whenever the physician or health care provider receives or otherwise becomes aware of information, from any source, that reasonably suggests that a HUD has or may have caused or contributed to the death or serious injury of a patient, the physician or health care provider must:
 1. Report such findings to the FDA and the IRB as soon as possible, but no later than 10 working days after the physician first learns of the event or problem. This reporting is in addition to, not a substitute for, FDA and/or manufacturer reporting requirements in accordance with 21 CFR 803.30.
 2. The Investigator must also promptly report any FDA action regarding the death or serious injury of a patient to the IRB.

References:

21 CFR 312.66

21 CFR 803.30

45 CFR 46.103(b)(5)

FDA Guidance for Clinical Investigators, Sponsors, and IRBs: Adverse Event Reporting to the IRBs – Improving Human Subject Protection, January 2009

MedWatch – “What Is a Serious Adverse Event?”

OHRP Guidance Document, “Adverse Event Reporting Requirements,” January 11, 2001

OHRP Guidance Document, “Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events,” January 15, 2007

ICH-GCP: 3.3.8, 4.10.2

Procedure Number: 19.A**Title: Reporting Unanticipated Problems Involving Risk to Participants or Others****Procedure:**

This procedure outlines the process for reporting unanticipated problems involving risk to participants or others.

I. LR Responsibilities

- A. The LR submits a Reportable Event as soon as possible, but no later than 5 working days after the LR first learns of the event/problem.
- B. The LR is responsible for the accurate documentation, investigation, and follow-up of all unanticipated problems.
- C. For clinical investigations, independent safety monitoring reports or DSMB reports must be reviewed by the LR and reported to the UCI IRB within 5 working days if the report constitutes an unanticipated problem or provided to the IRB at the time of continuing review.
- D. Relatedly, the Lead Researcher must notify the IRB of matters of (or potential matters of) serious and/or continuing non-compliance via Reportable Events as soon as possible, but no later than 5 working days after the LR first learns of the event/problem. (See Policy # 19.)

II. IRB Chair/Designated Committee Member Responsibilities

- A. All Reportable Events are provided to a Chair or a designated Committee Member for review either within 72 hours or during the weekly IRB Chair meeting, depending on the severity of the event/problem.
- B. The reviewer is provided:
 - 1. A copy of the report and all attachments; and
 - 2. The IRB Application file including the most recently approved protocol consent form and any other applicable documentation.
- C. The Chair reviews the materials to confirm whether the event represents an unanticipated problem.
 - 1. If the Chair cannot decide for each criterion, the event will be forwarded to the convened IRB Committee to make these decisions.
 - 2. If the Chair determines that the event meets all three criteria, then the event will be considered an unanticipated problem involving risk to participants or others and the event will be referred to the convened IRB Committee for further action. If participants are at immediate risk of harm and there is insufficient time to wait for review by the convened IRB, the Chair or designee can suspend the research. (See HRP Policy # 51.)
 - 3. If the Chair determines that the event does not meet one or more of the three criteria, then the event will be considered not to represent an unanticipated problem involving risk to participants or others. Documentation of this assessment will be maintained in the study file.

III. **IRB Committee Responsibilities**

- A. If the Chair confirms that the Reportable Event constitutes an unanticipated problem involving risk to participants or others, or when the determination is required by the IRB Committee, the UP report will be forwarded to the convened IRB Committee.
- B. Documentation for IRB review of unanticipated problems involving risk to participants or others, or possible unanticipated problem includes:
 - 1. All Committee members review:
 - a. The Reportable Event and all attachments;
 - b. Previously reported unanticipated problems;
 - c. The current IRB-approved Application and informed consent document(s); and
 - d. The Amendment Application, if applicable.
 - 2. The assigned member also reviews:
 - a. The sponsor's protocol, if applicable
 - b. The Investigator's Brochure, if applicable.
 - c. Data Safety Monitoring Charter, if applicable.
- C. The IRB may postpone a decision while awaiting additional information.
- D. If the IRB confirms that the event/problem meets all three criteria, then any of the following actions may be taken:
 - 1. The IRB may:
 - a. Accept the report with no changes;
 - b. Accept the report with changes to the risk/benefit profile, the protocol, or the informed consent documents (require submission of an Amendment);
 - c. Require notification/re-consenting of participants when such information might relate to the participants' willingness to continue participation in the research (the consent document or notification letter must be reviewed by the IRB prior to notification);
 - d. Require notification of past participants when such information might relate to long term risks (the notification letter must be reviewed by the IRB prior to notification);
 - e. Request further information from the LR or DSMB;
 - f. Increase the frequency of continuing review;
 - g. Impose additional monitoring requirements of the protocol, such as monitoring of the consent process;
 - h. Require additional training of the LR and research team;
 - i. Require notification of researchers at other sites;
 - j. Referral to other organizational entities;
 - k. Suspend the study per HRP Policy 51.
 - m. Terminate the study according to HRP Policy 51.
 - 2. The event will be reported according to HRP Policy 53.
 - 3. The IRB will consider whether the event represents serious or continuing non-compliance according to HRP Policy 52.
 - 4. In the case of changes to the protocol taken without prior IRB review to eliminate apparent immediate hazard to a research participant, the IRB will consider whether the changes were consistent with the rights and welfare of participants.
 - 5. If the IRB determines that the event does not meet one or more of the three criteria, then the event will be considered not to represent an unanticipated problem involving risks to participants or others.

IV. **IRB Administrator Responsibilities**

- A. The IRB Compliance Manager (EQUIP Team) monitors when potential UPs are reported to the IRB. The HRP staff works closely with the IRB Chair and IRB to manage potential UPs. When an UP may involve noncompliance the IRB Compliance Manager works closely with the IRB Chair and IRB to manage the potential UP. (See HRP Policy # 52.)
- B. All unanticipated problems reports made under HRP Policy 19 are provided to a Chair or a designated Committee Member for review either within 72 hours or during the weekly IRB Chair meeting, depending on the severity of the event/problem.
- C. Unanticipated problems involving risk to participants or others or where the IRB Chair is unable to confirm whether the event/problem qualifies as an unanticipated problem involving risk to participants or others are prepared for convened IRB Committee review. The Reportable Event is placed on the next convened Committee agenda, one IRB Reviewer is assigned, and the appropriate documents are included on the agenda for the Committee.
- D. Letters requesting information from the LR are drafted using an appropriate HRP memo template.
- E. Appropriate database entries are completed.

Policy Number: 20

Title: Completion of Study/Study Closure

Date of Last Revision: 01/21/07, 08/24/10, 01/29/15, 04/22/15, 10/01/16, 02/28/18, 03/26/22, 09/14/22

Definitions:

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to require reporting of study closure. In addition, the IRB may require an administrative study closure for studies that have been submitted to the but have not met the requirements for IRB review.

I. Final Closing Reports

- A. Investigators are required to submit a Final Closing Report to the IRB as soon as possible but no later than three months after the following has occurred:
 - 1. All subject accrual (i.e., recruitment and enrollment) is complete;
 - 2. All subject specimens, records, data have been obtained (i.e., no further collection of data/information from or about living individuals is required);
 - 3. No further contact with subjects is necessary (i.e., all interactions or interventions are complete and no further contact with enrolled subjects is necessary); and
 - 4. Analysis of subject identifiable data, records, and specimens are complete (i.e., use or access to subject identifiable data and review of source documents by study sponsors is no longer necessary).
 - B. If a study is canceled without participant enrollment, Investigators are still required to submit a Closing Report to the IRB.
- II. An Closing report is completed and submitted electronically to the Human Research Protections (HRP) staff.
- III. Investigators are required to report unanticipated problems involving risks to participants or others even if a closing report has been filed. The Investigator is required to submit the form to the IRB within 5 business days of the Investigator's awareness of the problem. (See IRB Policy # 19.)
- IV. Additional items relating to the study, such as the Sponsor's Completion Summary are accepted for the protocol file after the study has been closed.

V. **Administrative Closing**

- A. Full Committee: It is necessary for Investigators to submit to and address various ancillary committee requirements, along with HRP requirements upon submission of a new study. When a new study submission is determined not ready for IRB review (e.g., major information not provided, ancillary committee clearance not provided) it may take several weeks or months, over multiple IRB agendas for an item to be placed on an agenda.
- B. Expedited / Exempt: Likewise, for minimal risk research, sometimes it may take months for a researcher to respond to requests for required documentation.
- C. Studies that are not ready for IRB review will remain pending in the queue for a maximum of three (3) months from the date of submission. If the study is not ready for IRB review after 3 months, it will be administratively closed out.

Procedure:

This procedure outlines the process for reporting study closures and completing an administrative closure.

I. Lead Researcher (LR) Responsibilities

- A. The LR is required to submit a Closing Report to the IRB when:
 - 1. All subject accrual (i.e., recruitment and enrollment) is complete;
 - 2. All subject specimens, records, data have been obtained (i.e., no further collection of data/information from or about living individuals is required);
 - 3. No further contact with subjects is necessary (i.e., all interactions or interventions are complete and no further contact with enrolled subjects is necessary);
 - 4. Analysis of subject identifiable data, records, and specimens are complete (i.e., use or access to subject identifiable data and review of source documents by study sponsors is no longer necessary) or, if
 - 5. The study is canceled without participant enrollment.
- B. Investigators are required to report unanticipated problems involving risks to participants or others even if a closing report has been filed. The Investigator is required to submit the form to the IRB within 5 business days of the Investigator's awareness of the problem. (See IRB Policy # 19.)

II. IRB Chair/Designated Committee Member Responsibilities

- A. The IRB Chairperson, Vice-Chair or Designated Committee Member will review Closing Reports for protocols involving greater than minimal risk. The IRB Chairperson, Vice-Chair or Designated Committee Member will acknowledge study closure via their agreement to close the study in the electronic IRB submission and management system.
- B. When there is a discrepancy, the IRB Chair may request clarification.

III. IRB Analyst or Higher Responsibilities

- A. All Closing Reports are reviewed by the Analyst for completeness.
- B. The Analyst will assist in obtaining any additional information requested by the Committee Chairperson.
- C. The Analyst will process the Closing Report, and make the appropriate database entries.

Policy Number: 21

Title: Participant Compensation

Date of Last Revision: 08/10/05, 09/27/10, 01/24/11, 05/03/21, 03/28/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to review and approve payments to human research participants.

- I. **The IRB must determine that the risks to research participants are reasonable in relation to the anticipated benefits and that the informed consent document contains an adequate description of the study procedures as well as the risks and benefits.** Payment to research participants in studies is not considered a benefit. Rather, it should be considered compensation for time, effort, and inconvenience. The amount and schedule of all payments should be presented to the IRB at the time of initial review or via a modification request.
 - A. The IRB should review the amount of payment and the proposed method and timing of disbursement to assure that neither is coercive nor presents undue influence.
 - B. Timing of Payments. Credit for payment should accrue as the study progresses and not be contingent upon the participant completing the entire study. The participants should be paid in proportion to their time and inconvenience because of participation in the research study. Unless it creates undue inconvenience or a coercive practice, payment to participants who withdraw from the study may be paid at the time they would have completed the study (or completed a phase of the study) had they not withdrawn. For example, in a study lasting only a few days, an IRB Committee may find it permissible to allow a single payment date at the end of the study, even to participants who had withdrawn before that date. In general, a single payment date is not permissible especially for longitudinal studies lasting several months. Moreover, participants who withdraw before completion of a longitudinal study should receive accrued compensation in a timely manner.
 - C. Completion Bonus. While the entire payment should not be contingent upon completion of the entire study, payment of a small proportion as an incentive for completion of the study is acceptable, providing that such incentive is not coercive. The IRB will determine whether the amount paid as a bonus for completion is reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn.
 - D. Disclosure of Payments. All information concerning payment, including the amount and schedule of payments should be described in the informed consent document.
 - E. Advertisement of Payments. Advertisements may state that participants will be paid or compensated, but the payment or the amount to be paid should not be over-emphasized. (See IRB Policy # 22.)

- II. **Alterations in Payments** - Any alterations in research participant payment or liberalization of the payment schedule must be reported to the IRB prior to implementation as an Amendment. (See IRB Policy # 17.)
- III. **Reporting Payments to the IRS** - The Internal Revenue Service (IRS) requires that UC Irvine (or whomever is paying the research participants for their participation) report payments more than \$600 per calendar year on Form 1099-Misc. The filing of these forms necessitates that the name and social security number of the participant be collected (preferably on a Form W-9) and released to the Office of Accounting and Fiscal Services to process the Form 1099-Misc. The collection and release of this information must be addressed thoroughly in the informed consent document so that it is clear to participants that their identity will be released for the purpose of payment and reporting.
- IV. **Use of Sponsor Coupons** - **The use of sponsor coupons, as a form of participant compensation, good for a discount on the purchase price of the product once it has been approved for marketing is prohibited.**
- V. **When following a Department of Defense Addendum**
 - A. When research involves U.S. military personnel, policies and procedures require limitations on dual compensation as follows:
 - 1. Prohibit an individual from receiving pay from more than one position for more than 40 hours of work in one calendar week;
 - 2. Prohibit an individual from receiving pay of compensation for research during duty hours. U.S. Military personnel may be compensated for research if the participant is involved in the research while not on duty.
 - 3. The policy includes temporary, part-time, and intermittent appointments.

References:

45 CFR 46

21 CFR 50.20

U.S. Food and Drug Administration Information Sheets: "Guidance for Institutional Review Boards and Clinical Investigators," 1998 Update

IRB Management and Function; Amdur, R. and Bankert, E.; 2002 Jones and Bartlett Publishers, Inc.

DoDD: Dual Compensation Act, 24 U.S.C. 301

University of California – Policy D-371-12.1

Procedure Number: 21.A**Title: Procedure for Participant Compensation****Procedure:**

This procedure provides guidance for payment to research participants under the jurisdiction of the UC Irvine (UCI) Institutional Review Board (IRB).

I. Lead Researcher (LR) Responsibilities

- A. The LR will provide a detailed description of proposed payments to research participants in the IRB Application. This will include timing of payments, pro-rating schedule, payment for participants who withdraw before completion, and completion bonus plans, if applicable.
- B. Any alterations in payments to research participants are to be submitted as an Amendment to the IRB prior to implementation. (See IRB Policy # 17.)
- C. All information concerning payment should be incorporated into the informed consent document using the applicable IRB template. This information should be addressed in the consent template. Payments are not a benefit and are not to be included in the benefits section of the informed consent document.
- D. The LR should provide the Office of Accounting and Fiscal Services the name and social security number of participants who receive payments more than \$600 per calendar year preferably on Form W-9 for processing the Form 1099-Misc to be forwarded to the IRS.
 - 1. The collection and release of this information must be addressed thoroughly in the informed consent document so that it is clear to participants that their identity will be released for the purpose of payment and IRS reporting.

II. IRB Committee Responsibilities

- A. The IRB Committee, the Chairperson or designated Committee Member will review the planned research activities to determine that the risks to participants are reasonable in relation to the anticipated benefits and that the informed consent document contains an adequate description of the study procedures, as well as the risks and benefits.
- B. The IRB will review the amount of payment and the proposed method and timing of disbursement to assure that neither are coercive nor present undue influence.
- C. The IRB must assure the entire payment is not contingent upon the participant completing the entire study, unless the study is of short duration or only a one-time procedure. Payment should accrue as the study progresses.
- D. The IRB should determine that the amount paid as a bonus for completion is reasonable and not so large as to unduly influence participants to stay in the study when they would otherwise have withdrawn.
- E. The IRB will review advertisements to assure the advertisements are not coercive or present undue influence and do not over-emphasize the payment or the amount to be paid. (See IRB Policy # 22.)

- F. The IRB must determine if payment made directly to a child is appropriate or inappropriate by carrying the risk of undue inducement.

III. **IRB Analyst or Higher Responsibilities**

- A. The Analyst will conduct a pre-review of the IRB Application, the informed consent documents, and advertisements submitted to determine that the method of payment for participation in research is consistent with IRB policy, as well as ethical standards.
- B. If additional information regarding payments to participants is needed, the Analyst will contact the LR and request the additional information.

Policy Number: 22

Title: Advertisement and Recruitment

Date of Last Revision: 08/10/05, 09/09/10, 02/01/16, 04/06/18, 09/14/22, 12/05/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to review and approve all recruitment materials for participants in research conducted under its jurisdiction.

- I. The IRB must assure that appropriate safeguards exist to protect the rights and welfare of research participants. In fulfilling these responsibilities, the IRB must review all of the research documents and activities that bear directly on the rights and welfare of the participants of proposed research, including the methods and materials that Investigators propose to use to recruit participants.
 - A. Recruiting and advertising materials must be approved by the IRB. The Investigator must obtain IRB approval for all final versions of television, radio, videotape or print advertisements, e-mail solicitations, Internet websites, and other recruitment methods and materials intended for the recruitment of prospective research participants. All methods of advertisement require approval from the IRB prior to their use.
 - B. The following examples do not qualify as an advertisement:
 1. Communications intended only to be seen or heard by health professionals, such as “dear doctor” letters and doctor-to-doctor letters;
 2. News stories, so long as they are not intended for recruitment purposes (e.g. a phone number at the end to contact for more information to participate in a particular study, full details of inclusion/exclusion criteria of a particular study, etc.); and
 3. Publicity intended for other audiences (e.g., media releases regarding types of services available or offered by a particular clinic, institute or physician).
 - C. The IRB considers advertising or soliciting for study participants to be the start of the informed consent process and subject selection process. Advertisements must be reviewed and approved by the IRB as part of the package for initial review. When the Investigator decides after the initial approval to advertise for participants or to change the advertisement, the advertising is considered a modification to the ongoing study. The IRB reviews the advertising to assure that it is not unduly coercive and does not promise a certainty of cure beyond what is outlined in the consent and the protocol. This is especially critical when a study may involve participants who are likely to be vulnerable to undue influence.

- D. When advertising is to be used, the IRB must review the information contained in the advertisement and the mode of its communication, to determine that the procedure for recruiting participants is not coercive and does not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol. The IRB reviews the final copy of printed advertisements to evaluate the relative size of type used and other visual effects. When advertisements are to be taped for broadcast, the IRB reviews the final audio or video tape. The IRB may review and approve the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording.
 - E. **For Exempt and Expedited research that is not regulated by the Food and Drug Administration (FDA), the IRB may approve the UCI “Recruitment Material Master Template” in lieu of approving all recruiting and advertising materials.**
 - 1. When utilizing this template, researchers do not need to obtain IRB approval for the final versions of recruitment materials, provided that the materials:
 - a) Are limited to the information and text as described in the IRB approved master template AND
 - b) Adhere to the recruitment material standards and requirements set forth in in this policy.
 - 2. Investigators are responsible for maintaining copies of the final product in the research files.
 - 3. Any subsequent change in the content of the “Recruitment Material Mater Template”, that would also require a change to the approved protocol (i.e., eligibility criteria), must be submitted for IRB review and approval via an amendment.
- II. Any advertisement to recruit participants should be limited to the information the prospective participants need to determine their eligibility and interest. When appropriately worded, the following items may be included in advertisements:
- A. The name, address, and institution of the Lead Researcher or study coordinator (e.g., UC Irvine);
 - B. If applicable, include “investigational, meaning non-FDA approved”;
 - C. The condition under study and the purpose of the research;
 - D. In summary form, the criteria that will be used to determine eligibility for the study;
 - E. A brief list of participation benefits, if any (e.g., a no-cost health examination);
 - F. The time or other commitment required of the participants; and
 - G. The location of the research and the person or office to contact for further information.
- III. **Advertising materials should not include the following:**
- A. Claims, either explicitly or implicitly, that the drug, biologic, device or other type of intervention is safe or effective for the purposes under investigation;
 - B. Claims, either explicitly or implicitly, that the test article is known to be equivalent or superior to any other drug, biologic, device or intervention;
 - C. Claims, either explicitly or implicitly, about the drug, biologic, or device under investigation that are inconsistent with FDA labeling;

- D. Allow compensation for participation in a trial offered by a Sponsor to include a coupon good for a discount on the purchase price of the product once it has been approved for marketing;
 - E. Use terms such as "new treatment," "new medication" or "new drug" without explaining that the test article is investigational, meaning non-FDA-approved;
 - F. Promises of "free medical treatment," when the intent is only to say that participants will not be charged for taking part in the investigation;
 - G. Exculpatory language or
 - H. An emphasis of payment or the amount to be paid, by such means as larger or bold type.
- IV. **Recruitment Scripts** - The first contact prospective study participants make is often with an administrative staff contact that follows a script to determine basic eligibility for the specific study. The IRB must review the procedures to assure that they adequately protect the rights and welfare of the prospective participants. The IRB must have assurance that any information collected about prospective participants will be appropriately handled.
- V. **Internet Recruitment** - All advertisements and recruitment methods must be reviewed and approved by the IRB prior to implementation except for two specific clinical trial listing services which do not require prospective IRB approval as determined by the Food and Drug Administration. These include the National Cancer Institute's cancer clinical trial listing (PDQ) and the government-sponsored AIDS Clinical Trials Information Service (ACTIS). For other Internet recruitment sites, IRB review and approval is required to assure that the information does not promise or imply a certainty of cure or other benefit beyond what is contained in the protocol and the informed consent document. In addition, the Investigator must assure that the information shared for Internet recruitment is in accordance with their signed clinical trial agreement or grant.
- VI. **UCI Campus Communication E-mail** - Advertising submitted through mass email solicitation to the UC Irvine campus community should be simple, readable, and understandable. It should meaningfully and respectfully convey a message to a broad spectrum of the UCI community. It should be text-based and written in block paragraphs. The following format is recommended when utilizing this method of recruitment or advertisement:
- A. A headline that describes the study and volunteers needed;
 - B. Use complete sentences and paragraphs;
 - C. Statement 1 – include enough information to help readers self-select;
 - D. Statement 2 – purpose of the study;
 - E. Statement 3 – requirements of participation;
 - F. Statement 4 – benefit to the participant or a statement there is no benefit; and
 - G. Statement 5 – a contact person "for more information".
- VII. **Students as Participants** - The IRB should exercise oversight with the use of students as participants in research.

- VIII. **Data Base/Primary Care Physician Recruitment** - Often times Investigators request to use search methods of particular databases looking for potential participants that may be eligible for their research projects (e.g., disease, age, sex, etc.), or they request to contact primary care providers (PCP) for access to potential participants from the PCP's patient population. These recruitment methods require IRB approval prior to initiation.
- IX. **Inclusion of Women, Children and Minorities** - The inclusion of women, children, and minorities in research is important, both to ensure that they receive an appropriate share of the benefits of research and that they do not bear a disproportionate burden. To the extent that participation in research offers direct benefits to the participants, under-representation of children, men, women or minorities denies them the opportunity to benefit. Moreover, for purposes of generalizing research results, Investigators should include the widest possible range of population groups.
- X. **Involvement of Humans in Research** - NIH-supported Investigators must provide to the IRB details of the proposed involvement of humans in their research protocols, including the characteristics of the subject population, anticipated numbers, age ranges. The proposed research should specify the gender and racial/ethnic composition of the subject population, as well as criteria for inclusion or exclusion of any subpopulation.
- XI. **Finder's Fees and Bonus Payments – Although research sponsors may offer to pay Investigators or study personnel an additional fee to encourage participant recruitment efforts and the timely or accelerated opening of research studies, these payments are strictly prohibited per California Health and Safety Code Section 445 and UCI IRB policy.**
- A. It is not permissible to pay or accept a "finder's fees."
 - B. It is not permissible to accept bonus payments. UCI employees or students cannot accept personal payments from sponsors or other researchers in exchange for accelerated recruitment or referrals of patients. Cash or cash-equivalent payment to health care providers for referral of subjects or potential subjects is not permitted.
 - C. Other types of compensation (e.g., books, other non-cash gifts) are also prohibited.
 - D. The Council on Ethical and Judicial Affairs of the American Medical Association denounced the practice of finder's fees in December 1994;
 - E. The Federal anti-kickback statute can also be implicated by this practice; and
 - F. California Health and Safety Code (Section 445) states that "No person, firm, partnership, association or corporation, or agent or employee thereof, will for profit refer or recommend a person to a physician, hospital, health-related facility, or dispensary for any form of medical care or treatment of any ailment or physical condition."
- XII. **Use of a Lottery, Raffle or Drawing System**
- A. **According to the California Department of Consumer Affairs, "California law prohibits lotteries.** A lottery is any scheme for the disposition of property by chance among persons who have paid or promised to pay any value for the chance of obtaining the property, with

the understanding that it will be disposed of by chance.” (There are three exemptions to this prohibition including the California State Lottery, bingo for charitable purposes and a raffle conducted by a non-profit, tax-exempt organization for charitable purposes.)

Courts have used certain rules to decide whether a scheme includes consideration because it is not always clear. If a person is eligible to win a prize without purchase, there is no consideration, and the contest is legal. If some people may pay money - for example, an admission charge or buy a product - there is not necessarily consideration *if* others may enter the contest without such a purchase. If eligibility to win a prize is limited to those who have paid money, however, there is consideration and the contest is not legal.

Consideration in the context of research applies when subject compensation is a lottery or raffle to win a prize (e.g., gift certificate, iPad, etc.). If eligibility to win a prize is limited to those who participate in the research, there is consideration therefore the contest is not legal.

- B. The IRB will determine whether lotteries, raffles, and/or drawings may be used to recruit or retain participants. For the IRB to consider approving the use of lotteries, raffles, and/or drawings, the following must be considered:
1. The study involves minimal risk to participants (Exempt or Expedited).
 2. The prize is less than \$600 and will not unduly influence participation in the research.
 3. The subject compensation process must include the following:
 - a) Procedures to ensure that any individual who is asked to participate in the research study but declines, who consents/assents to enroll in the study, or who fails to complete the study, will be given equal compensation by having an equal chance of winning. In other words, if an individual is eligible to participate in the study, and therefore the lottery, raffle and/or drawing, they are not required to participate in the study to be eligible to participate in the lottery, raffle, and/or drawing;
 - b) Procedures for the inclusion of an individual who is not asked to participate in the study but wishes to be included in the lottery, raffle, and/or drawing;
 - c) A fair method of choosing the winner and how the winner will be notified; and
 - d) Disclosure of the approximate chance of winning (e.g., no less than 1 in 1000) in the consent/assent.

This information, along with specifically informing individuals that they are not guaranteed to win any prize in the drawing and that the only compensation they will receive is the “1 in X” chance of winning, must be provided in the consent/assent and recruitment materials for those who wish to participate in the lottery but not the research study.

- XIII. **When research is sponsored by the Department of Defense (DoD)**
- A. When research involves U.S. military personnel policies and procedures include additional protections for military research participants to minimize undue influence as follows:
1. Officers are not permitted to influence the decision of their subordinates;
 2. Officers and senior non-commissioned officers may not be present at the time of recruitment;
 3. Officers and senior non-commissioned officers have a separate opportunity to participate;
 4. When recruitment involves a percentage of a unit, an independent ombudsman is present.
- XIV. **When following Department of Justice Regulations and Guidance**
- A. When research is conducted within the Bureau of Prisons:
1. The selection of participants within any one organization must be equitable;
 2. Incentives may not be offered to help persuade inmate participants to participate. However, soft drinks and snacks to be consumed at the test setting may be offered;
 3. Reasonable accommodations such as nominal monetary recompense for time and effort may be offered to non-confined research participants who are both:
 - a) No longer in the Bureau of Prisons custody,
 - b) Participating in authorized research being conducted by Bureau employees or contractors.
- XV. **California Info Information Practices Act of 1977**
- A. An agency shall not disclose any personal information in a manner that would link the information disclosed to the individual to whom it pertains unless the information is disclosed as per **Cal. Civ. Code §1798.24(t)**, with all criteria satisfied as part of the Committee for the Protection of Human Subjects (CPHS) for the California Health and Human Services Agency (CHHSA) or an institutional review board.
1. The UCI IRB will ensure that personal information is protected in accordance with Cal. Civ. Code §1798.24(t) by reviewing and confirming the requisite elements as part of the IRB Application.

References:

21 CFR 56.107(a)
21 CFR 56.111(a)(3)
21 CFR 56.111(b)
21 CFR 50.20
21 CFR 50.25
21 CFR 812.20(b)(11)
California Health and Safety Code - Section 445
U.S. Food and Drug Administration Information Sheets: "Recruiting Study Subjects,"
1998 Update

Clarification of Ethics Opinion 6.03, 65. Finder's Fees: Payment for the Referral of
Patients to Clinical Research Studies
42 U.S.C. '1320a-7b(b)

SECNAVINST 3900.39D, para. 6a(6)
DoDD 3216.2, para. 4.4.4
DoJ: 28 CFR 512.11 (4,5)

Procedure Number: 22.A**Title: Procedure for Advertisement/Recruitment****Procedure:**

This procedure provides guidance for advertising associated with the recruitment of human participants for research conducted under the jurisdiction of the UC Irvine (UCI) Institutional Review Board (IRB).

I. Lead Researcher (LR) Responsibilities

- A. The LR will submit all types of advertisements (e.g., television ads, radio, videotape, print advertisements, e-mail solicitations, and Internet websites) associated with the recruitment of research participants to the UCI IRB for review and approval. This includes any sponsor-provided advertisements or Investigator-drafted advertisements.
- B. The IRB reviews advertisements in their final form prior to final IRB approval for use.
- C. The UCI IRB considers advertising or soliciting for study participants to be the start of the informed consent and participant selection processes. Therefore, advertisements should be included as part of the initial IRB Application.
- D. IRB review and approval for additional advertisements or changes in currently approved advertisements or recruitment methods will be submitted in the form of an Amendment request to the IRB for approval prior to implementation.
- E. Campus Community e-mail solicitations are first submitted to the UCI IRB for review and approval. The IRB will provide the Investigator with the approved advertisement with an IRB approval stamp. The Investigator submits the IRB stamped mass e-mail advertisement to their School's Communication Representative for mass e-mail posting.

II. IRB Committee Responsibilities

- A. The IRB will review and approve all advertisements or means of soliciting participants in human subjects research to assure that the rights and welfare of the prospective participants are protected, and that information collected about prospective participants will be appropriately handled.
- B. The IRB will review final versions of printed advertisements to evaluate the relative size of type used and other visual effects.
- C. When advertisements are to be taped for broadcast, the IRB will review of script and the final audio or video tape prior to approval.
- D. The IRB Committee Chair or designated Committee Member may review changes to advertisements. However, the Chair or designated Committee Member may refer the advertisement to the full, convened IRB Committee if the advertisement contains subjective material which in his or her opinion needs further review.

III. IRB Analyst or Higher Responsibilities

- A. The Analyst will review all initial study submissions to determine what type of advertisements will be used for recruitment. If advertisements are planned, but not provided, the Analyst will remind the LR that submission for IRB review and approval is required prior to use.
- B. The Analyst will stamp all written forms of advertisement that include local contact information with the official IRB approval stamp.
- C. Advertisements submitted as modifications may be approved by the IRB Chair or designated Committee Member on an expedited basis.
- D. If the Chair or designated Committee Member refers the advertisement to the full, convened IRB Committee, the Analyst will facilitate scheduling on the next available agenda.

Procedure Number: 22.B:**Title: Procedure for Advertisement/Recruitment of Students and Employees as Research Participants****Procedure:**

This procedure outlines the responsibilities of the UC Irvine (UCI) Institutional Review Board (IRB) and Investigators when recruiting students and employees as participants in research conducted under the UCI IRB's jurisdiction.

I. Lead Researcher (LR) Responsibilities

The LR must take into consideration the following when recruiting students and employees as participants in human subjects research.

- A. Recruitment of students by LRs who are also faculty members or instructors at UCI.
 - 1. Lead Researchers are to advertise and recruit student participants generally, rather than recruiting individual students directly.
 - 2. An exception to this rule may be allowed when the use of one's own students is integral to the research. For example, research into teaching methods may be allowed by the IRB when sufficient precautions have been taken to protect the student-participant (e.g., using a third party to obtain informed consent).

B. Student Participation as a Class Component

- 1. The IRB may approve the giving of course credit or extra credit to students who are expected to participate in research activities as part of a class curriculum only when alternative means of obtaining course credit or extra credit is made available to students who do not wish to volunteer as research participants. Students must be given other options for fulfilling the research participation component that are comparable in terms of time, effort, and educational benefit. For example, short papers, special projects, book reports, and brief quizzes on additional reading may be offered in lieu of research participation.
- 2. These research studies may not involve more than minimal risk and students must be told that they can withdraw from the study at any time without losing the extra credit.
- 3. The use of extra credit points for participation in research studies should be limited as a reward, used only when the research is closely tied to the course subject matter, and should not raise the student's grade by more than one-half of a letter grade (e.g., B to B+).
- 4. Students should be recruited through the Social Sciences Human Subjects Pool, bulletin board postings or online advertisements, rather than individual solicitations.
- 5. Research interventions should not be conducted during class time.
- 6. Lead Researchers should be cautious about recruiting students into research of a coercive or sensitive nature (e.g., drug use, alcoholism, sexual preferences, etc.).

C. Medical School Students

1. Medical school students may only participate in research involving minimal risk and minimal interruption of time.
2. The IRB has the authority to review and approve research involving medical students. However, any IRB concerns regarding the use of medical students should be promptly forwarded to the Senior Associate Dean for Educational Affairs for review.
3. Lead Researchers should be cautious about recruiting medical students into research of a coercive or sensitive nature (e.g., drug use, alcoholism, sexual preferences, etc.).

D. Student Recruitment

Although UCI IRB approval is granted, research activities that are targeted for or designed specifically to address students from a particular Department or School may require the approval of the appropriate Dean or Department Chair before the study may commence.

E. Student Records

1. UC Irvine is subject to the provisions of Federal law known as the Family Educational Rights and Privacy Act (also referred to as FERPA). This act affords matriculated students certain rights with respect to their educational records.
2. Generally, students have the right to consent to disclosures of personally identifiable information contained in the student's education records to third parties (such as researchers). Investigators must obtain student's consent to access personally identifiable information in the student's educational records, even if consent to participate in the research may have been waived by the IRB. There are some exceptions however. (See Policy # 32.)

F. Employees

1. Lead Researchers should minimize the likelihood that employees who participate in research programs perceive that the decision will affect performance evaluations or job advancement.
2. Employees should be recruited through general announcements or advertisements, rather than individual solicitations.
3. Employees of a particular Investigator or laboratory should not be directly recruited for participation in any study conducted by that Investigator or laboratory, although such employees may, on their own, volunteer to participate.
4. Lead Researchers who include colleagues or subordinates as research participants should be able to provide a rationale other than convenience for selecting those individuals and should show that the recruitment methods do not lead colleagues to think that they will be compromised by not participating.

II. IRB Committee Responsibilities

- A. The IRB should exercise oversight with the use of faculty, instructors, students, medical students, and employees as the targeted population in research.
- B. The IRB will review the proposed involvement of faculty, instructors, students, medical students, and employees as the targeted population in research activities and when making its final determination assure that:
 - 1. Consent for participation is sought only under circumstances which minimize the possibility of coercion or undue influence, which, clearly identify methods used to maintain confidentiality;
 - 2. There are genuinely equivalent alternatives to participation available;
 - 3. The selection of participants is equitable;
 - 4. The risk of undue influence or coercion is minimized; and
 - 5. If applicable, added protections for vulnerable populations have been assured.
- C. Any concerns regarding the use of students may be promptly forwarded to the Dean of the appropriate school or Department Chair.
- D. Any concerns regarding the use of medical students may be promptly forwarded to the Associate Dean for Medical Education.
- E. The IRB will review the submitted application in accordance with Information Practices Act of 1977 and as per Cal. Civ. Code §1798.24(t).

III. IRB Analyst or Higher Responsibilities

- A. The Analyst will conduct a pre-review of all initial applications or modifications that propose the use of students, medical students, or employees as a targeted population.
- B. The Analyst will assure that the IRB Chair or Committee is aware of the inclusion of students, medical students, or employees as a targeted population.
- C. If necessary, the Analyst will facilitate communication between the IRB Committee and the Dean of the appropriate school or Department Chair or the Associate Dean for Medical Education.

References:

45 CFR 46.111

California Civil Code 1798.24 (t)

University of California, Irvine
Human Research Protections
Standard Operating Policies and Procedures

Policy Number: 23

Title: Risk/Benefit Analysis

Date of Last Revision: 12/27/04, 10/29/10, 05/01/13, 01/27/15, 03/30/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to review all human subjects research to ensure that risks to participants are *minimized* by using procedures which are consistent with sound research design and *reasonable* in relation to any anticipated benefits.

- I. In order to approve human subjects research the IRB shall determine that the following requirements are satisfied:
 - A. Risks to subjects are *minimized* by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
 - B. 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 Committee will 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.
- II. Research cannot be approved when the risks are judged unreasonable in relation to the anticipated benefits.
- III. The IRB Committee is required to consider all types of potential risks including:
 - A. **Physical Harms:** Medical research may involve exposure to minor pain, discomfort, or injury from medical procedures, or harm from possible side effects of drugs. Research designed to evaluate new drugs, biological products, procedures, or medical devices may present more than minimal risk to subjects and could potentially cause serious or disabling injuries.
 - B. **Psychological Harms:** Undesired changes in thought processes and emotion (e.g., episodes of depression, confusion, or hallucination resulting from drugs, feelings of stress, guilt, and loss of self-esteem). Changes may be transitory, recurrent, or permanent.
 - C. **Social Harms:** Invasions of privacy and breaches of confidentiality may result in embarrassment. Areas of particular sensitivity are information regarding alcohol or drug abuse, mental illness, illegal activities, and sexual behavior. Some social and behavioral research may yield information about individuals that could "label" or "stigmatize" the subjects.
 - D. **Economic Harms:** Loss of employment, financial standing, and diminished employability are types of risks that could affect one's current or future financial situation.

- E. **Legal Harms:** Breaches of confidentiality could increase the risk of criminal or civil liability depending on the type of information being collected (e.g., drug use, previous crimes, other illegal behaviors).
- IV. The IRB assumes responsibility for scientific review in conjunction with the Biostatistics, Epidemiology and Research Design (BERD) unit in the Institute for Clinical and Translational Sciences (ICTS)- for certain types of research. (See Policy # 10.) The IRB relies on outside groups (e.g., NIH and NSF peer review, Cooperative Group review) and other campus units/entities (e.g., Department Chairs, and School Deans) to aid the IRB review of scientific or scholarly merit of the research relative to the research design and the likelihood of the research achieving its aims as follows. (See Policy # 10.)
- A. The Chao Family Comprehensive Cancer Center (Cancer Center) Protocol Review and Monitoring Committee (PRMC) reviews protocols that meet the following criteria:
 - 1. The research is cancer-related¹ and hypothesis-driven,
 - 2. The research involves interaction with participants, including obtaining consent.
 - B. IRB submission timing requirements:
 - 1. Investigator-initiated studies that are greater than minimal risk require Cancer Center approval prior to IRB submission.
 - 2. NCI National Clinical Trial Network, industry-sponsored studies, and minimal risk studies may be submitted to the Cancer Center and the IRB concurrently.
 - C. Scientific Review: As noted above, UCI's IRB assumes responsibility for scientific review in conjunction with the BERD unit in the ICTS. The IRB, in conjunction with BERD will assure that the research uses procedures consistent with sound research design, the study design can be reasonably expected to answer the proposed question, and the importance of the knowledge expected to result from the research is known. Scientific review is required for the following protocols:
 - 1. Investigator authored, biomedical or clinical human subject research studies involving greater than minimal risk that have not received prior scientific or scholarly review *or*
 - 2. As required by the IRB will render a scientifically valid interpretation of the results as defined by the study plan and objectives.
 - D. Human Stem Cell Research Oversight Committee (hSCRO): hSCRO considers the ethical and social issues presented by human stem cell activities. The hSCRO reviews the scientific/scholarly merit of human stem cell activities.
 - E. The deans, department chairs or directors of the UCI General campus academic and research units are responsible for ensuring that human research conducted by their faculty, staff, and students receive a sufficient level of scientific or scholarly review, and that adequate resources are available to protect participants involved as subjects in human research. The signature of the dean, department chair or director

¹ Studies involving participants with cancer, any active intervention (e.g., behavioral or pharmacological) involving cancer or pre-cancerous participants, or participants of a study involving a specific cancer focus (e.g., program evaluations, quality-of-life survey health education, etc.).

on the Institutional Review Board (IRB) Application certifies that these issues have been addressed and approved by the academic or research unit.

- V. For research conducted within the Bureau of Prisons, the research must also have an adequate research design and also contribute to the advancement of knowledge about corrections.
- VI. For studies that involve DoD-supported research with human subjects, independent review of the research for scientific merit or scholarship is required prior to IRB review.

Procedure Number: 23.A**Title: Procedure for Risk/Benefit Determination****Procedure:**

This procedure outlines the responsibilities of Investigators and the UC Irvine (UCI) Institutional Review Board (IRB) when conducting the analysis of the risks and benefits associated with the research.

I. Lead Researcher (LR) Responsibilities

- A. Complete the IRB Application in its entirety.
 - 1. Risk Assessment
 - a. The Investigator determines the level of review based upon his/her/ their assessment of the possible risks to participants; and
 - b. If the research qualifies for exempt or expedited review, the Investigator provides the applicable category and a justification for the level of review and category chosen.
 - 2. Risks and Discomforts
 - a. The Investigator describes the potential risks/discomforts (e.g., physical, psychological, social, economic) associated with each intervention or research procedure;
 - b. Estimates the probability (e.g., chance or likelihood of occurrence) that a given harm may occur and its severity (e.g., mild, moderate, severe);
 - c. Describes measures that will be taken to prevent and minimize any potential risks/discomforts; and
 - d. For research reviewed by the full IRB Committee, the Investigator states whether study procedures may involve risks to the subject (or embryo or fetus, if the subject is or may become pregnant) that are currently unforeseeable.
 - 3. Potential Benefits
 - a. The Investigator discusses the benefits that may accrue directly to the subjects and,
 - b. Describes the potential societal benefit(s) that may be expected from this research.
- B. Seek scientific or scholarly review prior to IRB review, as applicable.
- C. Ensure that the Informed Consent form(s) or Study Information sheet appropriately describes the potential risks and anticipated benefits of the research.
- D. Reply to all requests for revisions and/or a clarification requested by the pre-reviewers or reviewers, when applicable, and provides an explanation if the requested revisions are not made.

II. IRB Committee Responsibilities

- A. The assessment of risks and benefits includes the following steps:
 - 1. Identify the risks associated with the research, as distinguished from the risks of therapies the subjects would receive even if not participating in research;

- a) As applicable, evaluate the available clinical and nonclinical information on an investigational product to determine if the data is adequate to support the proposed clinical trial.
2. Consider all types of potential risks/harms:
 - a. Physical
 - b. Psychological
 - c. Social
 - d. Economic
 - e. Legal
3. Determine that the risks will be minimized to the extent possible;
4. Determine whether the research involves virtually no risk (Exempt); no greater than minimal risk (may qualify for Expedited review) procedures; or greater than minimal risk (requires review at a full IRB Committee at a convened meeting).
5. Identify the probable benefits to be derived from the research;
6. Determine that the risks are reasonable in relation to the benefits to participants, if any, and the importance of the knowledge to be gained;
7. Assure that potential subjects will be provided with an accurate and fair description of the risks or discomforts and the anticipated benefits; and,
8. Determine intervals of periodic review, and, where appropriate, determine that adequate provisions are in place for monitoring the data collected.
- B. Consider whether the provisions to protect the privacy of participants are adequate to maintain the confidentiality of the data (See IRB Policy # 24.)
- C. Where the subjects are likely to be members of a vulnerable population (e.g., mentally disabled), determine that appropriate additional safeguards are in place to protect the rights and welfare of the participants. (See IRB Policies # 36-40.)

III. **IRB Analyst or Higher Responsibilities**

- A. The Analyst will pre-review the IRB Application, and other documentation to assure that they meet the requirements under the IRB policies and procedures.
- B. Ensure that the results of the scientific or scholarly review, as applicable, are provided to the IRB committee.
- C. If additional information regarding potential risks/harms or possible benefits is needed, the Analyst will contact the LR and request the additional information.

References:

21 CFR 56.111(a)(1-2, 6)

45 CFR 46.111(a)(1-2, 6)

OHRP IRB Guidebook, Chapter 3: "Basic IRB Review", Section A, "Risk/Benefit Analysis."

IRB Policy 24, "Subject Privacy and Protection of Confidentiality"

IRB Policies 36-40, "Vulnerable Populations"

ICH-GCP (E6)

Guidance for IRBs: Clinical Investigators, and Sponsors: IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE is Needed

Policy Number 24

Title: Subject Privacy, Protection of Confidentiality and Data Security

**Date of Last Revision: 03/30/09; 10/11/10; 05/10/15; 03/03/16; 05/01/16; 09/27/17;
10/19/17; 06/13/18; 09/14/22**

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to consider whether adequate provisions exist for the protection of subject privacy, the maintenance of confidentiality of identifiable research data and data security. To ensure that risks related to a potential breach of confidentiality are minimized, all human subjects research protocols must have acceptable, effective, and documented procedures for the protection of identifiable and/or confidential information collected or examined for research purposes.

The UCI IRB, in its role as the Privacy Board for Research, also ensures that research data be used, stored and/or disclosed according to current HIPAA regulations.

I. Research Design

Research should be designed to minimize the intrusion on privacy to no more than is necessary. Confidentiality of the data obtained during the research should be protected throughout the project including after the research is completed.

II. Protection of Privacy

Privacy refers to a person's desire to control the access of others to themselves. For example, persons may not want to be seen entering a place that might stigmatize them, such as a pregnancy counseling center clearly identified by signs on the front of the building. The evaluation of privacy also involves consideration of how the researcher accesses information from or about potential participants (e.g., recruitment process). IRB members consider strategies to protect privacy interests relating to contact with potential participants, and access to private information.

III. Identification of Research Records

- A. Protocols should be designed to minimize the need to collect and maintain identifiable information about research subjects.
- B. If possible, data should be collected anonymously, or the identifiers should be removed and destroyed as soon as possible.
- C. When it is necessary to collect and maintain identifiable data, the IRB will ensure that the protocol includes the necessary safeguards to maintain confidentiality of identifiable data and data security appropriate to the degree of risk from disclosure.

- IV. **Health Insurance Portability and Accountability Act of 1996 (HIPAA)**
- A. HIPAA is the acronym for the Health Insurance Portability and Accountability Act of 1996.
 - B. HIPAA affects only that research which uses, creates, or discloses "Protected Health Information" or "Personal Health Information" (PHI).
 - C. Researchers often have legitimate needs to use, access, and disclose PHI to carry out a wide range of health research studies. The Privacy Rule protects PHI while providing ways for researchers to access and use PHI when necessary to conduct research.
 - D. The intention of HIPAA is to protect patients from inappropriate disclosures of PHI that can cause harm to a person's insurability, employability, etc.
 - E. PHI is information that can be linked to a particular person and that is created, used, or disclosed while providing a health care service (i.e., diagnosis or treatment).
 - 1. Examples of PHI include, but are not limited to, the following:
 - a. Names;
 - b. All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly available data from the Bureau of the Census:
 - (1) The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and
 - (2) The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people are changed to 000.
 - c. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older;
 - d. Telephone numbers;
 - e. Fax numbers;
 - f. Electronic mail addresses;
 - g. Social security numbers;
 - h. Medical record numbers;
 - i. Health plan beneficiary numbers;
 - j. Account numbers;
 - k. Certificate/license numbers;
 - l. Vehicle identifiers and serial numbers, including license plate numbers;
 - m. Device identifiers and serial numbers;
 - n. Web Universal Resource Locators (URLs)
 - o. Internet Protocol (IP) address numbers;
 - p. Biometric identifiers, including finger and voice prints;
 - q. Full face photographic images and any comparable images; and
 - r. Any other unique identifying number, characteristic or code.

- F. The Privacy Rule is a nickname for DHHS' regulation, "Standards for Privacy of Individually Identifiable Health Information," applicable to entities covered by HIPAA.
- G. In May 2002, the Board of Regents designated the University of California as a HIPAA hybrid covered entity and determined that UC would be a Single Health Care Component (SHCC) for the purposes of complying with the HIPAA Privacy Rule.
- H. The research function is excluded from HIPAA coverage at UC. Therefore, when a researcher conducting research pursuant to an IRB-approved protocol wants to obtain PHI from records maintained by the SHCC (such as those found in a hospital's medical records department), the Privacy Rule requires that the SHCC receive specific assurances from the UCI IRB.
- I. **The IRB acts as a Privacy Board for Research to review the use/disclosure of PHI and to determine whether participants should sign an "Authorization" (an addendum to the consent to participate in research) or if a Waiver of HIPAA Authorization (roughly analogous to a Waiver of Consent under the Common Rule) may be granted.**
- J. Waivers of HIPAA Authorization: Although it is always preferred to get permission to use an individual's PHI, HIPAA permits research using PHI without obtaining permission (called "Authorization"). To waive HIPAA Authorization, the IRB must determine that the study meets all the following criteria:
 - 1. The use or disclosure of PHI involves no more than minimal risk;
 - 2. Granting of the waiver will not adversely affect privacy rights and welfare of the individuals whose records will be used;
 - 3. The protocol could not practicably be conducted without a waiver;
 - 4. The protocol could not practicably be conducted without use of PHI;
 - 5. The privacy risks are reasonable relative to the anticipated benefits of research;
 - 6. An adequate plan to protect identifiers from improper use and disclosure is included in the research proposal;
 - 7. An adequate plan to destroy the identifiers at the earliest opportunity, or justification for retaining identifiers, is included in the research protocol;
 - 8. The research plan includes written assurances that PHI will not be re-used or disclosed for other purposes; and
 - 9. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
- K. If the IRB permits a waiver of HIPAA Authorization, the justification is documented in the protocol file and, if applicable, the IRB meeting minutes.
- L. **Limited Data Set (LDS)** - A limited set of identifiable information in which most of the identifiers for the individual, the individual's relatives, employers and household members have been removed.
 - 1. The only allowable PHI identifiers are:
 - a. 5-digit zip code (4-digit extension is not allowed)
 - b. Full dates of birth or death
 - c. Full date(s) of service (admission and discharge)
 - d. Geographic subdivision (other than street address)
 - 2. For direct access to the medical record to obtain a LDS, since an LDS is identifiable under HIPAA, a waiver of HIPAA Authorization is

required or a signed Data Use Agreement (DUA).

3. Investigators may be required to sign a DUA through UCI Sponsored Projects for data received or sent out of UCI, to give assurance that the information will be protected.

V. Protection of Confidentiality and Data Security

- A. A guiding principle of research involving human volunteers is that a participant's privacy must be respected, and confidentiality of person-identifiable data must be preserved.
- B. Access to research data should be based on a "need to know" and "minimum necessary" standard.
- C. Since a breach of confidentiality may present a risk of harm to subjects (e.g., as when the researcher obtains information about the participants that would, if disclosed by the researcher, jeopardize their employment, social standing, or lead to criminal or civil prosecution), the IRB carefully considers whether there is an appropriate plan to protect the confidentiality of research data (e.g., coding data, removal of identifying information, limiting access to data, use of Certificates of Confidentiality or other methods as appropriate).
- D. The IRB also evaluates the following:
 1. Whether methods used to identify and recruit potential participants protect subject privacy;
 2. Whether the consent form fully discloses the extent to which confidentiality will be protected and the potential risks to subject privacy/confidentiality; and
 3. Whether the appropriate physical safeguards are in place for protecting confidentiality of research data and data security (e.g., maintenance of records in locked files, separation of person-identifiable data from study data and/or use of unique study ID numbers in place of identifiers, etc.)
- E. When applicable, the IRB ensures that prospective subjects are informed of the following in the consent form:
 1. Whether records identifying the subjects will be maintained;
 2. How the subject identifiable data will be maintained to ensure confidentiality;
 3. How long the subject identifiable data will be maintained; and
 4. Who will have access to the data.
 - a. When FDA-regulated products are being studied; subjects are informed that the FDA may have access to their study records to protect their safety and welfare. Any information derived from the research project that personally identifies the subject will not be voluntarily released or disclosed by these entities without the subject's separate consent, except as specifically required by law; and
 - b. Research records provided to authorized, non-UCI entities will not contain identifiable information about the subject.
 5. Publications and/or presentations that result from the study will not include identifiable information about the subject.

VI. Certificates of Confidentiality

- A. Certificates of Confidentiality are issued by the DHHS' National Institutes of Health (NIH) to protect the privacy of research subjects by protecting researchers and institutions from being compelled to release information

that could be used to identify subjects with a biomedical, behavioral, clinical or other research study.

- B. Section 2012 of the 21st Century Cures Act, enacted December 13, 2016, enacts new provisions governing the authority of the Secretary of Health and Human Services (Secretary) to protect the privacy of individuals who are the subjects of research, including significant amendments to the previous statutory authority for such protections, under subsection 301(d) of the Public Health Service Act.
1. Specifically, the amended authority requires the Secretary to issue to investigators or institutions engaged in biomedical, behavioral, clinical, or other research in which identifiable, sensitive information is collected ("Covered Information"), a Certificate to protect the privacy of individuals who are subjects of such research, if the research is funded wholly or in part by the Federal Government.
 2. The authority also specifies the prohibitions on disclosure of the names of research participants or any information, documents, or biospecimens that contain identifiable, sensitive information collected or used in research by an investigator or institution with a Certificate.
 3. Certificates of Confidentiality are issued to institutions or universities where the research is conducted. Any investigator or institution for which identifiable sensitive information is shared is also subject to disclosure restrictions.
 4. The Certificates of Confidentiality protects the privacy of subjects by limiting the disclosure of identifiable, sensitive information. Under the new policy, disclosure is not up to the discretion of the investigator. Disclosure is only permitted in the following circumstances:
 - a) if required by other Federal, State, or local laws, such as for reporting of communicable diseases
 - b) if the subject consents; or
 - c) for the purposes of scientific research that is compliant with human subjects regulations.
 5. If the research is not federally funded, the Secretary may issue a Certificate to an investigator or institution engaged in such research, upon application.
- C. Because of the protections it affords, the IRB may require researchers to acquire a Certificate of Confidentiality as a condition of approval for research involving sensitive matters. Examples of sensitive research activities include, but are not limited to, the following:
1. Collecting genetic information;
 2. Collecting information on psychological well-being of subjects;
 3. Collecting information on subjects' sexual attitudes, preferences or practices;
 4. Collecting data on substance abuse or other illegal risk behaviors;
 5. Studies where subjects may be involved in litigation related to exposures under study (e.g., breast implants, environmental or occupational exposures).
- D. Not eligible for a Certificate are activities that are:
1. Not research;
 2. Not collecting personally identifiable information;
 3. Not reviewed and approved by the IRB as required by these guidelines; or
 4. Collecting information that if disclosed would not significantly harm or damage the participant.

- E. In general, certificates are issued for single, well-defined research protocols rather than groups or classes of protocols.
 - 1. In some instances, they can be issued for cooperative multi-site protocols. A coordinating center or "lead" institution designated by the NIH program officer can apply on behalf of all institutions associated with the multi-site project.
 - 2. The lead institution must ensure that all participating institutions conform to the application assurances and inform participants appropriately about the Certificate, its protections, and the circumstances in which voluntary disclosures would be made.
- F. A Certificate of Confidentiality protects all information identifiable to any individual who participates as a research subject (i.e., about whom the investigator maintains identifying information) during any time the Certificate is in effect.
- G. Generally, Certificates are effective on the date of issuance or upon commencement of the research protocol if that occurs after the date of issuance.
 - 1. The expiration date usually corresponds with the completion of the study.
 - 2. The Certificate states the date upon which it becomes effective and the date upon which it expires.
 - 3. Although an extension of coverage must be requested if the research extends beyond the expiration date of the original Certificate, the protection afforded by the Certificate is permanent (i.e., all personally identifiable information maintained about participants in the protocol while the Certificate is in effect is protected indefinitely).
- H. Limitations and Exceptions
 - 1. Subjects may authorize in writing the investigator to release their information to insurers, employers, or other third parties. In such cases, researchers may not use the Certificate to refuse disclosure.
 - 2. Additionally, while Certificates protect against involuntary disclosure, they do not protect subjects against voluntary disclosure of information by the subject (e.g., when research subjects voluntarily disclose their research data or information to their physicians or other third parties).
 - 3. In accordance with California law, researchers are not prevented from the voluntary disclosure of matters such as child abuse, elder abuse, reportable communicable diseases, or subject's threatened violence to self or others.
 - 4. Finally, Certificates do not authorize researchers to refuse to disclose information about subjects if authorized DHHS personnel request such information for an audit or program evaluation.
 - a. Researchers cannot refuse to disclose such information if it is required to be disclosed by the Federal Food, Drug, and Cosmetic Act.

VII. **Use of State Death Records**

- A. Effective January 1, 2003, California law requires local IRBs to review research using California state death data files containing personal identifying information (i.e., state issued death certificates and indices).
 - 1. This law is more restrictive than federal human research protection regulations, which govern use of living humans or identifiable data about living humans.

2. The state requires IRBs to protect information about deceased persons as carefully as information about living persons.
- B. In order for an IRB to permit such a study, the state requires that the researcher have a "valid scientific interest."
- C. State death records do not fall under the federal exemption from IRB approval for research on publicly available existing data (as these records are no longer publicly available); therefore, such studies may require expedited review.

VIII. **California Info Information Practices Act of 1977**

- A. An agency shall not disclose any personal information in a manner that would link the information disclosed to the individual to whom it pertains unless the information is disclosed as per **Cal. Civ. Code §1798.24(t)**, with all criteria satisfied as part of the Committee for the Protection of Human Subjects (CPHS) for the California Health and Human Services Agency (CHHSA) or an institutional review board.
 1. The UCI IRB will ensure that personal information is protected in accordance with Cal. Civ. Code §1798.24(t) by reviewing and confirming the requisite elements as part of the IRB Application.

References:

21 CFR §56.111(a)(7)
 21 CFR 50.25(a)(5)
 21 CFR 56.110
 21 CFR 312.68
 21 CFR 812.145(c)
 45 CFR 46.110
 45 CFR 46.116(a)(5)
 45 CFR §46.111(a)(7)
 45 CFR 164.514(e)
 45 CFR 528(a)(viii)
 California Health and Safety Code 102231
 Child Abuse and Neglect Reporting Act, Cal. Penal Code, Section 11165 et seq.; Elder Abuse and Dependent Adult Civil Protection Act, Cal. Welfare. & Inst. Code, Section 15601 et seq.; Reports of Injuries, Cal. Penal Code, Section 11160 et seq.
 National Institutes of Health, Office of Extramural Research, "Certificates of Confidentiality: Background Information", Web Posting: 7/22/2003
 OHRP Compliance Activities: Common Findings and Guidance #3, #4
 Section 301(d) of the Public Health Service Act (42 U.S.C. 241(d)).
 Privacy Rule of the Health Insurance Portability and Accountability Act of 1996, Section 64.514.
 Public Health Service Act, S 301(d), 42 U.S.C. s 241 (d), as added by Pub. L. No. 100-607, S 163 (November 4, 1988).
 DOJ: 28 CFR 22, 28 CFR 512.8,11,12,13,15
 UCOP HIPAA Glossary: <http://policy.ucop.edu/doc/1110170/HIPAA-11>
 UCOP HIPAA and Research: <http://policy.ucop.edu/doc/1100616/HIPAA%2014>
 Cal. Civ. Code §1798.24(t)
<https://www.energy.gov/eere/communicationstandards/collecting-personally-identifiable-information-through-web-and-user>

Procedure Number: 24.A**Title: Procedure to Ensure Subject Privacy and the Protection of Confidentiality****Procedure:**

This procedure outlines the responsibilities of the UC Irvine (UCI) Institutional Review Board (IRB) and guidance to Investigators to assure that all studies conducted at UC Irvine (UCI) ensure subject privacy and confidentiality of data and are in compliance with the HIPAA regulations.

I. Lead Researcher (LR) Responsibilities

- A. LRs should make every effort to reduce the likelihood of a potential breach in confidentiality; especially when a breach of research data could reasonably place subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, or reputation. The LR should consider the following methods of securing data when designing his/her research:
 - 1. Collect only the minimum necessary subject identifiers.
 - 2. Remove/destroy subject identifiers as soon as they are no longer needed.
 - 3. Limit physical access to any area or computer that contains subject identifiers.
 - 4. Limit electronic access to any computer that contains subject identifiers.
 - 5. Avoid storing subject identifiable data on portable devices as these devices are particularly susceptible to loss or theft. If there is a necessity to use portable devices for initial collection of subject identifiers, the data files should be encrypted, and subject identifiers transferred to a secure system as soon as possible.
 - 6. Remove necessary subject identifiers from data files and encrypt data files if stored electronically. Identifiers should be stored in a physically separate and secure location from the data files and associated with the data files through a key code that is also stored in a separate and secure location.
 - 7. If subject identifiers will be retained in the data files because of the specific needs of the research study, additional justification must be provided by the Researcher to justify retention.
 - 8. Use only secure modes of transmission of data; subject identifiers submitted over a public network should be encrypted.
 - 9. Review the UCI [Office of Information Technology \(OIT\) website](#) for additional recommendations on how to best secure confidential research data.
- B. In the Confidentiality section of the IRB Application, LRs must address the method of collecting, recording, coding and maintaining data, as well as specify who will have access to the data and at what point subject identifiable data will be de-identified or destroyed.
- C. In the Informed consent document, researchers must describe the extent, if any, to which confidentiality of records identifying the subject will be maintained.
- D. If there is an inadvertent breach of confidentiality of the research data which causes harm or places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm), the LR must

report this to the IRB through the Reportable Event reporting process within 5 working days of the researcher becoming aware of the event.

1. If there is such a breach, investigators should contact OIT to report that a potential security breach has occurred and request immediate notification of the OIT security staff and the Security Breach Lead Campus Authorities. Send additional information via email to security@uci.edu with a copy to security-lca@uci.edu.
 2. For a data security breach that involves protected health information under HIPAA, investigators should also contact the Hospital Compliance Office at 714-456-3674.
- E. LRs wanting to create, use, or disclose PHI as part of the research activities must indicate in the IRB Application which PHI identifiers will be accessed, created, or disclosed. The LR must also submit the informed consent documents to the IRB for review and approval prior to consenting participants.
- F. For studies requesting a waiver of authorization to use or disclose PHI, the LR must explain why the study meets all of the waiver criteria and submit to the IRB for review and approval.
- G. LRs may be required to sign a Data Use and Transfer Agreement through UCI Sponsored Projects for data sent and received by UCI to give assurance that the information will be protected.
- H. Investigators wanting, for research purposes, to obtain California state death data files containing personal identifying information must submit an IRB Application for IRB review.
- I. **Department of Justice (DOJ) Regulations and Guidance:** (Specifically in regard to research funded by the National Institute of Justice (NIJ)):
1. All projects are required to have a privacy certificate approved by the NIJ Human Subjects Protection Officer.
 2. All researcher and research staff are required to sign employee confidentiality statements, which are maintained by the responsible researcher.
 3. For National Institute of Justice-funded research, a copy of all data must be de-identified and sent to the National Archive of Criminal Justice Data, including copies of the informed consent document, data collection instruments, surveys or other relevant research materials.
- J. **Bureau of Prisons Requirements:**
1. A non-employee of the Bureau may receive records in a form not individually identifiable when advance adequate written assurance that the record will be used solely as statistical research or reporting record is provided to the agency.
 2. Except as noted in the informed consent statement to the subject, the researcher must not provide research information which identifies a subject to any person without that subject's prior written consent to release the information.
 - a) For example, research information identifiable to a particular individual cannot be admitted as evidence or used for any purpose in any action, suit or other judicial, administrative, or legislative proceeding without the written consent of the individual to whom the data pertains.
 3. Except for computerized data records maintained at an official Department of Justice site, records which contain non disclosable information directly traceable to a specific person may not be stored in, or introduced into, an electronic retrieval system.

4. If the researcher is conducting a study of special interest to the Office of Research and Evaluation (ORE), but the study is not a joint project involving ORE, the researcher may be asked to provide ORE with the computerized research data, not identifiable to individual subjects, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the project.
- K. **Department of Energy (DOE):** When Human Research is conducted or funded by the DOE, the IRB will review for the purposes of compliance with the DOE requirements for the protection of personally identifiable information.

II. **IRB Committee Responsibilities**

- A. The IRB Committee will consider as part of their review, whether security procedures regarding access and storage of the data are adequate.
- B. The IRB Committee will also consider whether the use of personal identifiers or codes linking the data to the participant is justifiable.
- C. Any unanticipated problems related to data security will be reviewed. (See HRP Policy # 19.)
- D. When a Certificate of Confidentiality has been issued for a protocol, the IRB ensures that the consent form includes:
 1. A statement that notifies subjects that a Certificate is in effect; and
 2. A fair and clear explanation of the protection that the Certificate affords, including the limitations and exceptions noted below.

III. **IRB Privacy Board Responsibilities**

- A. The IRB will review all IRB applications and human subject research proposals for adequate privacy measures and to maintain the confidentiality of the research participants and their data.
- B. The IRB will review all IRB applications involving HIPAA and determine whether:
 1. The Investigator should obtain authorization from the participants to access, create or disclose PHI, or
 2. The IRB may review and approve requests for a waiver of HIPAA authorization.
- C. The IRB may review and approve the disclosure of a limited data set through expedited procedures.

IV. IRB Analyst or Higher Responsibilities

- A. The Analyst will assess all new submissions to ensure that the Investigator addressed concerns regarding privacy, confidentiality provisions and data security.
- B. The Analyst will contact the LR to request additional information or documentation, as necessary to ensure that the LR addresses concerns/problems regarding privacy, confidentiality and data security as noted in the IRB Application, Amendment or Renewal.
- C. Any new information provided related to data security will be handled as specified in HRP Procedure # 19.A.
- D. The Analyst may prepare the study for IRB review and approval prior to receiving the appropriate template language. However, the reviewers must be made aware that the necessary revisions have been requested and the status of the approval must be pending receipt of these changes.

Policy Number: 25

Title: Investigator and Research Personnel Conflicts of Interest

Date of Last Revision: 07/28/06, 10/03/10, 08/08/11, 04/03/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) that all disclosable financial interests be captured as part of the IRB application for review by the COIOC and the IRB to assure protection of the rights and welfare of participants in human subjects research.

Disclosable Financial Interests are any of the following financial interests of any key research personnel (Lead Researcher and all individuals responsible for the design or conduct of the study), or his or her immediate family (spouse, domestic partner, and child), in aggregate:

1. Ownership interest, stock, stock options, or other financial interest related to the research, unless it meets all four tests:
 - a. Less than \$10,000 when aggregated for the immediate family and
 - b. Publicly traded on a stock exchange and
 - c. Value will not be affected by the outcome of the research and
 - d. Less than 5% interest in any one single entity.
2. Compensation related to the research, including salary, consultant payments, honoraria, royalty payments, dividends, loans, or any other payments or consideration with value, including payments made to the University Health Sciences Compensation Plan, unless it meets both of the following tests:
 - a. Less than \$10,000 in the past year when aggregated for the immediate family and the
 - b. Amount will not be affected by the outcome of the research.
3. Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright or licensing agreement.
4. Board or executive relationship (e.g., director, officer, partner, or trustee) related to the research, regardless of compensation.

References:

University Policy on Disclosure of Financial Interest in Private Sponsors of Research (APM-028), dated 10/23/18

University Guidelines for Disclosure and Review of Principal Investigator's Financial Interest in Private Sponsors of Research, dated April 27, 1984

UCI Policy on Disclosure of Principal Investigator's Financial Interests in Nongovernmental Sponsors of Research, revised December 15, 1999

UCI Research Policy for Conflict of Interest in Human Subjects Research

42 CFR 50.603

21 CFR 54.1

Procedure Number: 25.A**Title: Procedure for Investigator and Research Personnel Disclosure of Conflicts of Interest****Procedure:**

This procedure outlines the process for reporting and disclosing any conflicts of interest in human subjects research.

I. Lead Researcher (LR) Responsibilities

- A. A LR who is conducting human subjects research at UCI or utilizing UCI resources or facilities is required to disclose all disclosable financial interests:
 - 1. That would reasonably appear to be affected by the research; or
 - 2. In entities whose financial interests would reasonably appear to be affected by the research.
 - 3. This requirement applies to all studies, sponsored or non-sponsored.
- B. The LR is responsible for submitting financial disclosures, if any, from all research personnel listed on the application and protocol.
- C. Disclosures must be submitted:
 - 1. At initial IRB submission via the electronic IRB submission and management system;
 - 2. As applicable through the Amendment Application.
 - 3. Within 30 days of becoming aware of any previously undisclosed financial interest using the "Disclosure of Investigator's Financial Interests" form.
- D. The Investigator must comply with the recommendations of the Conflict-of-Interest Oversight Committee (COIOC) and IRB to minimize the conflict.

II. IRB Committee Responsibilities

- A. The IRB will have final authority to decide whether an investigator's financial interest and the COIOC management plan, if any, allow the research to be approved.
- B. The IRB will review the research protocol along with the COIOC report and will either accept the management plan or revise the management plan to ensure the rights and welfare of the participants are adequately protected.

III. IRB Analyst or Higher Responsibilities

- A. When the IRB receives an IRB application where a researcher has disclosed a financial interest:
 - 1. Ensure that the COIOC Ancillary Review tab has been selected in the electronic IRB submission and management system.
 - 2. The COIOC Administrator will provide the COIOC report in the electronic IRB submission and management system and "clear" the COIOC Ancillary Review tab.
 - 3. IRB review runs concurrent with COIOC review.
 - 4. IRB final approval is pending:
 - a. COIOC review,

- b. Acceptance of the COIOC recommendations by the Associate Vice Chancellor for Research, utilizing the current email template language.
- c. After reviewing the Associate Vice Chancellor's recommendations, the IRB Chair / Vice Chair (VC) may accept or recommend full board IRB (re)review. If the IRB Chair / VC accepts the COIOC recommendations and the IRB documentation includes the required statements, IRB approval may be released. (See Section II above.)
- d. If the IRB determines that additional protections are required, the IRB Administrator informs the LR and the COIOC Administrator.

IV. **Conflict of Interest Oversight Committee (COIOC) Responsibilities**

- A. The COIOC considers the research project according to traditionally held principles of ethical conduct and academic freedom. The COIOC evaluates whether the financial interest will adversely affect the integrity of the research; there is sufficient separation of University and private interests, the proposed research is appropriate to the University, the teaching and research environment is open, freedom to publish and to disseminate research results is preserved, the University's intellectual property rights are protected, the University's facilities and resources are used appropriately, and the University receives proper compensation for their use.
- B. The COIOC also considers the effects of the disclosed financial interests on the rights and welfare of the human subject participants. The COIOC considers whether the rights of the participants would be better protected by reduction or elimination of a financial interest, separation of responsibilities for financial and research decisions, additional oversight, implementation of an independent data and monitoring committee, or any other mechanism that would mitigate the effects of the financial interest.
- C. The COIOC makes a recommendation on each disclosure to the Associate Vice Chancellor for Research, who decides whether the financial interests are acceptable or should be reduced, managed or eliminated.

V. **COIOC Administrator Responsibilities**

- A. The COIOC Administrator pre-reviews the Disclosure of Investigator's Financial Interests form to assure that the information is complete and meets the requirements under COIOC policies and procedures.
- B. The COIOC Administrator will prepare reports including, but not limited to, information obtained from a COIOC questionnaire completed by the Investigator and a copy of the protocol, for consideration by the COIOC.
- C. If additional information regarding an Investigator's financial interests is required, the Administrator will contact the Investigator and request the additional information.
- D. The COIOC Administrator enters the decision of the Committee into the COI database.
- E. The COIOC Administrator forwards the decision of the Associate Vice Chancellor for Research
- F. Once the Associate Vice Chancellor for Research accepts the financial

disclosures, the COIOC Administrator prepares the COIOC report to inform the IRBs of the results of the COIOC evaluation and management plan. The report includes the:

1. IRB Protocol number and study title;
2. Disclosing Individual's name;
3. Lead Investigator's name;
4. Study Sponsor and Award Type;
5. Description of the disclosable financial interest;
6. Scientific rationale for the research;
7. The COIOC determination;
8. An explanation for the determination; and
9. Suggested informed consent language, if any.

- G. The COIOC Administrator sends a memo to the Investigator via e-mail of the outcome of the COIOC review.

**University of California, Irvine
Human Research Protections
Standard Operating Policies and Procedures**

Policy Number: 26

Title: Compensation for Injury that Occurs During Participation in Research

Date of Last Revision: 08/10/2005, 09/23/2019, 09/25/2019, 09/15/2022

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to assure that research participants have knowledge of compensation and treatment availability for injury that may occur as a result of participation in research activities.

- I. For studies that involve greater than minimal risk, unless waived by the IRB, all participants must be provided with an explanation in the consent form as to whether any medical treatments are available if injury occurs and, if so, what they consist of and where further information may be obtained.
- II. For commercially sponsored studies, compensation or payment of immediate necessary care for injury related to participation in research activities shall be provided according to the contractual agreement between the sponsor and UC Irvine. In general, if a participant is injured as a direct result of participation in this study, the sponsor is required to reimburse the University for reasonable and necessary medical care to treat the injury. Contractual agreements are negotiate through Sponsored Projects in the Office of Research Administration.

References:

45 CFR 46

UC Operating Requirement No. 95-5: Administration of Agreements with Private Sponsors for Drug and Device Testing Using Human Subjects

OHRP Report Emergency Medical Care, May 15, 1991.

Procedure Number: 26.A**Title: Procedure for Compensation for Medical Treatment if Injury Occurs During Participation in Research****Procedure:**

This procedure provides guidance for compensation or medical treatment if injury occurs while participating in research conducted at UCI or by UCI investigators as part of their institutional responsibilities.

I. Lead Researcher (LR) Responsibilities

- A. The LR conducting greater than minimal risk research must ensure that UCI template language regarding compensation for immediate necessary care for study-related injury is included in the informed consent document template. The informed consent template is located on the IRB website at <https://research.uci.edu/human-research-protections/irb-forms/> under "IRB Consent Forms."
- B. Sponsors often request different wording for the treatment and compensation for injury policy statement, minor changes to the UC statement, or conditions for when the sponsor will pay for injury. **Such requests cannot be honored.** The wording of the statement was formulated with the advice of UC legal counsel with the intent of adhering to the requirements of federal regulations and UC's subject injury policy. The sponsor may include its name or the sponsor may remain silent on this point, in which case the reference to the sponsor should be removed from the treatment and compensation for injury policy statement. The clinical trial contract language specifies under what conditions and process a Sponsor has a duty to reimburse the University for any costs the University incurs in meeting its obligation to participants.

II. IRB Committee Responsibilities

- A. The IRB will review and approve the proposed compensation and injury language as a part of the new study submission.
- B. The IRB will render its determination for approval of compensation or medical treatment for medical injury as follows:
 - 1. The IRB will verify that the template language for injury is contained in the informed consent document.
 - 2. The IRB may verify that the compensation language is congruent with the sponsor's contract as approved by Sponsored Projects in the Office of Research Administration.
 - 3. The IRB will review the injury language to assure readability and comprehension in relation to the proposed target study population.
 - 4. For studies that involve an IRB reliance, UCI will maintain consent template injury language, as applicable in the UCI consent form/ document and for those sites where the UCI Lead Researcher is engaged in conducting research at the non-UCI site.

III. IRB Administrator Responsibilities

- A. The Administrator will review the informed consent documents verifying

that the UCI template language for compensation for immediate necessary care is detailed in the informed consent document.

- B. The Administrator may verify with Sponsored Projects that the compensation for injury language in the sponsor's agreement is congruent with the compensation for injury statement in the informed consent document.

Policy Number: 27

Title: Research Conducted at International Performance Sites

Date of Last Revision: 12/27/2004, 11/04/2010, 04/20/2012, 05/01/2016, 09/14/2018, 04/07/2020, 04/03/2022

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to assure that adequate provisions are in place for research under its jurisdiction conducted at international sites.

I. IRB Review of International Research

- A. When research is performed in other countries the IRB will ensure that the research meets equivalent levels of protection that would be required domestically considering local laws and cultural context.
 - 1. The IRB follows European Union General Data Protection Regulations for the use of identifiable data within countries of the European Union.
 - 2. The IRB abides by China's Personal Information Protection Law for processing of personal information of individuals living in *mainland China* on or after November 1, 2021.
- B. The IRB will seek the advice of legal counsel, as necessary, to resolve conflicts among applicable laws.
- C. When the non-US institution or site is a performance site "engaged" in research.
 - 1. Because UCI holds an assurance with OHRP, any non-US institution or site that will receive federal funds must file an International Federalwide Assurance (FWA) with OHRP.
 - 2. IRB or equivalent ethical board review must be conducted by a non-US IRB or equivalent ethical board review of the locality where the research will be performed. The UCI IRB must receive and review documentation of approval from the non-US IRB or equivalent ethical board review prior to the commencement of the research at the non-US institution or site.
- D. When the non-US institution or site is a performance site "not engaged" in research:
 - 1. When the non-US institution or site has an established IRB or equivalent ethical board review, the Investigator must obtain approval to conduct the research from the site's IRB or equivalent ethical board review or provide documentation that the site's IRB or equivalent ethical board has determined that approval is not necessary for the Investigator to conduct the proposed research at the site.
 - 2. When the non-US institution or site does not have an established IRB, a letter of cooperation must be obtained demonstrating that the appropriate institutional or oversight officials are permitting the research to be conducted at the performance site.
 - 3. UCI IRB approval to conduct research at the non-US institution or site is contingent upon receiving documentation of approval from the non-US IRB or equivalent ethical board review, or letter of cooperation, as applicable.

4. It is the responsibility of the UCI Investigator and the non-US institution or site to assure that the resources and facilities are appropriate for the nature of the research.
5. It is the responsibility of the UCI Investigator and the non-US institution or site to notify the UCI IRB promptly if a change in research activities alters the performance site's engagement in the research (e.g., performance site "not engaged" begins consenting research participants, etc.)
- E. When the research is funded by the Department of the Defense, the following requirements apply:
 1. The Investigator must have permission to conduct the research in that country by certification, or local ethics review (or local Naval IRB review if the research is funded by the Department of the Navy).
 2. The Investigator will follow all local laws, regulations, customs, and practices.
 3. These additional safeguards might not be applicable to social-behavioral research involving no more than minimal risk the Investigator should check with the Program Officer.
- F. The Office of Foreign Assets Control (OFAC) of the US Department of the Treasury administers economic and trade sanctions against specific countries, individuals and entities. The Lead Research should work with the Office of Research – Export Control Officer to confirm feasibility to conduct research in sanctioned countries, as well as obtain the necessary license as applicable.
- G. UCI IRB can serve as the IRB of Record for an external site engaged in non-exempt research as well as cede IRB review to a non-UCI IRB. *To ensure that appropriate regulatory requirements are addressed as part of the IRB review process, typically, international sites are excluded from these agreements.*

II. **IRB Considerations for Approval**

- A. For Federally funded research, approval of research for non-US institutions or sites "engaged" in research is only permitted if the non-US institution or site holds an Assurance with OHRP and local IRB or equivalent ethical board approval is obtained.
- B. The IRB will consider local research context (including local applicable laws) when reviewing international studies to assure protections are in place that are appropriate to the setting in which the research will be conducted. (See IRB Policy # 3.) The IRB may require an expert consultant to address issues of local research context if the IRB does not have the expertise or knowledge required to adequately evaluate the research.
- C. The informed consent documents including recruitment materials must be in a language understandable to the proposed participants. The IRB may review the translation and back translation, as applicable, of the foreign language informed consent document. The Investigator must provide the certification or credentials of the translator. (See IRB Policy # 31.)

III. **Monitoring of Approved International Research**

- A. The IRB is responsible for the ongoing review of international research conducted under its jurisdiction (including renewals and amendments).
- B. The IRB may require documentation of regular correspondence between the Investigator and the non-US institution or site.

- C. The IRB may require verification from sources other than the Investigator that there have been no substantial changes in the research since its last review as a measure of post-approval monitoring.

References:

45 CFR 46

21 CFR 50 & 56

OHRP, IRB Guidebook, Chapter VI, "Special Classes of Subjects"

71 Fed Reg. 10511 (July 7, 2006)

SECNAVINST 3900.39D, para.6i

DoDD 3216.2, para.4.9

OHRP Link to International Issues:

<http://www.hhs.gov/ohrp/international/index.html#regstd>

International Compilation of Human Research Protections – 2010 Edition:

<http://www.hhs.gov/sites/default/files/ohrp-international-compilation-2021.pdf>

Europe's [General Data Protection Regulation \(GDPR\)](#)

China's Personal Information Protection Law (PIPL):

<https://digichina.stanford.edu/work/translation-personal-information-protection-law-of-the-peoples-republic-of-china-effective-nov-1-2021/>

Procedure Number: 27.A**Title: Procedure for Research Conducted at International Performance Sites****Procedure:**

This procedure outlines the responsibilities of the UCI Institutional Review Board (IRB) and the Investigator for human subjects research conducted at international performance sites.

I. Lead Researcher (LR) Responsibilities

- A. Researchers must provide the same or equivalent protections to human participants in research conducted in other countries.
- B. When conducting international research, researchers must be aware of local laws and cultural context in all locations where the research is conducted and comply with local laws and adhere to cultural norms.
- C. It is the LR's responsibility to provide the following to the UCI IRB for International performance sites "engaged" in research:
 - 1. Adequate information and materials to evaluate local research context for the location in which the proposed research will be conducted.
 - 2. Protocol documentation that aligns with European Union General Data Protection Regulations for the use of identifiable data within countries of the European Union.
 - 3. Protocol documentation that aligns with China's Personal Information Protection Law (PIPL).
 - 4. If applicable: adequate information and materials to evaluate local research context for ethnographic research / field work proposals.
 - 5. An Office of Human Research Protections (OHRP) approved International Federalwide Assurance (FWA) for the non-US institution or site, if federally funded;
 - 6. Local IRB or equivalent ethical board approval letter for the proposed research, as applicable; and
 - 7. A translated informed consent document encompassing all of the required elements of informed consent as well as translated recruitment materials in the language appropriate to the location of the research. An English language back translation of the exact content may be requested by the IRB. The qualifications of the translator must be included in the IRB Application or Amendment request. (See IRB Policy # 31.)
- D. It is the LR's responsibility to provide to the UCI IRB the following for international performance sites "not engaged" in research:
 - 1. When the non-US institution or site has an established IRB, the Investigator must submit to the UCI IRB approval to conduct the research at the "not engaged" site from the site's IRB or provide documentation that the site's IRB has determined that approval is not necessary for the Investigator to conduct the proposed research at the site; or
 - 2. When the non-US institution or site does not have an established IRB, the Investigator must submit to the UCI IRB a letter of cooperation demonstrating that the appropriate institutional or oversight officials are permitting the research to be conducted at the performance site.
 - 3. It is the responsibility of the UCI LR and the non-US institution or site to assure that the resources and facilities are appropriate for the nature of the research;

- i. A translated informed consent document encompassing all of the required elements of informed consent in the language appropriate to the location of the research as well as translated recruitment materials must be submitted to the UCI IRB for review and approval, and upon request an English language back translation of the exact content on the translated consent. The qualifications of the translator must be included in the IRB Application or Amendment request.
- ii. Adequate information and materials are provided to evaluate local research context in the location in which the proposed research will be conducted.
- iii. It is the responsibility of the UCI LR and the non-US institution or site to notify the UCI IRB promptly if a change in research activities alters the performance site's engagement in the research (e.g., performance site "not engaged" begins consenting research participants, etc.).
- iv. The LR is responsible for providing to the IRB any reports of correspondence with the non-US institution or site and appropriate documentation of data and safety measures throughout the course of the study, including subject complaints, issues of non-compliance and unanticipated problems involving risk(s) to participants or others (e.g., a breach of participant confidentiality resulting in local ramifications).

II. IRB Responsibilities

- A. The IRB must demonstrate that it has obtained necessary information about the local research context through written material or discussions with IRB Members knowledgeable of the local context or appropriate expert consultants. The level of local knowledge required is based on the degree of risk presented by the research. Extra considerations may include the following to enhance human research protections:
 1. The economic prosperity of the area;
 2. The influence of local officials on the population;
 3. Whether the country or area allows foreign visitors;
 4. The nature of the procedures conducted (some may not allow invasive procedures such as in poorer regions);
 5. The literacy rate of the area;
 6. The local legal rights of the population;
 7. How complaints will be reported and to whom;
 8. The relevance of the research to the area's needs; and
 9. The possibility of including officials from the area in the monitoring of the research.
- B. The IRB will review the consent process taking into consideration the following additional issues:
 1. Disclosure of scientific and/or medical facts to individuals who may be unfamiliar with and distrustful of the concepts;
 2. Differences in cultural and societal norms;
 3. Differences in the role of women in society;
 4. Differences in the role of family and community in the consent process;
 5. Multiple local languages; and
 6. Literacy level.

- C. The IRB must assure that adequate provisions are outlined for data and safety monitoring keeping in mind that some non-US IRB/EC may not require continuing review of approved research.
- D. UCI IRB approval to conduct research at the non-US institution or site is contingent upon receiving documentation of the non-US performance site's IRB/EC determination, or letter of cooperation, as applicable.

III. IRB Analyst or Higher Responsibilities

- A. The Analyst will pre-review the proposed research according to applicable IRB policies and procedures.
- B. The Analyst will assure the required documents are present for adequate review by the IRB.
- C. The Analyst will provide guidance to the LR as needed (e.g., recommending a translation service, verifying OHRP IRB registration and FWA approval for the non-US site).

Policy Number: 28

Title: Research Involving Use of the Internet

Date of Last Revision: 01/21/2007, 04/03/2022

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to review the use of the internet for human research activities, including participant recruitment, in human subjects research conducted under its jurisdiction.

I. IRB Considerations in Review and Approval of Research Activities Involving the Use of the Internet

- A. The IRB must review all research activities involving the use of the internet with the same considerations and standards for approval of research (45 CFR 46.111), for informed consent, and voluntary participation as all other research activities under the jurisdiction of the UCI IRB.
- B. The informed consent process and documentation of such must include all relevant elements of informed consent as listed in the Federal regulations.
- C. The IRB review must include a consideration for the delineation of personal boundaries (i.e., would the participant consider the access private or public space of the internet).
- D. The IRB review must consider the risks to the participants and must assure that there is an appropriate level of protection.
 - 1. The IRB must consider that each communication carries the risk of a breach of confidentiality. Even when data is collected without names, web sites or email programs may still be capable of collecting identifiers.
 - 2. The IRB must consider that admonishing participants that they must be 18 years of age to participate, does not guarantee compliance.
 - 3. The IRB must consider all additional requirements for the approval of research that involves a vulnerable population as all other studies recruiting those populations.
- E. The use of online surveys must include mechanisms, if applicable, for withdrawal such as how to retrieve and discard responses from a participant who has decided to withdraw.
- F. Because there is no standard for identifying distressed participants online, the IRB must take into consideration potential participant experiences (the sensitive nature of the research) that may be distressing when evaluating the risk/benefit ratio.

II. Requirements for Evaluating the Use of the Internet for Participant Recruitment

- A. The IRB must approve all materials used for posting recruitment materials on the internet, (e.g., through a website, a banner advertisement, or an email solicitation) (See IRB Policy # 22).

- B. Investigators must follow the appropriate procedures required by UCI Communications in addition to IRB approval.
- III. **Requirements for Consideration of Data Collection and Security to Ensure Confidentiality of Data**
- A. All data must be protected as it moves along the communication pathways (e.g., from the participant to the server, from the server to the Investigator). Additionally, all databases storing identifiable information or data must be protected regardless of the source creating the data (e.g., encryption of the database, de-identifying the data).
 - B. The IRB must review and approve the method and procedures for data collection and security.
 - C. Investigators must provide information regarding the transmission and storage of the data.

References:

IRB Policy 22, "Advertisement and Recruitment."

Policy Number: 29

Title: Applicable State Laws/Regulations

Date of Last Revision: 10/12/2007, 11/02/10, 04/05/2013, 05/01/16, 09/19/22, 08/21/24

Policy:

In addition to the Office for Human Research Protections (OHRP) regulations at 45 CFR 46 and Food and Drug Administration (FDA) regulations 21 CFR 50 and 21 CFR 56, along with University of California requirements, it is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) that Investigators follow state and local laws. The following California state laws may be directly relevant to human subjects research. *(References are included in text below for ease of reference.)*

- I. **Abortion:** California Health and Safety Code (Sections 123420-123450, 123110 (a), 123115 (a), California Civil Code 56.10, 56.11)
 - A. Except in a medical emergency requiring immediate medical action, no abortion shall be performed upon a minor unless she first has given her written consent (assent) to the abortion and also has obtained the written consent (permission) of one of her parents or legal guardian.¹
 - B. The health care provider is not permitted to inform a parent or legal guardian without the minor's consent. The provider can only share the minor's medical records with the signed consent of the minor.
- II. **Acquired Immune Deficiency Syndrome (AIDS) Immunization:** California Health and Safety Code (Sections 121280, 121310, Section 121315 (a), Section 121320 (a))
 - A. States that it is in the interest of the people of California to develop a vaccine to prevent the HIV infection, and the process for the development of that vaccine, including the development of a prototype to be given to HIV negative people to determine toxicity and efficacy, the need for insurers to not withhold settlement or coverage and confidentiality measures.
 - B. A manufacturer, research institution, or researcher shall, prior to the administration of an AIDS vaccine to a research subject, obtain that woman's informed consent, that shall comply with all applicable statutes and regulations.
 1. The informed consent shall contain a statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject.
 2. A copy of the informed consent shall be maintained with the woman's medical records.

¹ *(Highlight remains in this document intentionally):* American Academy of Pediatrics v. Lungren (1997) 16 Cal.4th 307. **A minor may consent to an abortion without parental consent and without court permission.** California Health and Safety Code remains unchanged.

- C. A manufacturer, research institution, or researcher shall not be strictly liable for personal injury or wrongful death resulting from the administration of any AIDS vaccine to a research subject participating in the clinical trials described in this chapter.
 - D. No person shall be denied the opportunity to be a research subject because of the inability to pay for medical treatment.
- III. **Assisted Oocyte Production:** California Health and Safety Code (Sections 125330-125355)
- A. Prior to obtaining informed consent from a subject for assisted oocyte production (AOP) or any alternative method of ovarian retrieval on a subject for the purpose of procuring oocytes for research or the development of medical therapies, a physician and surgeon shall provide to the subject a standardized medically accurate written summary of health and consumer issues associated with AOP and any alternative methods of oocyte retrieval.
- IV. **Children / Minors:** (California Family Code, Sections 6920-6929): Describes when minors (children) may consent for themselves in various scenarios where treatment may be provided.
- A. Consent: Additional Guidance and Requirements:
 1. Children - For subjects < 18 years of age, their parents or legal guardians are the legally authorized representatives who may grant permission for their participation in research.
 2. Parents - Only the parents may grant permission for their child's participation in research. *Assent is to be sought from the child, only after permission has been obtained from the parents.* Grandparents and other relatives or caregivers may not grant permission unless they have been granted formal custody of the child by a court. In such cases, the LR must obtain a copy of the court order as evidence of that person's authority to grant permission for participation in research on the child's behalf.
 3. Children in State Custody - According to the California Department of Children's Services' (DCS) applicable policies by virtue of the court order granting DCS legal custody of certain children (e.g., foster children) that Department is the agency that is authorized to grant permission for participation in research for children in their custody. The decision of whether to grant permission for research is made on a case-by-case basis by DCS. In such cases, the LR must obtain a copy of the court order from DCS.
 4. Mature Minors or Emancipated Minors - In certain limited circumstances, it may be appropriate to allow a mature minor to consent to participation in a research study in the absence of the permission of a parent or legal guardian if the minor has the sufficient capacity to consent to the procedures involved in the research study.
 5. The IRB will determine whether the inclusion of mature minors or emancipated minors in research activities in the absence of the permission of a parent or legal is appropriate. Further, each situation is judged on a case-by-case basis. *Legal counsel may be appropriate to consider as part of this decision.* Documentation of those decisions must be included in the research file.

6. The following information provides examples of circumstances under which California law combined with federal regulations permits individuals under 18 to enroll in research without permission from parent(s) or guardian(s):
- (1) Minors may consent for themselves to medical care related to the prevention or treatment of pregnancy, but not necessarily to sterilization or abortion [California Family Code Section 6925; Health and Safety Code Section 123450 for abortion].²
 - (2) Minors 12 years of age or older have the legal right to consent on their own behalf, for:
 - a) Mental health treatment or counseling on an outpatient basis or residential shelter services (in limited circumstances) [California Family Code Section 6924].
 - b) Medical care related to the diagnosis or treatment of infectious, contagious, or communicable diseases that are required to be reported to the local health officer or a related sexually transmitted disease [California Family Code Section 6926].
 - c) Medical care related to the diagnosis or treatment of the condition and collection of medical evidence about alleged rape or sexual assault [California Family Code Section 6927].
 - d) Medical care and counseling related to the diagnosis and treatment of an alcohol or drug-related problem [California Family Code Section 6929].
 - (3) Self-sufficient minors who are:
 - a) 15 years of age or older;
 - b) living separately from their parents/guardians; and
 - c) managing their own financial affairs have the legal right to consent on their own behalf to medical or dental care [California Family Code 6922].
 - (4) Emancipated minors, those who are:
 - a) married or divorced
 - b) on active duty in the U.S. armed forces **or** emancipated by the court; and
 - c) have the legal right to consent on their own behalf to medical, dental, or mental health treatment. They also have extensive other rights to enter into legal and business arrangements, and so can consent to be included in other research (e.g., interviews, surveys) [California Family Code 7000-7143].
 - (5) Capacity to consent depends upon:
 - a) The age, ability, experience, education, training, and degree of maturity and judgment of the minor. A minor between the ages of fourteen (14) and eighteen (18)

² (Highlight remains in this document intentionally): American Academy of Pediatrics v. Lungren (1997) 16 Cal.4th 307. **A minor may consent to an abortion without parental consent and without court permission.** California Health and Safety Code remains unchanged.

- may have such capacity, but a minor under the age of fourteen (14) would rarely have such capacity;
 - b) The conduct and demeanor at the time consent is to be given;
 - c) The totality of the circumstances;
 - d) The nature of the proposed research procedures and their risks, probable consequences, benefits, and alternatives to the treatment; and
 - e) The minor's ability to appreciate the nature, risks, consequences, benefits, and alternatives of the proposed research procedures.
 - B. Emancipated Minors (California Family Code, Sections 7000-7002; 7050-7052; 7120-7123): Further defines an emancipated minor and rights of emancipated minors.
 - C. Experimental Use of Drugs and Consent for Minors Provision (California Health and Safety Code, Sections 111515– 111545): Minor consent is required prior to administering an experimental drug. Parental or legal guardian consent (permission) is required, and minor consent (assent) is required for children 7 years of age or older.
 - D. Mandatory Reporting of Child Abuse or Neglect (California Penal Code, Section 11164 -11174.3) Identifies who is a “mandated reporter” required to report known or reasonably suspected child abuse or neglect.
 - E. Parental Consent for Children to Participate in Research (California Education Code, Section 51513): For K-12 students - tests, questionnaires, surveys, or examinations containing any questions about the pupil's or the pupil's family's personal beliefs or practices in sex, family life, morality, and religion require written parental consent (permission).
- V. **Cloning:** California Health and Safety Code (Sections 24185-24187)
- A. No person shall clone a human being or engage in human reproductive cloning; no person shall purchase or sell an ovum, zygote, embryo, or fetus for the purpose of cloning a human being.
 - 1. "Clone" means the practice of creating or attempting to create a human being by transferring the nucleus from a human cell from whatever source into a human or nonhuman egg cell from which the nucleus has been removed for the purpose of, or to implant, the resulting product to initiate a pregnancy that could result in the birth of a human being.
 - 2. "Human reproductive cloning" means the creation of a human fetus that is substantially genetically identical to a previously born human being. The department may adopt, interpret, and update regulations, as necessary, for purposes of more precisely defining the procedures that constitute human reproductive cloning.
- VI. **Consent:** (California Code of Regulations, Section 650)
- A. **Anti-Kickback:** In relevant part, Section 650 provides as follows:
 - 1. The offer, delivery, receipt, or acceptance by any person licensed under this division or the Chiropractic Initiative Act of any rebate,

refund, commission, preference, patronage dividend, discount, or other consideration, whether in the form of money or otherwise, as compensation or inducement for referring patients, clients, or customers to any person, irrespective of any membership, proprietary interest or co-ownership in or with any person to whom these patients, clients, or customers are referred is unlawful.

B. **Consent:** (California Administrative Codes 4734, 4735):

1. Except as provided in Sections 4734 and 4735, a health care provider or health care institution providing care to a patient shall do the following:
 - i. Comply with an individual health care instruction of the patient and with a reasonable interpretation of that instruction made by a person then authorized to make health care decisions for the patient.
 - ii. Comply with a health care decision for the patient made by a person then authorized to make health care decisions for the patient to the same extent as if the decision had been made by the patient while having capacity.
2. California Code of Regulations, Section 50423: Describes specific consent criteria for release of confidential information or records, the need for consent only after appropriate IRB approval, that the information is provided to subjects (or their representative) in a language that is understandable, and that consent language must not appear to be exculpatory.
3. California Health and Safety Code 24173 further defines “informed consent” as the authorization given pursuant to Section 24175 to have a medical experiment performed after each of the following have been satisfied:
 - i. The subject or subject’s conservator or guardian, or other representative, as specified in Section 24175, is provided with a copy of the experimental subject’s bill of rights, prior to consenting to participate in any medical experiment, containing all the information required by Section 24172, and the copy is signed and dated by the subject or the subject’s conservator or guardian, or other representative, as specified in Section 24175.
 - ii. A written consent form is signed and dated by the subject or the subject’s conservator or guardian, or other representative, as specified in Section 24175.
 - iii. The subject or subject’s conservator or guardian, or other representative, as specified in Section 24175, is informed both verbally and within the written consent form, in nontechnical terms and in a language in which the subject or the subject’s conservator or guardian, or other representative, as specified in Section 24175, is fluent, of the following facts of the proposed medical experiment, which might influence the decision to undergo the experiment, including, but not limited to:
 - (1) An explanation of the procedures to be followed in the medical experiment and any drug or device to be utilized, including the purposes of the

procedures, drugs, or devices. If a placebo is to be administered or dispensed to a portion of the subjects involved in a medical experiment, all subjects of the experiment shall be informed of that fact; however, they need not be informed as to whether they will actually be administered or dispensed a placebo.

- (2) A description of any attendant discomfort and risks to the subject reasonably to be expected.
 - (3) An explanation of any benefits to the subject reasonably to be expected, if applicable.
 - (4) A disclosure of any appropriate alternative procedures, drugs, or devices that might be advantageous to the subject, and their relative risks and benefits.
 - (5) An estimate of the expected recovery time of the subject after the experiment.
 - (6) An offer to answer any inquiries concerning the experiment or the procedures involved.
 - (7) An instruction to the subject that he or she is free to withdraw his or her prior consent to the medical experiment and discontinue participation in the medical experiment at any time, without prejudice to the subject.
 - (8) The name, institutional affiliation, if any, and address of the person or persons actually performing and primarily responsible for the conduct of the experiment.
 - (9) The name of the sponsor or funding source, if any, or manufacturer if the experiment involves a drug or device, and the organization, if any, under whose general aegis the experiment is being conducted.
 - (10) The name, address, and phone number of an impartial third party, not associated with the experiment, to whom the subject may address complaints about the experiment.
 - (11) The material financial stake or interest, if any, that the investigator or research institution has in the outcome of the medical experiment. For purposes of this section, "material" means ten thousand dollars (\$10,000) or more in securities or other assets valued at the date of disclosure, or in relevant cumulative salary or other income, regardless of when it is earned or expected to be earned.
- iv. The written consent form is signed and dated by any person other than the subject or the conservator or guardian, or other representative of the subject, as specified in Section 24175, who can attest that the requirements for informed consent to the medical experiment have been satisfied.

(1) At UCI, the researcher finalizing the consent process and signing the written consent form satisfies this requirement.

- v. Consent is voluntary and freely given by the human subject or the conservator or guardian, or other representative, as specified by Section 24175, without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence.
- C. **Disclosure** (Regents of University of California, 51 Cal.3d 120, 271 Cal. Rptr. 146, 793 P.2d 479 (Cal. 1990)):
 - 1. In obtaining a patient's consent to a procedure, a physician must disclose personal interests unrelated to the patient's health, whether research or economic, that may affect the physician's professional judgment.
- D. **Health Plan Coverage for Clinical Trials** (California Health and Safety Code 1370.6): States in part:
 - 1. An individual or group health care service plan contract that is issued, amended, or renewed on or after January 1, 2020, shall not:
 - i. Deny a qualified enrollee's participation in an approved clinical trial.
 - ii. Deny, limit, or impose additional conditions on the coverage of routine patient care costs for items and services furnished in connection with a qualified enrollee's participation in an approved clinical trial.
 - iii. Discriminate against an enrollee based on the qualified enrollee's participation in an approved clinical trial.
- E. **No Profit from Referral** (California Health and Safety Code, Section 445): Prohibits any person from profiting from the referral of a person to a health-related facility as follows:
 - 1. No person, firm, partnership, association or corporation, or agent or employee thereof, shall for profit refer or recommend a person to a physician, hospital, health-related facility, or dispensary for any form of medical care or treatment of any ailment or physician condition. The imposition of a fee or charge for any such referral or recommendation creates a presumption that the referral or recommendation is for profit.
- F. **Protection of Human Subjects in Medical Experimentation Act** (California Health and Safety Code, Sections 24170– 24179.5): Requires that individuals be provided the Subject's Bill of Rights as part of the informed consent process prior to participation in a medical experiment.
 - 1. A "medical experiment" is defined as: (a) The severance or penetration or damaging of tissues of a human subject or the use of a drug or device, as defined in Section 109920 or 109925, electromagnetic radiation, heat or cold, or a biological substance or organism, in or upon a human subject in the practice or research of medicine in a manner not reasonably related to maintaining or improving the health of the subject or otherwise directly benefiting the subject; (b) The investigational use of a drug or device as provided in Sections 111590 and 111595; and (c) Withholding medical treatment from a human subject for any purpose other than maintenance or improvement of the health of the subject.

2. The Subject's Bill of Rights is a separate document and must be provided in addition to the Informed Consent document approved by the IRB. Per Section 24172, those rights include that the subject:
 - i. Be informed of the nature and purpose of the experiment.
 - ii. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.
 - iii. Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.
 - iv. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.
 - v. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.
 - vi. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.
 - vii. Be given an opportunity to ask any questions concerning the experiment or the procedures involved.
 - viii. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.
 - ix. Be given a copy of the signed and dated written consent form as provided for by Section 24173 or 24178.
 - x. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.
 3. The Subject' Bill of Rights is to be including for protocols involving patient care (e.g., Expanded Access, CA Right to try).
 4. The Subject's Bill of Rights is not required for protocols involving Humanitarian Use Device/s.
 5. To view the UCI Experimental Subjects Bill of Rights (available in 10 languages) go to the HRP Website, then click on "IRB Forms", then "Consent Forms": <https://research.uci.edu/human-research-protections/irb-forms/>
- G. **Signatures:** Per Health and Safety Code Section 24170-24179.5, holding an HHS Federal wide Assurance exempts UCI researchers from the requirement to obtain a signature on the California Bill of Rights. The requirement is to provide the Bill of Rights to all research participant s in medical experiments. This Bill of Rights is attached as necessary to the IRB approved Consent Form.
- H. **Surrogate Decision Maker** (California Health and Safety Code, Section 24178):
1. With respect to medical experiments that relate to the cognitive impairment, lack of capacity, or serious or life-threatening diseases and conditions of adult research participants, investigators may obtain surrogate informed consent by following a specific hierarchy for nonemergency and emergency room environments. (See Policy # 30.)
 2. Non-Medical Research: California law addresses surrogate consent in the context of medical research. The Office of the President has

acknowledged that campuses may permit the same surrogates authorized by Section 24178 may also be considered in the context of non-medical research.

3. Per the Common Rule, for research that is no more than minimal risk, the IRB may approve a request to waive some or all of the required elements of informed consent under specific circumstances, and in such cases the need for surrogate consent may also be waived. (See Policy # 30.)

VII. **Controlled Substance Research / Illegal Drug Research** - Research Advisory Panel of California, CA Health and Safety Code (Section 11480-11481; 11212-11213; 11603)

- A. California requires proposed research projects involving certain opioid, stimulant, and hallucinogenic drugs classified as Schedule I and Schedule II controlled substances to be pre-reviewed and authorized by the Research Advisory Panel of California in the Attorney General's Office.
- B. Investigators must submit applications to the panel for research projects involving:
 1. Any Schedule I controlled substance;
 2. Human research using any Schedule I or Schedule II controlled substance; or
 3. Research for the treatment of drug abuse using any drug, scheduled or not.
- C. Persons who, under applicable federal laws or regulations, are lawfully entitled to use controlled substances for the purpose of research, instruction, or analysis, may lawfully obtain and use for such purposes those substances classified in paragraphs (45) and (46) of subdivision (b) of Section 11054 of the Health and Safety Code, upon registration with and approval by the California Department of Justice for use of those substances in bona fide research, instruction, or analysis.
 1. That research, instruction, or analysis shall be carried on only under the auspices of the individual identified by the registrant as responsible for the research. Complete records of receipts, stocks at hand, and use of these controlled substances shall be kept.
 2. The Department of Justice may withdraw approval of the use of such substances at any time. The department may obtain and inspect at any time the records required to be maintained by this section.
- D. Persons who, under applicable federal laws or regulations, are lawfully entitled to use controlled substances for the purpose of research, instruction, or analysis, may lawfully obtain and use for such purposes such substances as are defined as controlled substances in this division, upon approval for use of such controlled substances in bona fide research, instruction, or analysis by the Research Advisory Panel established pursuant to Section 11480 and 11481.
 1. Such research, instruction, or analysis shall be carried on only under the auspices of the head of a research project which has been approved by the Research Advisory Panel pursuant to Section 11480 or Section 11481. Complete records of receipts, stocks at hand, and use of these controlled substances shall be kept.

- E. The Attorney General, with the approval of the Research Advisory Panel, may authorize persons engaged in research on the use and effects of controlled substances to withhold the names and other identifying characteristics of individuals who are the subjects of the research. Persons who obtain this authorization are not compelled in any civil, criminal, administrative, legislative, or other proceeding to identify the individuals who are the subjects of research for which the authorization was obtained.
- VIII. **Death Data Records:** California Health and Safety Code (Section 102231 – 102232)
- A. Death data files containing personal identifying information may be released to persons expressing a valid scientific interest, as determined by the appropriate committee constituted for the protection of human subjects that is approved by the DHHS and has a general assurance pursuant to 45 CFR Part 46.
- IX. **Drug and Alcohol Abuse, Diagnosis, or Treatment:** (Federal law 45 CFR 2, Cal. Health & Safety Code § 11845.5(c)(3).)
- A. Records containing information pertaining to alcohol and drug abuse patients are subject to special protection under federal and state law.
 - B. Federal law, 42 C.F.R. Part 2 (“Part 2”), applies to federally assisted substance use disorder programs.
 - 1. A program is “federally assisted” when it receives federal funding or is registered to dispense controlled substances related to the treatment of substance use disorders.
 - 2. A program is considered to be a “substance use disorder” program when: (1) a program or unit of a medical facility holds itself out as providing substance use disorder diagnosis, treatment, or referral for treatment; or (2) medical personnel or other medical facility staff primarily provide substance use disorder diagnosis, treatment, or referral for treatment and who are identified as such providers. [42 C.F.R. § 2.11.](#)
 - C. Part 2 allows identifiable patient information to be disclosed for the purpose of conducting scientific research without patient authorization, but only where the Part 2 Program Director makes specific determinations, described below. If the location has a program or unit dedicated to substance abuse disorders, the individual designated as director or managing director, or otherwise vested with authority to act as the chief executive officer of the Part 2 Program is the Program Director. Otherwise, the Program Director is the individual medical personnel providing substance use disorder medical services. [42 C.F.R. § 2.11.](#)
 - D. Specifically, in order for Part 2 identifiable information to be disclosed for research purposes without patient authorization, the Part 2 Program Director must determine:
 - 1. The recipient of the patient identifiable information has obtained a waiver of authorization consistent with the HIPAA Privacy Rule; and
 - 2. The research is in compliance with the Common Rule and FDA regulations regarding the protection of human subjects (21 C.F.R. Parts 50 and 56), as applicable.
 - E. In addition, the researcher is subject to certain requirements. The

researcher must:

1. Comply with Part 2's requirements on the use and disclosure of the information;
 2. Not re-disclose patient identifying information except back to the Part 2 Program from where the information was obtained, or otherwise permitted by Part 2;
 3. Only include Part 2 data in research reports in aggregate form in which patient identifying information has been rendered non-identifiable such that the information cannot be re-identified and serve as an unauthorized means to identify a patient as having, or having had, a substance use disorder;
 4. Maintain and destroy patient identifying information in accordance with specified security requirements under the regulations (see 42 C.F.R. Section 2.16 for security requirements), or more stringent requirements; and
 5. Retain records in compliance with applicable record retention laws.
- F. The researcher must also comply with specific requirements where they request linkages to data sets from a data repository holding identifiable Part 2 patient information. [42 C.F.R. § 2.52\(c\)](#). This includes:
1. Seeking review and approval from the IRB for the project;
 2. Ensuring that patient identifiable information is not provided to law enforcement agencies or officials.
- G. California law applies to patient information maintained in connection with alcohol and other drug abuse treatment or prevention conducted, regulated, or directly or indirectly assisted by the California Department of Health Care Services. This type of information may be disclosed to "qualified personnel" for the purposes of conducting scientific research, who must have training and experience appropriate to the nature and level of work in which they are engaged, and who, when working as part of an organization, are performing that work with adequate administrative safeguards against unauthorized disclosures. However, these personnel may not identify, directly or indirectly, any individual in any report or otherwise disclose patient identities in any manner. [Cal. Health & Safety Code § 11845.5\(c\)\(3\)](#).
- X. **Embryos:** California Health and Safety Code (Sections 124320-125300)
- A. A physician and surgeon or other health care provider delivering fertility treatment shall provide his or her patient with timely, relevant, and appropriate information to allow the individual to make an informed and voluntary choice regarding the disposition of any human embryos remaining following the fertility treatment; covers consent requirements for donation of embryos for research.
- XI. **Experimental use of Devices:** California Health and Safety Code (Section 109920): Defines a device as a: means any instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, that is any of the following:
1. Recognized in the official National Formulary or the United States Pharmacopoeia, or any supplement to them.

2. Intended for use in the diagnosis of disease or other condition, or in the cure, mitigation, treatment, or prevention of disease in humans or any other animal.
3. Intended to affect the structure or any function of the body of humans or any other animal and that does not achieve any of its principal intended purposes through chemical action within or on the body of humans or other animals and that is not dependent upon being metabolized for the achievement of any of its principal intended purposes.

XII. **Experimental Use of Drugs**: California Health and Safety Code (Section 111515-111545)

- A. Under the California Health and Safety Code 111515, an “experimental drug” means a drug intended for investigational use under Section 111595.
 1. Section 111595 indicates that Section 111550 does not apply to any any drug or device intended solely for investigational use by investigators qualified by scientific training and experience to investigate the safety and effectiveness of drugs or devices. A drug or device is an “experimental drug” only if the drug or device complies with all of the provisions in federal law relating to exemption from investigational new drug requirements for drugs 21 U.S.C. Section 355(i), and all of the following additional requirements are met:
 - i. The investigator must submit to the California Department of Health Services (hereinafter “the Department”), before any clinical testing of a drug or device, reports by the manufacturer or sponsor of the investigation of the drug or device of preclinical tests, including tests on animals, of the drug or device adequate to justify the proposed clinical testing.
 - ii. The manufacturer or the sponsor of the investigation of a drug or device proposed to be distributed to investigators for clinical testing must obtain a signed, notarized agreement from each of the investigators involved that patients to whom the drug or device is administered will be under the investigator’s personal supervision, or under the supervision of investigators responsible to them, and that they will not supply the drug or device to any other investigator, or to clinics, for administration to human beings.
 - iii. The manufacturer or the sponsor of the investigation of a drug or device must establish and maintain records and make reports to the Department of data, including, but not limited to, analytical reports by investigators obtained as a result of the investigational use of the drug or device as the Department finds will enable it to evaluate the safety and effectiveness of the drug or device in the event of the filing of an investigational new drug (IND) or device application to the Department.
 - iv. The manufacturer or sponsor of the investigation must require investigators using the drugs or devices for investigational purposes to certify to the manufacturer that they will comply with the requirements of California Health and Safety Code Sections 111515-111545.

- v. The investigator(s), manufacturer(s), or sponsor(s) shall additionally comply with any other conditions the Department may adopt as regulations necessary for the protection of the public health, even if these additional regulations provide protections beyond those required under federal law.
 - vi. *An “experimental drug” does not include any investigational new drug for which a investigator has submitted an IND application and received approval of that application from either the FDA (if the investigational new drug application was submitted to the FDA) or the Department (if the investigational new drug application was submitted to the Department).*
 - vii. Prior to prescribing or administering an experimental drug, the investigator must obtain the informed consent of all subjects to whom they intend to administer the experimental drug.
 - B. California Health and Safety Code (Section 111525) states that prior to prescribing or administering an experimental drug, consent to the use of the drug shall be obtained in the manner specified in Section 24170 (also known as the Protection of Human Subjects in Medical Experimentation Act).
 - C. The Right to Try Act is defined at Section 111548. (See Policy # 41.)
- XIII. **Hereditary Disorders:** California Health and Safety Code (Section 1124975, 1124980)
- A. Hereditary disorders can be understood to include any disorder transmitted through the hereditary process. See [Cal. Health & Safety Code § 124975](#).
 - B. Both federal and state law allow for the disclosure of genetic test information for research purposes without a patient’s authorization; however, state imposes specific requirements on such disclosure.
 - C. Specifically, California law provides that all testing results and personal information from “hereditary disorders programs” may be disclosed for research purposes without patient authorization, provided that, pursuant to the Common Rule:
 - 1. [T]he research has first been reviewed and approved by an [IRB] that certifies the approval to the custodian of the information and further certifies that in its judgment the information is of such potentially substantial public health value that modification of the requirement for legally effective prior informed consent of the individual is ethically justifiable. [Cal. Health & Safety Code § 124980\(j\)](#).
 - D. Hereditary Disorders Act: States in part, that each person in California is entitled to health care commensurate with their needs, detection through screening of hereditary disorders can lead to further understanding an accumulation of medical knowledge and carriers of most deleterious genes should not be stigmatized and discriminated against. Participation of persons in hereditary disorders programs in the State of California should be wholly voluntary, except for initial screening for phenylketonuria (PKU) and other genetic disorders treatable through the California newborn screening program. All information obtained from persons involved in hereditary disorders programs in the state should be held strictly confidential.

- E. California Health and Safety Code (Section 124980) States that all testing results and personal information from hereditary disorders programs obtained from any individual, or from specimens from any individual, shall be held confidential and be considered a confidential medical record except for information that the individual, parent, or guardian consents to be released, provided that the individual is first fully informed of the scope of the information requested to be released, of all of the risks, benefits, and purposes for the release, and of the identity of those to whom the information will be released or made available.
 - F. Except for data compiled without reference to the identity of any individual, and except for research purposes, provided that pursuant to 45 CFR Part 46 the research has first been reviewed and approved by an institutional review board that certifies the approval to the custodian of the information and further certifies that in its judgment the information is of such potentially substantial public health value that modification of the requirement for legally effective prior informed consent of the individual is ethically justifiable.
- XIV. **HIV/AIDS Testing Information:** California Health and Safety Code (Sections 121075, 120775, 120980, 121090)
- A. HIV/AIDS testing information is regulated by state law. In general, the disclosure of an HIV test result in a manner that identifies or provides identifying information, must be pursuant to a written authorization. [Cal. Health & Safety Code § 120980.](#)
 - 1. An HIV test includes any clinical test, laboratory or otherwise, used to identify HIV, a component of HIV, or antibodies or antigens to HIV. [Cal. Health & Safety Code § 120775\(c\).](#)
 - 2. *Written authorization* applies only to the disclosure of test results by a person responsible for the care and treatment of the person subject to the test. Written authorization is required for each separate disclosure of the test results and shall include to whom the disclosure would be made.
 - B. The California AIDS Research Confidentiality Act provides for the confidentiality of the records of HIV- or AIDS-related research [[Cal. Health & Safety Code § 121075 et seq.](#)]. The Act requires that research records developed or acquired by any person while conducting research or a research study relating to HIV or AIDS not be disclosed without the person's prior written consent.
 - C. Confidential research records may be disclosed in accordance with the prior written consent of the research subject to whom the confidential research records relate, but only to the extent, under the circumstances, to the persons and for the purposes the written consent authorizes. Any disclosure made pursuant to such prior written consent shall contain the following statement:
 - i. *"This information has been disclosed to you from a confidential research record the confidentiality of which is protected by state law and any further disclosure of it without specific prior written consent of the person to whom it pertains is prohibited. Violation of these confidentiality guarantees may subject you to civil or criminal liabilities."*

- D. Confidential research records may be disclosed without prior written consent of the research subject to whom the confidential research records relate in the following circumstances:
 - 1. To medical personnel to the extent it is necessary to meet a bona fide medical emergency of a research subject; and
 - 2. To the California Department of Health Services for the conduct of a special investigation of the sources of morbidity and mortality and the effects of localities, employments, conditions and circumstances on the public health and for other duties as may be required in procuring information for state and federal agencies regarding the effects of those conditions on the public health.
 - E. The content of any confidential research record shall be disclosed to the research subject, the legal representative of the research subject if the research subject is a child, or the personal representative of a deceased research subject to whom the record pertains within 30 days after a written request is made for such records by the research subject, the legal representative.
 - F. Nothing in this policy shall preclude the disclosure of information in order to further research efforts, including, but not limited to, the publication, dissemination, or sharing of raw data, statistics, or case studies, so long as no confidential research records concerning any research subject are disclosed.
- XV. **Mandatory Reporting of Sexually Transmitted Disease:** (California Health and Safety Code, Section 120500 -120605): Describes the requirements for reporting sexually transmitted disease to CA Department of Health. **Mandatory Reporting of Sexually Transmitted Disease - California Health and Safety Code (Section 120500-120605)**
- A. Every physician or other person who makes a diagnosis of, treats or prescribes for a case of sexually transmitted disease designated as reportable is required to report the case immediately to the Department of Health. Reports include the name, address, age, sex, race, stage of disease, treatment, and control of the disease.
 - B. Children 13 years of age or younger must be reported to the Department of Health.
 - C. Reporting is required for children where sexual abuse is suspected regardless of injury to the Department of Health. The Department of Health will notify the Department of Children's Services.
- Prisoners in Biomedical and Behavioral Research** (California Penal Code, Section 3500 – 3523) (Section 3369.5 of Title 15 of the California Code of Regulations) (See Policy # 37.) Describes the requirements for biomedical and behavioral research conducted in CA prisons.
- XVI. **Special Populations:**
- A. **Elder Abuse and Dependent Adult Civil Protection Act** (California Welfare and Institutions Code, Section 15600 - 15637) Describes the requirements for reporting harm and neglect to elder or dependent adults.
 - B. (California Penal Code 11160): A health practitioner investigator, while conducting human subjects research, who discovers or reasonably

suspects that a study subject: (1) Has been the victim of a wound or other physical injury caused by a firearm (either self-inflicted or inflicted by another); or (2) Is suffering from any wound or other physical injury inflicted upon the study subject where the injury is the result of assaultive or abusive conduct, has a legal obligation to make two reports to the local law enforcement agency.

- C. The first report must be made immediately by telephone or as soon as practically possible. The second report must be made in writing within two working days on a "Suspicious Injury Report" Form published by California's Office of Emergency Services (Form OES-920). Both the oral and written report must include the name of the injured person, if known; the injured person's whereabouts; the character and extent of the person's injuries; and the identity of any person the injured person alleges inflicted the assault or abusive conduct.
- D. In the event a health practitioner investigator becomes aware of or reasonably suspects that a study subject has been the victim of any of the injuries set forth in this policy, the physician investigator should immediately notify the IRB to ensure that the proper reports are made.
- E. When the investigator is not a physician or "mandated reporter," the investigator can make a voluntary report to the appropriate agency. If such information is discovered unexpectedly (i.e., not anticipated given the study design or subject population), the Investigator should seek advice from his/her department chair or dean or from the Executive Director of Research Protections or designee, who may refer the question to UC Legal Counsel.
- F. If an Investigator is planning a study that is designed or likely to elicit information about sexual or physical abuse, or neglect of an elder or dependent adult, the IRB application and consent/assent forms must indicate how discovery of such information will be managed.

XVII. Stem Cell Research and Cures Act

- A. On November 2, 2004 California voters approved Proposition 71, the California Stem Cell Research and Cures Act ("Act"), a \$3 billion bond measure to advance stem cell research over the next ten years. The Act also created the California Institute for Regenerative Medicine (CIRM) and the Independent Citizens Oversight Committee (ICOC) which will govern the Institute and make grants and loans for stem cell research and research facilities.
- B. (Section 125290.35): Institute will develop its own standards for scientific and medical research.
- C. (Section 125290.55): States a scientific and medical accountability standard working group will be established. The composition of the working group is specified.
- D. (Section 125300): The policy of the State of California shall be that research involving the derivation and use of human embryonic stem cells, human embryonic germ cells, and human adult stem cells, including somatic cell nuclear transplantation, shall be reviewed by a stem cell research oversight committee.

XVIII. Surrogate Decision Maker: (California Health and Safety Code Section 24178) (See Procedure # 30C.)

- XIX. **Women and Minorities:** California Health and Safety Code (Section 100238)
- A. In conducting or supporting a project of clinical research, a grantee shall, except as provided in subdivision (b) or (e), do all of the following:
 - 1. Ensure that women, including, but not limited to, women over the age of 40 years, are included as subjects in each research project.
 - 2. Ensure that minority groups are included as subjects in each research project.
 - 3. Conduct or support outreach programs for the recruitment of women and members of minority groups as subjects in projects of clinical research.
 - 4. The requirement established in subdivisions (a) and (d) regarding women and members of minority groups shall not apply to a project of clinical research if the inclusion, as subjects in the project, of women and minority groups is inappropriate for either of the following reasons:
 - i. With respect to the health and safety of the subjects.
 - ii. With respect to the purpose of the research.
 - B. In the case of any clinical trial in which women or members of minority groups will, under subdivision (a), be included as subjects, a grantee shall ensure that the trial is designed and carried out in a manner sufficient to provide for a valid analysis of whether the variables being studied in the trial affect women or members of minority groups, as the case may be, differently than other subjects in the trial.
 - C. In any grant, or in any contract by a grantee under a grant, the grantee or contracting party shall acknowledge, agree to, and be bound by, the terms of this section. If a grantee is in compliance with the 1993 National Institutes of Health guidelines, the grantee shall be deemed to be in compliance with this section.

- XX. **Committee for the Protection of Human Subjects** of the California Health and Human Services Agency (CHHSA) and California Information Practices Act, Civil Code, Section 1798.24 (SB 13)
- A. For identifiable UC data sent to Data Repositories under California Civil Code 1798.24, the Lead Investigator is responsible for complying with all applicable federal and state laws regarding the confidentiality of information (such as the California Information Practices Act).
 - 1. Research funded by CHHSA or any of its departments must be sent to the CHHSA Committee for the Protection of Human Subjects for review. The CPHS serves as the institutional review board (IRB) for the California Health and Human Services Agency.
 - 2. The CHHSA CPHS must also review when identifiable data held by the University of California (UC) will be released or when identifiable data will be received from another state agency, as these situations both fall under the terms of the California Civil Code 1798.24, as amended in 2005. Unless subjects have provided informed consent no more than 30 days before the disclosure, or in the time limit specified in the informed consent document, or another exception exists as outlined in the law, the release of identifiable information to or by UC requires review by the Committee for the Protection of Human Subjects of the California Health and Human Services Agency.
- XXI. **Prisoners in Biomedical and Behavioral Research**
- A. Penal Code (Section 3500 – 3523) (Section 3369.5 of Title 15 of the California Code of Regulations) (See Policy # 37.)
 - B. 15 California Code of Federal Regulations Section 1454 states expectations for conducting research on juveniles.
 - C. 15 California Code of Federal Regulations Section 3369.5 states expectations for conducting research on adult inmates and parolees including the approval of a research advisory committee.
- XXII. **Research Conducted by or at State Hospitals, Regional Centers, or by Other Persons or at Places Subject to Section 4514 of the Welfare and Institutions Code** (17 Code of California Regulations 50403-50429; 50401-50429 includes definitions and rules for the conduct of research.)
- XXIII. **Responsibilities of IRB Members**
- A. IRB members are to be aware of the state law that may be relevant to the conduct of human subject research and to apply to the consideration of whether research meets the criteria for approval.
 - B. IRB members are to be aware of the state law that may be relevant to the conduct of human subject research and to consider whether disclosure of the implications of the law is required for legally effective informed consent.
- XXIV. **Responsibilities of Legal Counsel**
- A. In general, the IRB will apply the most stringent law when federal law and other applicable laws apply. However, legal counsel, as needed, will provide assistance to resolve conflicts between federal law and other applicable laws.

- B. Legal counsel will provide assistance, as needed, when applying state and local laws that govern research involving human subjects, including when the research is conducted outside State of California. (See Policy # 27.)

References:

California Health and Safety Code - Section 11480-11481

California Health and Safety Code - Section 24170-24179.5

California Health and Safety Code - Sections 24185-24187

California Health and Safety Code - Section 102231 – 102232

California Health and Safety Code - Section 111515-111545

California Health and Safety Code - Section 120500-120605

California Health and Safety Code - Section 121075-121125

California Health and Safety Code - Sections 123420-123450

California Health and Safety Code - Sections 124320-125300

California Health and Safety Code - Section 124980

California Health and Safety Code - Sections 125330-125355

California Penal Code - Section 3500 – 3520

California Penal Code - Section 11164-11174.3

California Education Code - Section 51513

California Welfare and Institutions Code - Section 15601

Committee for the Protection of Human Subjects of the California Health and Human Services Agency (CHHSA) and **California Information Practices Act**, Civil Code, Section 1798.24 (SB 13)

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Panetta J, Wetherell J, Mehok M. California Stem Cell Research and Cures Act: what to expect from stem cell research? J Biolaw Bus. 2005;8(4):3-12. PMID: 16619447.

Estanol, L. (2019). Post-Approval Investigator Responsibilities (PAIR) Worksheet. *UC Irvine: Human Research Protections (HRP), Education and Quality Improvement Program (EQUIP)*. Retrieved from <https://escholarship.org/uc/item/2kc9373m>

[Moore v. Regents of the University of California](#)

UCOP: [Use of Specimens \(Moore Clause\) Disclosure in the Informed Consent Form](#)

DRAFT RPAC Guidance Memo on Use of HIPAA Auth for Certain Information 12.13.23

Policy Number: 30

Title: Prospectively Obtained and Legally Effective Informed Consent

Date of Last Revision: 07/28/06, 09/13/10, 06/05/13, 05/11/15, 09/16/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to assure that provisions are made to obtain legally authorized informed consent prospectively from each research participant or permission from his or her legally authorized representative or surrogate decision maker.

I. General Requirements for Informed Consent Process

- A. Before involving a human subject in research covered by this policy, an investigator shall obtain the legally effective informed consent of the subject or the subject's legally authorized representative.
- B. An investigator shall seek informed consent only under circumstances that provide the prospective subject or the legally authorized representative sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence.
- C. The information that is given to the subject or the legally authorized representative shall be in language understandable to the subject or the legally authorized representative.
- D. The prospective subject or the legally authorized representative 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.
 - 1. Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative 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.
 - 2. Informed consent must present information in sufficient detail relating to the research 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 legally authorized representative's understanding of the reasons why one might or might not want to participate.
- E. No informed consent may include any exculpatory language through which the subject or the legally authorized representative 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, the institution, or its agents from liability for negligence.
- F. The IRB evaluates and assures that provisions are made to obtain legally effective informed consent prospectively from each research participant or permission from their legally authorized representative. There are circumstances in which the IRB may grant a waiver of informed consent in accordance with Federal regulations. (See IRB Policy # 32.)

- G. Documentation of informed consent is obtained unless alternate procedures are approved by the IRB. (See IRB Policy # 31.) The IRB reviews all informed consent documents to assure the adequacy of the information contained in the consent document, and adherence to Federal regulations regarding the required elements of informed consent. (See IRB Procedure # 30.B.)
- H. The consent process includes recruitment and screening procedures. The researcher will give either the participant or the representative adequate opportunity to read the consent form before it is signed. Alternatively, this form may be read to the subject or the subject's legally authorized representative.
- I. Unless documentation is waived by the IRB, informed consent shall be:
 - 1. Documented using a written informed consent form approved by the IRB and signed (either on paper or electronically) by the participant or the participant's legally authorized representative prior to initiating research activities. A written copy of the consent document will be given to the person signing the consent document. Per UCI Health IT, FDA-Regulated Studies must use DocuSign Part 11 for obtaining electronic signatures on the Informed Consent Form.
 - 2. Alternatively, a short form written informed consent form stating that the elements of informed consent required by [§46.116](#) have been presented orally to the subject or the subject's legally authorized representative, and that the key information required by [§46.116\(a\)\(5\)\(i\)](#) was presented first to the subject, before other information, if any, was provided. The IRB shall approve a written summary of what is to be said to the subject or the legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Only the short form itself is to be signed by the subject or the subject's legally authorized representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the subject's legally authorized representative, in addition to a copy of the short form.
- J. Lead Researchers (LRs) that plan on enrolling research participants in other states or countries should take care to comply with local law in determining who qualifies as a legally authorized representative/surrogate decision maker. (See Policy # 29.)
- K. If a prospective adult subject lacks the capacity to consent, his or her legally authorized representative may grant permission, on their behalf, for their participation in research. See IRB Procedure # 30.C for the hierarchy of individuals who qualify as surrogate decision makers.
- L. The State of California requires that all subjects enrolled in medical experimentation projects receive and sign a copy of the Experimental Subject's Bill of Rights. (See Policy # 57 for definition(s) of medical experimentation). (See *"General Information Often Requested by Study Sponsors"* for reason why UCI does not have signature lines on the Bill of Rights.)

- M. For projects that meet the definition of a clinical trial, the consent form will include a statement that a description of the clinical trial will be available on <http://www.clinicaltrials.gov>. The website will not include information that can identify the participant. At most, the website will include a summary of the results. The participant can reach the website at any time. (See Policy # 57 for definition(s) of a clinical trial.)
- N. For each clinical trial conducted / supported by HHS initially approved, or has transitioned to comply with the revised 2018 common rule requirements prior to enrollment closure on or after January 21, 2019, 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 Web site that will be established as a repository for such informed consent forms.
 - 1. 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 Web site (e.g., confidential commercial information), such Federal department or agency may permit or require redactions to the information posted.
 - 2. The informed consent form must be posted on the Federal Web site 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.

II. Requirements for Informed Consent- Basic Elements

- A. The basic required elements of consent to be included in each informed consent document are as per the 2018 Common Rule and include:
 - 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 that 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 that 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 will 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 (See Policy # 26);
 - 8. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled; and

9. One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:
 - a) 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
 - b) 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.

III. **Requirements for Informed Consent- Additional Elements**

- A. One or more of the following elements of information, when appropriate, shall also be provided to each subject or the legally authorized representative:
 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) that are currently unforeseeable;
 2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's or the legally authorized representative's consent;
 3. Any additional costs to the subject that may result from participation in the research;
 4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
 - a) When a participant withdraws from a study, the data collected on the participant to the point of withdrawal remains part of the study database and may not be removed. *The consent document cannot give the participant the option of having data removed.*
 - b) A researcher may ask whether the participant wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under these circumstances, the discussion with the participant would distinguish between study-related interventions and continued follow-up of associated clinical outcome information and address the maintenance of privacy and confidentiality of the participant's information.
 - c) The researcher must obtain the participant's informed consent for this limited participation in the study (assuming such a situation was not described in the original consent form). The IRB approves the consent document prospectively.
 - d) If a participant withdraws from the interventional part of the study and does not consent to continued follow-up of associated clinical outcome information, the researcher must not access for purposes related to the study the participant's medical record or other confidential records requiring the participant's consent.

However, a researcher may review study data related to the participants' withdrawal from the study, and may consult public records, such as those that establish survival status.

5. A statement that significant new findings developed during the research that may relate to the subject's willingness to continue participation will be provided to the subject;
 - a) If there are significant new findings, the LR (with Committee input) should update the consent form to include this information and submit the re-consent cover letter to summarize the major changes. The re-consent cover letter template is available on the IRB Forms website.
 - b) Examples of when re-consenting should be required:
 - c) Increase in risk;
 - d) New risks identified;
 - e) Decrease in anticipated benefits; and
 - f) Change in research procedures.
 - g) The IRB will also consider other situations where re-consenting may be necessary (e.g., Change in LR).
 6. The approximate number of subjects involved in the study;
 7. 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;
 8. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and
 9. 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).
 10. Study treatment(s) and the probability of random assignment to placebo or to each treatment;
 11. A statement noting the possibility that the FDA may inspect the study records;
 12. The type and amount of compensation, if any, the participant is to receive for study participation, and the schedule of compensation (i.e., whether it will be pro-rated).
 13. Notification of any potential conflict of interest.
 14. Any additional information that may be required by state law or institutional policy to obtain legally effective informed consent.
 15. The IRB may require that information, in addition to that required in Federal regulations, be given to research participants when in its judgment the information would meaningfully add to the protection of the rights and welfare of participants.
- B. UCI has elected to not implement the 2018 Common Rule elements of broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens.

IV. **Requirements for Informed Consent - Additional Consent Language Requirements**

- A. No Omission of Required Elements unless a Waiver is granted. Required elements of informed consent may not be omitted unless waived by the IRB. (See IRB Policy # 32.) In addition, there may not be discrepancies within the informed consent documents, the IRB Application, the Sponsor's or Investigator's Protocol, the Investigator's Brochure, the grant and/or the contract regarding the purpose, risks, and benefits of the research. The IRB encourages Investigators to use the IRB template informed consent document when developing consent documents. Biomedical and Social/Behavioral templates are available on the IRB website at <https://research.uci.edu/human-research-protections/irb-forms/> under the heading "IRB Consent Forms."
- B. Second Person. The language of the consent documents should be in the second person style (i.e., "you, your"), which may help convey that there is a choice to be made by the participant rather than a presumption of the participant's consent with the use of the first-person style (i.e., "I, me, my").
- C. No Unproven Claims of Effectiveness. No unproven claims of effectiveness or certainty of benefit, either implicit or explicit, may be included in the informed consent documents.
- D. No Complex Language. The information provided in the informed consent documents must be in a language understandable to the participant (target population). The informed consent documents should not include complex language that would not be understandable to all participants. Technical and scientific terms should be adequately explained using common or lay terminology consistently. Generic names are preferable when describing pharmaceuticals unless the brand name is more commonly known and understood. Regardless of which name is preferred, it should be used consistently throughout the informed consent documents. Devices and procedures should also be described consistently throughout the documents and explained in simple language. It is generally recommended that the adult consent documents be written at a sixth to eighth grade reading level.
- E. No Exculpatory Language. The informed consent documents may not contain any exculpatory language through which the participant is made to waive or appear to waive any of the participant's legal rights, or releases or appears to release the investigator, the sponsor, the University, or its agents from liability for negligence.
- F. FDA Regulated Test Articles. For all research involving test articles regulated by the U.S. Food and Drug Administration (FDA), informed consent documents should include a statement that a purpose of the study includes an evaluation of the test article. Statements that test articles are safe or statements that the safety has been established in other studies are not appropriate when the purpose of the study includes determination of safety. In studies that also evaluate the effectiveness of the test article, informed consent documents should include that purpose, but should not contain claims of effectiveness.
- G. Phase I Studies. Potential participants should be told, and a statement included in the purpose of the informed consent document, that Phase I studies are designed to determine safety, but not effectiveness. They are also designed to determine toxicity, and severe toxicity is a planned event for a subset of participants, and direct benefit is both not intended and extremely unlikely. In addition, the informed consent document should

include an explicit statement that the dose administered is not chosen to maximize the chance of effect.

- H. Phase II and Phase III Studies. Potential participants should be told, and a statement included in the purpose of the informed consent document, that Phase II and III studies are designed to determine both safety and effectiveness.

References:

45 CFR 46.109(b)

45 CFR 46.111

45 CFR 46.116 and 46.117

21 CFR 50.20

21 CFR 56.109(b)

21 CFR 56.111 (a)(4)

21 CFR 50.27(a)

21 CFR 56.111(a)(5)

21 CFR 50.24, 50.25 and 50.55

Information Sheet: A Guide to Informed Consent

OHRP Guidance Document: Informed Consent, Legally Effective and Prospectively Obtained (OPRR REPORTS 95-03)

IRB Procedure Section 30.C – “Procedure for Determining Surrogate Decision-Maker for Research”

IRB Policies 36-40 - “Vulnerable Populations”

California Family Code - Sections 6922-6929

California Family Code - Sections 7000-7143

Health and Safety Code - Section 123450

2018 Common Rule Changes to 45 CFR 46

Procedure Number: 30.A**Title: Procedure for Obtaining Prospective and Legally Effective Informed Consent****Procedure:**

This procedure outlines the responsibilities of the UCI Institutional Review Board (IRB) and the Investigator in obtaining legally effective and prospective informed consent from research participants or their legally authorized representatives.

I. Lead Researcher (LR) Responsibilities

- A. The LR provides a detailed description of the intended method and process for obtaining informed consent in the initial IRB Application.
- B. All informed consent documents (full written consent documents, oral scripts, study information sheets, and assent forms) are submitted for review and approval by the UCI IRB prior to use.
- C. Any changes in the informed consent process or documents are submitted as an Amendment request to the IRB for review and approval prior to use.
- D. The informed consent process must:
 - 1. Be solicited in circumstances that minimize the possibility of coercion and undue influence;
 - 2. Utilize language understandable to the participant or their legally-authorized representative – recommended 6 – 8th grade reading level;
 - 3. Not waive or appear to waive participant's or representative's rights; and
 - 4. Include each of the required elements and applicable additional elements of informed consent describing the research and the nature of research participation as required by Federal regulations. (See IRB Procedure # 30.B.)
- E. Unless specifically waived by the IRB, informed consent is documented in writing through the use of a current IRB-approved informed consent document signed and dated by the participant or by the participant's legally authorized representative prior to enrollment or participation in any phase of the research study.
- F. The LR assures the informed consent process in research is an ongoing exchange of information between the research team and the study participants throughout the course of a research study. Informed consent is a continuous process of communication and acknowledgement over time, not just a signed document.

II. IRB Committee Responsibilities

- A. The IRB Committee, the Chairperson or their designee reviews the planned research activities to assure that the informed consent document is congruent with the IRB Application, Investigator's brochure, Sponsor's or Investigator's protocol, grant and/or contract, and contains the necessary elements of informed consent as required by the applicable regulations.
- B. When reviewing the informed consent document, the Reviewers may request necessary revisions to the content, language, punctuation, and/or grammar in order for the intended target population to clearly understand the proposed research activities and make an informed decision on whether to participate in the research.

- C. The IRB Committee, the Chairperson or their designee ensures that research subjects are provided with the "Experimental Subjects' Bill of Rights" document during the IRB approved consent process to inform prospective research participants of their rights as research subjects.
- D. The IRB Committee, the Chairperson or their designee evaluates the circumstances of the informed consent process and method of documentation, indicating whether the process is appropriate for the proposed research activities and the target population as a part of the overall IRB approval of the study.
- E. The IRB Committee, the Chairperson or their designee evaluates whether the research involves participants who have diminished decision-making capacity, and if so, provides additional safeguards to ensure appropriate consent. (See IRB Policies # 33, 36, 38 and 39.)
- F. When following a Department of Defense (DoD) Addendum, the IRB must determine that the disclosures included in the consent document includes those provisions for research-related injury follow the requirements of the DoD component.
- G. When following Department of Justice regulations and guidance, for research funded by the National Institute of Justice, the following applies:
 - 1. The confidentiality statement on the consent document must state that confidentiality can only be broken if the participant reports immediate harm to participants or others.
 - 2. Under a privacy certificate, researchers and research staff does not have to report child abuse unless the participant signs another consent form to allow child abuse reporting.
- H. For research conducted within the Bureau of Prisons, required elements of disclosure in the consent document include:
 - 1. Identification of the principal investigator(s);
 - 2. Anticipated uses of the results of the research;
 - 3. A statement that participation is completely voluntary and that the participant may withdraw consent and end participation in the project at any time without penalty or prejudice (the inmate will be returned to regular assignment or activity by staff as soon as practicable);
 - 4. A statement regarding the confidentiality of the research information and exceptions to any guarantees of confidentiality required by federal or state law. For example, a researcher may not guarantee confidentiality when the subject indicates intent to commit future criminal conduct or harm himself/herself or someone else, or, if the subject is an inmate, indicates intent to leave the facility without authorization and
 - 5. A statement that participation in the research project will have no effect on the inmate participant's release date or parole eligibility.

III. **IRB Analyst or Higher Responsibilities**

- A. As applicable to the level of review, and considering the IRB review timeframe, the Analyst conducts a pre-review of the informed consent process and documents submitted with an IRB application to determine that the correct forms have been utilized for the targeted population; assesses the readability of the document and assures that all the necessary elements as required by the Federal regulations are present for adequate informed consent, including if any additional elements are appropriate.

- B. If additional information regarding the informed consent process or documentation is needed, the Analyst contacts the LR and requests the additional information.

References:

45 CFR 46.111

45 CFR 46.116 and 46.117

21 CFR 50.24 and 50.25

OHRP Guidance Document: Informed Consent Tips, March 1993

OHRP Guidance Document: Informed Consent, Legally Effective and Prospectively Obtained (OPRR REPORTS 95-03)

IRB Policies 36-40 "Vulnerable Populations"

DoD: DoDD 3216.2, para. 5.3.4; SECNAVINST 3900.39D, para. 6a(5)

28 CFR 512.16

Procedure Number: 30.B**Title: Procedure for Incorporating Elements of Informed Consent****Procedure:**

This procedure outlines the responsibilities of the UCI Institutional Review Board (IRB) and the Investigator in incorporating the required elements into the informed consent document as required by the Federal regulations.

I. Lead Researcher (LR) Responsibilities

- A. **Required Elements of Informed Consent:** The LR is responsible for incorporating the basic and additional elements of informed consent as required by Federal Regulations and as applicable to the context of the study into each informed consent document.

II. IRB Committee Responsibilities

- A. The IRB Committee, the Chairperson or their designee will review the informed consent documents to assure the documents contain all the required elements of consent as defined by the Federal Regulations and determine the additional elements that are appropriate and should be incorporated into the documents.
- B. The IRB will ensure there are no discrepancies within the informed consent documents by utilizing the "Informed Consent Checklist" ensure the basic and additional elements of informed consent are incorporated, the IRB application, the Sponsor's or Investigator's Protocol, or the Investigator's Brochure, regarding the purpose, risks, and benefits of the research.

III. IRB Analyst or Higher Responsibilities

- A. As applicable to the level of review, and considering the IRB review timeframe, the Analyst conducts a pre-review of the informed consent process and documents submitted with an IRB application to determine that the correct forms have been utilized for the targeted population; assesses the readability of the document and assures that all the necessary elements as required by the Federal regulations are present for adequate informed consent, including if any additional elements are appropriate.
- B. If additional information regarding the informed consent process or documentation is needed, the Analyst will contact the LR and request the additional information.

Procedure Number 30.C**Title: Procedure for Determining Surrogate Decision-Maker for Research****Procedure:**

This procedure outlines the responsibilities of the UCI Institutional Review Board (IRB) and the Lead Researcher (LR) in the approval and appropriate utilization of a Surrogate Decision-Maker in the context of research.

I. Specific Terminology Associated with Surrogate Decision-Maker

- A. Cognitively Impaired: Having either a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorder, or dementia) or a developmental disorder (e.g., mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Others, including persons under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interests.
- B. Legally Authorized Representative (LAR): A person authorized either by statute or by court appointment to make legal decisions on behalf of another person. In human subjects research, an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.
- C. Surrogate Consent: If a prospective subject cannot consent on their own behalf, federal regulations permit researchers to obtain consent from a Surrogate Decision-Maker. Surrogate consent may be permitted by the IRB only in research studies relating to the cognitive impairment, lack of capacity, or serious or life-threatening diseases and conditions of the research subjects.

II. Surrogate Consent in Non-Medical Research

- A. California law addresses surrogate consent in the context of medical research. The Office of the President has acknowledged that campuses may permit the same surrogates authorized by Section 24178 may also be considered in the context of non-medical research. Per the Common Rule, for research that is no more than minimal risk, the IRB may approve a request to waive some or all of the required elements of informed consent under specific circumstances, and in such cases the need for surrogate consent may also be waived.

III. Lead Researcher (LR) Responsibilities

- A. IRB Approval
 - 1. New studies: The LR must indicate in the IRB Application that the protocol will utilize consent of a Surrogate Decision-Maker and submit a consent document with the surrogate signature lines.
 - 2. Ongoing studies: If the LR later decides to utilize consent of a Surrogate Decision-Maker, an Amendment request must be submitted requesting the use of surrogate consent along with a revised informed consent document that incorporates the surrogate signature lines.

- B. Assessing Capacity: Participants should be assessed on their abilities to understand and to express a reasoned choice concerning the following:
1. Nature of the research and the information relevant to their participation;
 2. Consequences of participation for their own situation, especially concerning their health condition; and
 3. Consequences of the alternatives to participation.
- Investigators may use the Decision-Making Capacity Assessment Tool to assess the understanding of the consent process of persons who may have cognitive impairments or may elicit the information using clinical interview procedures. The IRB may permit less formal procedures to assess capacity (e.g., assessment of capacity through routine **interactions with** the participant) when the study is no more than minimal risk.
- C. Identifying the Surrogate Decision-Maker (SDM)
1. The SDM identified to make health care decisions on the patient's behalf is generally the individual who should make decisions regarding the patient's participation in IRB-approved clinical research studies.
 2. California Health & Safety Code § 24178 identifies the individuals who are legally authorized in California to provide surrogate consent for research.
 - a. For purposes of obtaining informed consent required for medical experiments in a **non-emergency room environment**, if a person is unable to consent and does not express dissent or resistance to participation, surrogate informed consent may be obtained from a SDM with reasonable knowledge of the subject, who shall include any of the following persons, in the following descending order of priority:
 - (1) The agent named in the potential research participant's advance health care directive. The conservator or guardian of the potential research participant, with authority to make healthcare decisions for the potential participant.
 - (2) The spouse of the potential research participant.
 - (3) The registered domestic partner of the potential research participant as defined in Section 297 of the Family Code.
 - (4) An adult child of the potential research participant.
 - (5) A custodial parent of the potential research participant.
 - (6) An adult sibling of the potential research participant.
 - (7) An adult grandchild of the potential research participant.
 - (8) An available adult relative with the closest degree of kinship to the potential research participant, whose relationship to the potential participant does not fall within one of the above listed categories (e.g., aunt; uncle; cousin; etc.).
 - b. The investigator is responsible for making a reasonable effort to determine if that individual is available to serve as surrogate. Potential surrogates must be advised that if a higher-ranking surrogate is identified at any time, the investigator will defer to the higher-ranking surrogate's decision regarding the subject's participation in the research. When there are two or more available persons who may provide surrogate consent and who are in the same order of priority (e.g., an adult son and daughter of the potential participant), if any of those persons in the same

order of priority expresses dissent as to the participation of the person in the medical experiment, consent shall not be considered as having been given.

- c. For purposes of obtaining informed consent required for medical experiments in an **emergency room environment**, if a person is unable to consent and does not express dissent or resistance to participation, surrogate informed consent may be obtained from a SDM who is any of the following persons:
 - (1) The agent named in the potential research participant's advance health care directive.
 - (2) The conservator or guardian of the potential research participant, with authority to make health care decisions for the potential participant.
 - (3) The spouse of the potential research participant.
 - (4) The registered domestic partner of the potential research participant as defined in Section 297 of the Family Code.
 - (5) The adult child of the potential research participant.
 - (6) A custodial parent of the potential research participant.
 - (7) An adult sibling of the potential research participant.
 - (8) In emergency room research settings, no surrogate consent may be utilized if there is a disagreement whether to consent among any available surrogates.
 - (9) SDMs described in this section shall exercise substituted judgment, and base decisions about participation in accordance with the person's individual health care instructions, if any, and other wishes, to the extent known to the SDM. Otherwise, the SDMs shall make the decision in accordance with the person's best interests. In determining the person's best interests, the SDM shall consider the person's personal values and his or her best estimation of what the person would have chosen if he or she were capable of making a decision per Cal. Health & Safety Code § 24178(g).
- d. A surrogate decision-maker is prohibited from receiving financial compensation for providing consent per Cal. Health & Safety Code § 24178(i).
- e. Section "2a" and "2c" above do not apply to any of the following persons, except as otherwise provided by law:
 - (1) Persons who lack the capacity to give informed consent and who are involuntarily committed pursuant the California Welfare and Institutions Code § 5000 *et seq*; or
 - (2) Persons who lack the capacity to give informed consent and who have been voluntarily admitted or have been admitted upon the request of a conservator pursuant to Chapter 1 (commencing with Section 6000) of Part 1 of Division 6 of the California Welfare and Institutions Code.

C. Required Documentation. In all cases involving adult patients who are incompetent or lacks decision-making capacity for healthcare decisions and consent of a Surrogate Decision-Maker is utilized, the LR, shall document in the medical record:

- 1. The basis for their determination that the individual lacks decision-making capacity;
 - a. The investigator must detail a decision-making capacity assessment which the IRB reviews and approves.

- b. If the determination that the prospective participant lacks decision making capacity is based on a diagnosis of mental illness, the researcher obtains consultation with a psychiatrist or licensed psychologist.
- c. The identity of the SDM and the rationale for the selection of the individual as SDM, which shall be documented on the [Investigator Certification of Surrogate Decision Makers for Potential Subject's Participation in University of California Research](#) form. A copy of the form should be provided to the SDM. In addition, the researcher must keep the original, signed form in the research records with the signed informed consent document.

D. Obtaining Surrogate Consent

1. Investigators must describe to potential SDMs the nature of ongoing decisions during the study regarding the subject's participation, decision to participate in certain procedures, changes to the study, etc., in order to ensure that the SDM is willing to undertake these ongoing responsibilities.
2. Disclosures to be made to the participant must be made to the participant's legally authorized representative or SDM.
3. Forcing or coercing participants to participate in a research study is prohibited.
4. The Investigator must complete the Investigator Certification of Surrogate Decision Makers for Potential Subject's Participation in University of California Research form as an attachment to the informed consent document for the study, and be given a copy of this form along with a copy of the consent to keep.
5. The Investigator must keep the signed form in the research records along with the signed consent. The Investigator Certification of Surrogate Decision Makers for Potential Subject's Participation in University of California Research form verifies the criteria for the use of a surrogate decision maker and the category of the potential surrogate.
6. Potential SDMs must be advised that if a higher-ranking surrogate is identified at any time, the investigator will defer to the higher-ranking surrogate's decision regarding the subject's participation in the research.
7. For non-emergency room environment research only: If the potential SDM identifies a person of a higher degree of surrogacy, the investigator is responsible to contact such individuals to determine if they want to serve as SDM.
8. Surrogate decision-makers are prohibited from receiving any financial compensation for providing consent. This does not prohibit the SDM from being reimbursed for expenses the SDM may incur related to their participation in the research.
9. Assessment of the decision-making capacity *of the SDM* should be implemented when the Investigator has reason to believe that the SDM's decision-making capacity may be impaired.

III. IRB Committee Responsibilities

- A. The IRB Committee, the Chairperson, or their designee will review the informed consent documents.
- B. The IRB Committee, the Chairperson or their designee will review the LR's rationale for the need to utilize consent by a Surrogate Decision-Maker assuring:
 - 1. There are appropriate safeguards in place for cognitively impaired participants;
 - 2. The LR has a thorough understanding of the appropriate use of consent of a Surrogate Decision-Maker in clinical research; and
 - 3. The LR has detailed how reconsenting will take place when and if an individual becomes competent to consent for oneself.
- C. The IRB should consider whether and when to require a reassessment of decision-making capacity. Additionally, after taking into account the study's anticipated length and the condition of the individuals to be included, whether and when periodic reconsenting of the SDM should be required to assure that a participant's continued involvement is voluntary.

IV. IRB Analyst or Higher Responsibilities

- A. As applicable to the level of review, and considering the IRB review timeframe, the Analyst conducts a pre-review of the informed consent process and documents submitted with an IRB application to determine that the correct forms have been utilized for the targeted population; assesses the readability of the document and assures that all the necessary elements as required by the Federal regulations are present for adequate informed consent, including if any additional elements are appropriate.
- B. If additional information regarding the informed consent process or documentation is needed, the Analyst will contact the LR and request the additional information.
- C. The Analyst will assure that the IRB database is updated appropriately to reflect IRB approval for the use of consent of a Surrogate Decision-Maker for the research.
- D. The Analyst will draft all approval letters and stamp the informed consent document. (See Policy # 34.)

References:

University of California Guidance Memo 21-01: Surrogate Consent for Research – Updated Guidance, Dated 02/16/202.

Policy Number: 31

Title: Documentation of Informed Consent for Human Subjects Research

Date of Last Revision: 01/21/2007; 01/16/2010; 04/19/2012; 02/06/2013; 04/04/2013; 04/19/2013; 06/05/2013; 10/17/2013; 02/11/2015; 04/10/2017; 06/19/2017; 07/21/2017; 06/27/2018; 08/21/19; 12/04/19; 01/15/20; 04/04/22, 06/24/22, 05/12/23, 08/21/24

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) that informed consent is documented in writing as determined in the IRB review and approval process.

I. Three Options for Documentation of Informed Consent

- A. The IRB may approve procedures for documentation of informed consent that involve either:
 - 1. A written consent form signed by the participant;
 - 2. A short form written consent with oral presentation; or
 - 3. In specific circumstances, a waiver of the signed written consent form.
- B. It is the responsibility of the IRB Committee to determine which of the procedures described below is appropriate for documenting informed consent in research applications that it reviews.

II. Option One: Written Consent Form Signed by the Participant or Legally Authorized Representative

- A. In most circumstances, the IRB should require that informed consent be documented by the use of a written consent form approved by the IRB and signed by the participant or the participant's legally authorized representative.
- B. This consent form must embody the required elements of informed consent required by IRB Policy # 30, in addition to any applicable additional elements that are required by the Federal regulations.
- C. This form may be read to the participant or the participant's legally authorized representative. However, the Lead Researcher should allow the participant or the legally authorized representative sufficient opportunity to read and consider the consent document before it is signed. A copy of the document must be given to the person signing the form.
- D. The written informed consent document should embody, in language understandable to the participant, all the required elements necessary for legally effective informed consent (See IRB Procedure # 30.B).
- E. Participants who do not speak English should be presented with an informed consent document written in a language understandable to them.

III. Option Two: Oral Presentation Using Short Form – Short Form Signed by Participant

- A. Participants Who Do Not Speak English
 - 1. It is preferable that the written informed consent documents for non-English speaking participants embody, in a language understandable

to the participant, all the required elements necessary for legally effective informed consent.

2. Alternatively, regulations permit an oral presentation of (long) informed consent information in conjunction with a short form written consent document, written in the language understandable to the participant. A witness to the oral presentation is required, and the participant must be given copies of the short form informed consent document and the IRB approved English version of the consent document.
3. The "short form" method for obtaining informed consent may be used for the **occasional and unexpected enrollment** of a non-English-speaking participant in a study for which no consent form in the participant's language has been prepared. Prospective IRB approval for the use of Short Forms is required.
4. Should a researcher believe that enrollment of non-English speaking participants is due to the nature of the disease or condition being studied and the anticipated study enrollment, study specific justification for the use of short forms must be provided in the IRB Application.
5. When this procedure is used the following steps are required:
 - a. The oral presentation and the short form written informed consent document should be in a language understandable to the participant;
 - b. A witness who is fluent in both English and the language of the participant should be present. The witness must sign and date both the short form written informed consent document and a copy of the IRB approved English version of the consent document.
 - c. The person obtaining consent may not also be the witness to the consent.
 - d. The participant must sign and date the short form written consent document.
 - e. The person obtaining consent (e.g., the Lead Researcher) must sign and date a copy of the IRB approved English version of the consent document that is presented orally.
 - f. Only those study team members who are approved by the IRB to obtain informed consent from research participants may obtain short form consent.
 - g. A copy of the Experimental Subject's Bill of Rights (in a language understandable to the participant) should also be provided to all research participants considering participation in a medical experiment, per California Health & Safety Code. These are available on the IRB Forms page under the heading, 'Human Research Protections / Foreign Language Translations' – on the HRP webpage: <https://research.uci.edu/human-research-protections/irb-forms/>
 - a. Additional Experimental Subject's Bill of Rights translations may be requested by contacting the HRP office.
 - h. Once the participant has consented and eligibility is confirmed, the IRB approved English version of the consent document must be translated into the participant's language by a professional or certified translator.

- a. *The translated consent form must be provided to the participant within one month from the date that eligibility is confirmed.*
6. In general, for studies that involve greater than minimal risk a request for Short Forms will require full committee review. The IRB Chair or Vice Chair's has discretion on a protocol-by-protocol basis however and may decide that review of a request for Short Forms can occur at a subcommittee level. The reason for the level of review (full committee or subcommittee) should be appropriately documented in the IRB Checklist.
7. In the instance that the UCI IRB has approved Short Form use but the specific foreign language translation of the English Short Form is not immediately available on the UCI HRP webpage, UCI researchers may use the appropriate language translation of the Short Form as found on the Western IRB (WIRB) or Central IRB for the National Cancer Institute (CIRB) websites.

IV. **Option Three: Waiver of Documentation – No Participant Signature**

- A. The IRB may waive the requirement for the Lead Researcher to obtain a signed consent form for some or all participants if the IRB finds either:
 1. That the only record linking the participant, and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality (Note: When the IRB waives the requirement for documentation under this condition, each participant must be asked whether the participant wants documentation linking the participant with the research, and the participant's wishes will govern);
 2. That the research presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context; or
 3. If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.
- B. **For FDA regulated research**, when the clinical investigation involves no more than minimal risk, **an alteration of consent (e.g., waiver of documentation of consent) may be granted when:**
 1. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
 2. The clinical investigation could not practicably be carried out without the waiver or alteration; and
 3. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
- C. In cases in which the documentation requirement is waived, the IRB may require that the LR provide participants with a written statement regarding the research (e.g., Study Information Sheet).

V. **No Verbal Consent** - Verbal agreement to participate in a research study is not permitted unless the documentation or process of informed consent is waived by the IRB.

- VI. **Use of Facsimile, Mail or Electronics to Document Informed Consent**
- A. The IRB may approve a process that allows the informed consent document to be delivered by mail, facsimile or electronically to the potential participant or the potential participant's legally authorized representative and to conduct the consent interview by telephone when the participant or the legally authorized representative can read the consent document as it is discussed.
 - B. In addition, there may be times when the use of an electronic consent documentation process is most appropriate. The consent may be electronically delivered to the potential participant's legally authorized representative (e.g., via DocuSign). Again, the consent process may be conducted by phone or video, while the participant or the legally authorized representative read the consent document as it is discussed.
 - C. OHRP and FDA regulations permit the use of electronic signatures when written informed consent is required.
 - D. FDA regulations set forth the criteria under which FDA considers electronic records, electronic signatures, and handwritten signatures executed to electronic records to be trustworthy, reliable, and generally equivalent to a handwritten signature executed on paper (see 21 CFR 11.1(a)). In order to be considered equivalent to full handwritten signatures, electronic signatures must comply with all applicable requirements under 21 CFR part 11. The electronic system must also capture and record the date that the participant or participant's LAR provides consent (see 21 CFR 50.27(a)).
 - E. All other applicable conditions for documentation of informed consent must also be met when using any of the above procedure.

References:

45 CFR 46.111

45 CFR 46.116 and [46.117](#)

21 CFR 50 and 56

21 CFR 11

OHRP Guidance Document, "Informed Consent, Non-English Speakers" dated November 1995.

FDA Information Sheets, "Guidance for Institutional Review Boards and Clinical Investigators", 1998

FDA Information Sheet, "IRB Waiver of Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects", July 2017:

<https://www.fda.gov/media/106587/download>

OHRP "Use of Electronic Informed Consent: Questions and Answers":

<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/use-electronic-informed-consent-questions-and-answers/index.html#tocq6>

Procedure Number: 31.A**Title: Procedure for Documentation of Informed Consent for Human Subjects Research****Procedure:**

The purpose of this procedure is to provide guidance on documentation of prospective, legally effective informed consent from research participants or their legally authorized representative.

I. Lead Researcher (LR) Responsibilities

- A. All informed consent documents (full written documents, oral scripts, Study Information Sheets, short forms, and assent forms) will be submitted to the IRB with the new study submission.
 - 1. It is highly recommended that UCI informed consent templates be used to draft all written informed consent documents. Biomedical and Social/behavioral templates are located on the IRB website at <https://research.uci.edu/human-research-protections/irb-forms/> and under the heading “IRB Consent Forms.”
 - 2. Informed consent documents (ICD) will be written in language that is at the appropriate reading and comprehension level for the targeted population. Generally, a sixth to eighth grade reading level is recommended for adult consent documents.
 - 3. When considering which researchers names should be included on the ICD as those who are capable of *finalizing* the consent process (i.e., those authorized to obtain verbal or written consent from participants), the following guidelines apply:
 - a. For minimal risk research, the LR must list their name on the ICD.
 - b. For greater than minimal risk research, the LR and Co-Researchers (CR) who are approved by the IRB to finalize consent must be listed on the ICD.
 - c. When UCI is the IRB of record for multisite, investigator-initiated trials (IITs), the UCI IRB may require a cover sheet specific to each relying site, listing the UCI LR, site-specific lead collaborating researcher/s and site-specific CR’s approved to finalize consent. This cover sheet may be appended to the top of the single, IRB approved, ICD. This efficiency will allow CR changes at study sites to be handled at the respective site only (along with verification of human research subject trainings).
 - d. For greater than minimal risk research that involves the application of an investigational drug, device, or surgical procedure, only a United States (US) licensed medical doctor or US licensed nurse practitioner may finalize the consent process.
 - (1) We realize and appreciate that Departments may have specific policies related to consent that may be more restrictive. Researchers should be aware of these policies and adhere accordingly.
 - 4. The IRB recommends that the informed consent documents apply to

the following division of target populations:

- a. Age 18 or older utilizing the adult informed consent document;
- b. Ages 13 to 17 utilizing a combination assent/parental permission form, in the same language as the adult informed consent document;
- c. Ages 7 to 12 utilizing an assent form written simply and at a comprehension level appropriate for a 7 year old; and
- d. Less than 7 years of age utilizing an oral script in very simple language appropriate for children of this age group.

B. Obtaining Informed Consent

1. The LR will provide a copy of the currently approved and IRB date-stamped informed consent documents to the participant or his or her legally authorized representative.
2. A surrogate decision-maker may grant permission for an individual to participate in research provided that use of the surrogate consent process has been requested by the LR and approved by the IRB.
3. The LR will provide the participants or his or her legally authorized representative adequate time to read the consent, ask questions, and consider the risks and/or benefits to participation in the research study prior to obtaining their signature.
4. Assent or dissent and documentation of such are to be obtained as directed by the determination of the IRB Committee.
5. Participants or the participant's legally authorized representative will provide a signature and the date of signature on all informed consent documents, unless a waiver of documentation has been requested by the LR and approved by the IRB.
6. For FDA-Regulated Studies using an electronic process to document consent, the LR must use [DocuSign Part 11](#) for obtaining signatures on the Informed Consent Form.

C. Non-English Speaking Participants

1. Translation of English Language ICD and all recruitment material: Participants who do not speak English should be presented with an informed consent document and recruitment materials written in a language understandable to them.
 - a. Translations for targeted populations that are non-English speaking must be submitted for review and approval. The LR may wish to delay translation until IRB approval is granted for the English version informed consent documents (including recruitment materials) to avoid extra translation costs.
 - b. Translation Requirements:
 - (1) **Greater than minimal risk studies:** professional or certified translation of ICD and recruitment materials is required for studies that pose more than minimal risk to participants.
For a professional translation the LR must provide the qualifications of the individual who translated the informed consent documents and recruitment materials. Include any credentials, certifications, education, native language fluency, etc. For a certified translation, a copy of the certification from the translator or translation service should be attached to the translation of any informed consent documents and recruitment materials.
 - (2) **Minimal risk studies:** Studies that are eligible for expedited

review also require translation of ICD and recruitment materials; however, certified translation is not required. The IRB will accept documents translated by an individual fluent (i.e., can speak, read, and write) in a given language. The qualifications of the individual performing the translation will be assessed by the IRB. A letter or statement from the translator describing their qualifications must be provided with the translation documents.

2. Use of Short Form Consent Document

- a. Investigators requesting the short form consent process must request this use via the IRB application.
- b. When informed consent is documented using the short form consent procedure for non-English speaking participants, the following is applicable:
 - (1) The IRB approved English version of the consent document and the short form consent documents will be provided in a language understandable to the participant.
 - (a) This includes a verbal translation of the English version of the consent form (i.e., the “long form”), along with a hard copy of the short form, written in a language understandable to the participant;
 - (2) A copy of the Experimental Subject’s Bill of Rights should be provided to all research participants considering participation in a medical experiment (provided in a language understandable to the participant);
 - (3) A witness who is fluent in both English and the language understandable to the participant should be present; and
 - (4) Once the participant has consented and eligibility is confirmed, the IRB approved English version of the consent document must be translated into the participant’s language by a professional or certified translator. *The translated consent form must be provided to the participant within one month from the date that eligibility is confirmed.*
- c. Required signatures for short form consent procedures include:
 - (1) The short form document should be signed and dated by the participant;
 - (2) The IRB approved English version of the consent document should be signed and dated by the person obtaining consent as authorized under the protocol; and
 - (3) The short form document and the IRB approved English version of the consent document should be signed and dated by the witness. When the person obtaining consent is assisted by a translator, the translator may serve as the witness.
- d. It is important to note that the FDA states that investigators should carefully consider the ethical/legal ramifications of enrolling participants when a language barrier exists. If the participant does not clearly understand the information presented, the participant’s consent will not truly be informed and may not be legally effective.

D. Waiver of Documentation of Informed Consent

1. The Investigator will assess the proposed research to determine if it meets regulatory requirements for a waiver of documentation of informed consent.

2. The Investigator will complete and submit for review a justification for the Request for a waiver of written (signed) informed consent.
 3. When the IRB waives the requirement for documentation of informed consent because the principal risk would be potential harm resulting from a breach of confidentiality, each participant must be asked whether he or she wants documentation linking him or her with the research, and the participant's wishes will govern.
- E. Any revisions to the informed consent process or documents will be submitted to the IRB for review and approval as presented in the amendment policy and procedure (See IRB Policy # 17).

II. **IRB Committee Responsibilities**

- A. The LR's plan to obtain informed consent should be assessed by the IRB Committee, the Chairperson, or designee must determine that the appropriate requirements are met.
1. The IRB should consider the nature of the proposed participant population, the type of information to be conveyed, and the circumstances under which the consent process will take place (e.g., manner, timing, place, personnel involved);
 2. All elements of consent as required by the Federal Regulations, as well as any appropriate additional elements are incorporated into the documents;
 3. Provisions have been made if the study is to include non-English speaking participants and the translated documents have been (will be) verified to be in a language understandable to the participant;
 4. The IRB Reviewers must assure that provisions for obtaining surrogate decision-maker consent are reviewed for appropriateness, when applicable;
 5. The reviewers are to verify that the informed consent documents match the protocol narrative and IRB application. If not, the Reviewer or Committee will request revisions prior to granting approval;
 6. The Reviewers will assure that the written language is in lay terms with correct grammar, spelling, and punctuation for readability and understanding.
- B. In order to determine that the use of the short form process is acceptable, consider whether the investigator has addressed or acknowledged all of the following criteria as outlined in the IRB Application:
1. Provided a compelling and sound rationale for use of the short form consent.
 2. The short form states that the elements of disclosure required by regulations have been presented orally to the participant or the participant's legally authorized representative.
 3. A written summary (i.e., IRB approved English version of the consent document) that embodies the basic and required additional elements of disclosure has been included.
 4. A witness will be present for the oral presentation.
 5. For participants who do not speak English, the witness will be conversant in both English and the language of the participant.
 6. The participant or the participant's legally authorized representative will sign and date the short form consent document.
 7. The witness will sign both the short form and a copy of the IRB

- approved English version of the consent document.
8. The investigator or designee actually obtaining consent will sign a copy of the IRB approved English version of the consent document.
 9. A copy of the short form consent will be given to the participant or the legally authorized representative.
 10. A copy of the IRB approved English version of the consent document will be given to the participant or the legally authorized representative.
 11. A copy of the Experimental Subject's Bill of Rights should also be provided to all research participants considering participation in a medical experiment.
- C. The IRB must review all amendments to the informed consent process or documentation. A determination of the necessity of re-consenting participants must also be rendered.
 - D. When the research includes children, the IRB must determine whether assent is required, for what ages assent is required, and how assent is to be documented.
 - E. Decisions to waive documentation of informed consent are documented in the IRB approved protocol and IRB minutes, if applicable.

III. IRB Analyst or Higher Responsibilities

- A. The Analyst will conduct a pre-review of all informed consent documents submitted for IRB review and approval utilizing the informed consent checklist.
- B. Correspondence recommending pre-review changes to the informed consent documents are sent to the LR by the Analyst in the electronic IRB submission and management system.
- C. Once final approval is granted by the IRB, the informed consent documents will be stamped with current "Date of IRB Approval" (See IRB Policy # 34).
- D. Changes to the informed consent process and/or documents are to be completed according to the IRB amendment request policy and procedure.
- E. Appropriate electronic IRB submission and management system entries are to be completed.

References:

45 CFR 46.111

45 CFR 46.116 and 46.117

21 CFR 56.109

OHRP Guidance Document, "Informed Consent, Non-English Speakers" dated November 1995.

OHRP IRB Guidebook, "Protecting Human Research Subjects: Institutional Review Board Guidebook"

FDA Information Sheets, "Guidance for Institutional Review Boards and Clinical Investigators", 1998

2018 Common Rule 45 CFR 46

Policy Number: 32

Title: Waiver or Alteration of Informed Consent for Human Subjects Research

Date of Last Revision: 01/21/07; 11/20/10, 09/14/18, 04/07/22, 07/29/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to grant a waiver or alteration of informed consent for research in accordance with the Federal regulations and IRB policies and procedures.

Generally, the IRB must assure that provisions are made to obtain legally effective informed consent prospectively from each research participant or the participant's legally authorized representative.

If the research involves accessing Student Records the research must comply with Family Educational Rights and Privacy Act (FERPA) (20 U.S.C. § 1232g; 34 CFR Part 99): The federal regulation that protects the privacy of student education records. This regulation applies to all schools that receive funds under an applicable program of the U.S. Department of Education. Generally, a waiver of the consent process is prohibited. The parent or eligible student must provide permission or consent to obtain any information from a student's education record for research purposes.

When research involves a [test article](#) and is subject to Food and Drug Administration (FDA), except as provided in 21 CFR 50.23 and 21 CFR 50.24 and described below in sections V, VI and VII, no investigator may involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative.

In order for an IRB to waive or alter consent, the IRB must find and document one of the following options:

- I. **Requirements for Waiver or Alteration of Consent – Screening, Recruiting or Determining Eligibility (Common Rule 2018)**
 - A. 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.

- II. **Broad Consent Preclusion for Waiver of Consent (Common Rule 2018)**
 - A. If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements of Broad consent at 45 CFR 46.116(d) and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.
 - B. **UCI has elected to not implement Broad Consent.**
- III. **Requirements for Waiver or Alteration of Consent (Items in blue are shared with the FDA per the July 2017 Information Sheet Guidance)**
 - A. The research or clinical investigation involves no more than minimal risk (per 21 CFR 50.3(k) or 21 CFR 56.102(i)) to the participant; and
 - B. 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; and
 - C. The waiver or alteration will not adversely affect the rights and welfare of the participants; and
 - D. The research or clinical investigation could not practicably be carried out without the waiver or alteration; and
 - E. Whenever appropriate, the participants will be provided with additional pertinent information after participation
- IV. **Requirements for Alteration of Consent (45 CFR 46.117(c)(1)) (also known as a waiver to obtain a signed informed consent form)**
 - A. That the only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject (or legally authorized representative) will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; and
 - B. That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context; or
 - C. If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.
 - D. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects or legally authorized representatives with a written statement regarding the research.
- V. **FDA Enforcement Discretion for In Vitro Diagnostics**

Under FDA's regulations governing the conduct of in vitro diagnostic (IVD) device studies, the definition of "subject" includes individuals on whose specimens an investigational device is used [see 21 CFR 812.3(p)]. This means that this research is subject to FDA regulations and thus a waiver of consent cannot be granted. The FDA believes that it is possible in certain circumstances for IVD device investigations to be conducted using leftover specimens obtained without

informed consent while protecting the human subjects who are the source of such specimens.

The FDA intends to exercise enforcement discretion as to the informed consent requirements for clinical investigators, sponsors, and IRBs if an in vitro diagnostic device investigation is performed and all of the following are true:

1. The investigation meets the IDE exemption criteria at 21 CFR 812.2(c) (3): A diagnostic device, if the testing:
 - (i) Is noninvasive,
 - (ii) Does not require an invasive sampling procedure that presents significant risk,
 - (iii) Does not by design or intention introduce energy into a subject, and
 - (iv) Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
2. The study uses leftover specimens, that is, remnants of specimens collected for routine clinical care or analysis that would have been discarded. The study may also use specimens obtained from specimen repositories or leftover specimens that were previously collected for other research purposes.
3. The specimens **are not individually identifiable**, i.e., the identity of the subject is **not known to and may not readily be ascertained by the investigator or any other individuals associated with the investigation**, including the sponsor. If the specimen is coded, it will be considered to be not individually identifiable if neither the investigator(s) nor any other individuals associated with the investigation or the sponsor can link the specimen to the subject from whom the specimen was collected, either directly or indirectly through coding systems.
4. The specimens may be accompanied by clinical information as long as this information does **not make the specimen source identifiable** to the investigator or any other individual associated with the investigation, including the sponsor.
5. The individuals **caring for the patients are different from and do not share information about the patient** with those conducting the investigation.
6. The **specimens are provided to the investigator(s) without identifiers** and the supplier of the specimens has established policies and procedures to prevent the release of personal information.
7. The **study has been reviewed by an IRB**.

VI. **Emergency use of a Drug or Device Exception to the Requirement for Consent at 21 CFR 50.23(a)-(c)**

Emergency Use means the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval. FDA regulations exempt research from prior IRB review for the use of a test article in a life-threatening situation in which no standard treatment is available. Exception

The use of informed consent is required unless the physician imposing an emergency use situation and another physician not otherwise participating in the clinical investigation certify in writing that all of 21 CFR 50.23(a) have been met:

- A. The human subject is confronted by a life-threatening situation necessitating the use of the test article.
- B. Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.
- C. Time is not sufficient to obtain consent from the subject's legal representative.
- D. There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

(See Policy # 45.)

VII. Exception from Informed Consent Requirements for Planned Emergency Research (21 CFR 50.24 or 45 CFR 46.101(i))

The IRB may approve planned research in an emergency setting without the informed consent of the participants or their legally authorized representatives in a limited class of emergency situations when the following criteria are met and documented:

- A. The target population for the research is in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
- B. Obtaining informed consent is not feasible because:
 - 1. The subjects will not be able to give their informed consent as a result of their medical condition;
 - 2. The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and
 - 3. There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.
- C. Participation in the research holds out the prospect of direct benefit to the subjects because:
 - 1. The subjects are facing a life-threatening situation that necessitates intervention;
 - 2. Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and
 - 3. The risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of the proposed intervention or activity.
- D. The clinical investigation could not practicably be carried out without the waiver.
- E. The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the Investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The Investigator must agree to summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing

review.

- F. The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with Federal regulations and IRB policies and procedures. The informed consent procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible.
- G. Additional protections of the rights and welfare of the subjects will be provided, including, at least:
 - 1. Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;
 - 2. Prior to the initiation of the clinical investigation, public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn of plans for the investigation and its risks and expected benefits;
 - 3. At the completion of the clinical investigation there are plans for public disclosure of sufficient information to apprise the community and researchers of the study. The information must include the demographic characteristics of the research population and results of the clinical investigation.
 - 4. Establishment of an independent data and safety monitoring committee to exercise oversight of the clinical investigation; and
 - 5. If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the Investigator must commit to attempting to contact within the therapeutic window, the subject's family member who is not a legally authorized representative and asking whether he/she objects to the subject's participation in the clinical investigation. The Investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.
- H. Procedures must be in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document, specifically that the he/she may discontinue the subject's participation at any time without penalty or loss of benefits of which the subject is otherwise entitled.
- I. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible.
- J. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.
- K. All clinical investigation records, including regulatory files, must be maintained for at least 3 years after the completion of the clinical investigation and will be accessible for inspection and copying by the regulatory authorities, as applicable.
- L. Clinical investigations that are granted an exception to the informed

consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies that the clinical investigation may include subjects who are unable to consent. The submission of these clinical investigations to the FDA for a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for this IND/IDE may not be submitted as an amendment to the existing IND/IDE.

- M. If the IRB determines it cannot approve a request for exception from informed consent requirements in planned emergency research because the clinical investigation does not meet the criteria according to Federal regulations, IRB policies and procedures, or other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the Lead Researcher who will forward to the sponsor of the clinical investigation.

VIII. **Planned Emergency Research Not Subject to FDA Regulations (Informed Consent Requirements in Emergency Research (OPRR Letter, 1996))**

The IRB Committee determines:

- A. The research does not meet FDA regulations in 21 CFR 50; and Items A-J as stated above are met. The term “clinical investigation” may be replaced by “research.”
- C. For the purposes of this waiver “family member” means any of the following legally competent persons: spouses; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the participant was the equivalent of a family relationship.

IX. **Planned Emergency Research funded by a Department of Defense entity:** If the research subject meets the definition of “experimental subject,” a waiver of the consent process is prohibited unless a waiver is obtained from the Secretary of Defense.

- A. If the research participant does not meet the definition of “experimental subject”, policies and procedures allow the IRB to waive the consent process.

X. **Waiver for Research Activities Designed to Study Certain Aspects of Public Benefit or Service Programs**

- 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
 - 2. The research could not practicably be carried out without the waiver or alteration.

References:

45 CFR 46
45 CFR 46.116

21 CFR 50 and 56

21 CFR 50.24

DoD: 10 USC 908(b)

ED: 34 CFR 99

Informed Consent Requirements in Emergency Research (OPRR Letter, 1996):

<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/emergency-research-informed-consent-requirements/index.html>

FDA Information Sheets- Exception from Informed Consent for Studies Conducted in Emergency Settings: <https://www.fda.gov/media/80554/download>

FDA Guidance Waiver of Consent/ Minimal Risk:

<https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM566948.pdf>

FDA Guidance / In Vitro Devices:

<https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm071265.pdf>

FDA Guidance/ Children:

<https://www.fda.gov/scienceresearch/specialtopics/runningclinicaltrials/ucm119111.htm>

Procedure Number: 32.A**Title: Procedure for Waiver or Exception of Informed Consent****Purpose:**

This procedure provides guidance on obtaining a waiver of informed consent; and requesting approval for exception from informed consent in planned emergency research from the UCI Institutional Review Board (IRB).

I. Lead Researcher (LR) Responsibilities

- A. Waiver or alteration of informed consent.
 - 1. The LR will assess the proposed research to determine if it meets regulatory requirements for a waiver or alteration of informed consent.
 - 2. The LR will complete and submit the applicable documentation to support the request for a waiver or alteration of informed consent, in accordance with the current and any related IRB policies.
- B. Exception from informed consent requirements for planned emergency research.
 - 1. The LR is responsible for providing all study documents and any additional materials requested by the IRB to prepare and conduct community consultation and public disclosure of the proposed research.
 - 2. The LR will prepare and submit to the IRB materials in preparation for public disclosure following completion of the research.
 - 3. The LR will establish an independent data and safety monitoring committee to exercise oversight of the clinical investigation.
 - 4. When the LR is unable to locate a legally authorized representative, the LR will attempt to contact, within the therapeutic window, the participant's family member who is not a legally authorized representative, to ask whether he or she objects to the individual's participation. A summary of efforts to contact the legally authorized representative and family members is made available to the IRB at the time of continuing review.

II. IRB Committee Responsibilities

- A. The IRB Reviewers will consider the request for a waiver of informed consent and the LR's justification verifying and documenting those regulatory conditions are applicable to the proposed research activity.
- B. If the IRB differs in their determination from the LR's request, this will be documented in the electronic IRB submission and management system.
- C. IRB determinations will be noted on the final, IRB approved IRB Application, along with the IRB approval letter.
- D. When amendments are made to a currently approved research study, the waiver of informed consent is reassessed by the IRB Committee, Chairperson or their designee, and a determination made as to whether the conditions for the waiver have been altered, necessitating the rescinding of the waiver. If this occurs, the IRB also determines whether currently enrolled participants must be re-consented by the LR.
- E. Exception from informed consent requirements for planned emergency research requires additional protections for the rights and welfare of the participants including, but not limited to the following:
 - 1. Consultation with representatives of the communities in which the investigation is conducted and from which the participants are drawn;

2. Public disclosure of plans for the investigation and its risks and expected benefits to the communities in which the research is conducted and from which the participants are drawn;
3. Public disclosure at the completion of the research to apprise the community and researchers of the study. This may include the demographic characteristics of the research population and study results.

III. IRB Analyst or Higher Responsibilities

- A. As applicable to the level of review, and considering the IRB review timeframe, the Analyst conducts a pre-review of the informed consent process and documents submitted with an IRB application to determine that the correct forms have been utilized for the targeted population; assesses the readability of the document and assures that all the necessary elements as required by the Federal regulations are present for adequate informed consent, including if any additional elements are appropriate.
- B. If additional information regarding the informed consent process or documentation is needed, the Analyst contacts the LR and requests the additional information.

Policy Number: 33

Title: Assent/Dissent by Children or Cognitively Impaired Adults who Lack Decision-Making Capacity

Date of Last Revision: 07/28/06, 08/20/10, 04/07/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to assure that adequate provisions are made for soliciting the assent or dissent of children and cognitively impaired adults who lack decision-making capacity.

- I. In instances where the participant is not legally capable of giving informed consent (e.g., children) or where the participant is cognitively impaired, the IRB must find that adequate provisions are made for soliciting the assent of the participant when in the judgment of the IRB, the participant is capable of providing assent. (See IRB Policies #36 and #39.)
- II. In determining whether participants are capable of assenting, the IRB shall take into account the age, maturity, and psychological state of the participant involved. This judgment may be made for all participants to be involved in research under a particular protocol, or for each participant, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the participants 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 participant and is available only in the context of the research, the assent of the participant is not a necessary condition for proceeding with the research. Even where the IRB determines that the participants are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with IRB Policy #36.
- III. When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

References:

The *Belmont Report*

45 CFR 46, Subpart D

21 CFR 50, Subpart D

IRB Policy 30, "Legally Effective and Prospectively Obtained Informed Consent"

IRB Policy 32, "Waiver of Informed Consent for Human Subjects Research or Exception of Informed Consent Requirements for Emergency Research"

IRB Policy 36, "Vulnerable Populations: Children"

IRB Policy 39, "Individuals Who Are Cognitively Impaired or Mentally Disabled"

Procedure Number: 33.A**Title: Procedure for Obtaining Assent/Dissent by Children or Cognitively Impaired Adults who Lack Decision-Making Capacity****Procedure:**

The purpose of this procedure is to outline the process for obtaining assent in children and cognitively impaired adults who lack the capacity for decision-making for participation in research activities.

I. Lead Researcher (LR) Responsibilities

- A. The LR will indicate the targeted study population as instructed in the IRB Application and provide a description. When the targeted population includes children or cognitively impaired adults who lack decision-making capacity, the LR will also provide a detailed description on how assent will be obtained and documented, or request consideration of a waiver of assent.
- B. The LR will draft the assent documents and may utilize the assent template located on the IRB Website at <https://research.uci.edu/human-research-protections/irb-forms/> under the heading "IRB Consent Forms."
- C. The LR will obtain permission from the child's parents or legal guardians in conjunction with assent requirements. Documentation of permission from the child's parents or legal guardians is provided by their signature and date on the informed consent document.
- D. Permission must also be obtained for research participants who are cognitively impaired and/or lack decision-making capacity from the individual's legally authorized representative, unless a waiver of informed consent has been granted by the IRB. Permission will be documented by the legally authorized representative's signature and date on the informed consent document.

II. IRB Committee Responsibilities

- A. The IRB Committee will review research involving children and cognitively impaired adults who lack decision-making capacity to determine whether assent is:
 - 1. Required of all participants in the proposed research; or
 - 2. Required on a case-by-case basis, when in the Investigator's opinion, the individual is able to comprehend the proposed research purpose and associated activities and procedures.
- B. The IRB Committee will also consider granting a waiver of assent in circumstances in which the targeted population does not have the ability to comprehend the proposed research purpose and/or associated procedures.
- C. The IRB Committee will consider granting a waiver of assent in circumstances in which the research holds out the prospect of direct benefit that is important to the health or well-being of the participant and is available only in the context of the research.
- D. The IRB shall take into account the age, maturity, and psychological state of the participants involved to determine if and when assent is required and the method of documenting assent.
- E. The IRB will review the LR's plan for assessment of the research participant's ability to provide assent and determine if the plan is appropriate. The IRB will make recommendations for additional

requirements, when necessary.

III. IRB Analyst or Higher Responsibilities

- A. The Analyst will complete a pre-review of the initial study submission involving children or cognitively impaired adults who lack decision-making capacity for the inclusion of assent plan, or a request for a waiver of assent in these targeted populations.
- B. If the plan for assent is not included in the initial submission, the Analyst will request additional information from the LR.
- C. The Analyst will pre-review the assent documents assuring that each has been presented in an age-appropriate language for children and in simple lay language for the cognitively impaired adults who lack decision-making capacity. The Analyst may forward recommendations for revisions to the LR prior to the meeting through the electronic IRB submission and management system.
- D. The Analyst will assign the study to Reviewers who have the expertise in the area of the proposed research and the population targeted. If a member with those qualifications is not a regular Committee member, an expert consultant will be sought.

References:

The *Belmont Report*

45 CFR 46, Subpart D

IRB Policy 30, "Legally Effective and Prospectively Obtained Informed Consent"

IRB Policy 32, "Waiver of Informed Consent for Human Subjects Research or Exception of Informed Consent Requirements for Emergency Research"

IRB Policy 36, "Vulnerable Populations: Children"

Policy Number: 34

Title: Approval Dates on Informed Consent Documents

Date of Last Revision: 08/10/05, 09/27/10, 06/05/13, 09/01/15, 04/07/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to stamp all IRB-approved informed consent documents with the Date of IRB Approval.

- I. Neither the Food and Drug Administration (FDA) or the Office for Human Research Protections (OHRP) mandate that the IRB stamp the final IRB-approved copy of the consent document. As part of UCI HRP policy, HRP staff affix the IRB approval date to all approved informed consent documents and recruitment materials. Copies of the current, date stamped as approved documents are the only versions that may be used by Investigators in recruiting and obtaining consent for research activities.
- II. **Date of IRB Approval** - The approval date is the date that the IRB application and informed consent documents were reviewed and granted approval by the IRB, either at initial review, amendment or renewal. The date of IRB approval which appears on the informed consent documents is the date of approval for the latest version of the informed consent documents.
- III. **Date of IRB Expiration** - The expiration date is the date that signifies the end of the current IRB approval period. The Federal 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 on or before the date when IRB approval expires. *In a measure to reduce administrative burden, HRP Staff do not include the expiration date on the final, IRB-approved copy of the consent document(s), as part of the IRB stamp.*

Procedure Number: 34.A**Title: Procedure for Stamping IRB Approval Dates on Informed Consent Documents****Procedure:**

The purpose of this procedure is to provide guidance on stamping IRB approval dates on informed consent documents.

I. Lead Researcher (LR) Responsibilities

- A. LRs are to electronically submit all informed consent documents as a part of a new study submission for review and approval. It is recommended that the LR use the informed consent template located on the IRB website at <https://research.uci.edu/human-research-protections/irb-forms/> under the heading “IRB Consent Forms.”
- B. Investigators are required to submit an electronic copy of the most recent informed consent documents with amendment requests. For continuing reviews, Investigators need to indicate on the continuing review application which informed consent documents need to be kept active. When reviewed and approved by the IRB, if changes have been made, a new approval date will be date-stamped on the active informed consent documents.
- C. Informed consent documents do not need to be reviewed in continuing reviews with no intent to enroll additional participants. However, the research study cannot be re-opened to enrollment without an amendment request to reactivate the consent form.
- D. It is the LR’s responsibility to only use the most current version of the informed consent documents bearing the approval date when obtaining informed consent from research participants. All current approved informed consent documents are available to the study team in the electronic IRB submission and management system.

II. IRB Committee Responsibilities

- A. The IRB Committee is to determine the appropriate review interval based on the Federal regulations and IRB policies and procedures regarding review and approval.

III. IRB Analyst or Higher Responsibilities

- A. Calculating the “Date of IRB Approval” on the Informed Consent Documents
 - 1. Approval at a convened meeting - When the convened IRB Committee approves the IRB application, the date of the convened IRB Committee meeting is the “Date of IRB Approval” stamped on the informed consent documents.
 - 2. Minor revisions required at a convened IRB Committee meeting - When the IRB application is approved with specific changes requested, pending review and approval by the Chair, the date that the changes are verified by the Chairperson or his or her designee is the “Date of IRB Approval” stamped on the informed consent documents.

3. Expedited Review - When the IRB application is approved through an expedited review process, the date that final approval is extended by the Chairperson or his or her designee is the “Date of IRB Approval” stamped on the informed consent documents.
4. Renewal
The “Date of IRB Approval” for the Renewal application is based on the type of review or determination as described above. For example, when an Expedited Renewal is approved pending changes at a subcommittee meeting; the date that the changes are verified by the Chairperson or his or her designee is the date of IRB approval stamped on the informed consent documents.
5. Amendments - The “Date of IRB Approval” for amended informed consent documents and for reconsent cover memos, if applicable, is based on the type of review or determination as described above. For example, when an amendment is approved pending changes at a convened IRB Committee meeting, the date that the changes are verified by the Chairperson or his or her designee is the date of IRB approval stamped on the informed consent documents.

IV. **IRB Analyst or Higher Responsibilities**

- A. How to Date Stamp Informed Consent Documents
 1. Once approval is granted, the Analyst will electronically affix the official stamp in the footer of each page.
 2. The date of IRB Approval and the assigned Human Subjects Number (HS#) will be entered in the official stamp. The date of IRB approval will match the date indicated in the IRB Approval Letter. The date of IRB expiration will be noted in the IRB Approval Letter only.
 3. The Analyst will electronically affix the IRB approval stamp upon initial approval to the informed consent documents and upon amendment (and IRB approval) to the informed consent documents.
- B. The Analyst will notify the Lead Researcher and administrative contact when the approval is available for downloading through the electronic IRB submission and management system.
- C. A copy of the date-stamped informed consent documents will be maintained in the electronic IRB submission and management system.

Policy Number: 35

Title: Policy for the Role of a Witness and/or Participant Advocate

Date of Last Revision: 05/13/2008; 06/16/2010; 02/26/2020; 04/11/2022

Policy:

The UCI Institutional Review Board (IRB) has the authority to observe or have a third party (i.e., an impartial witness) observe the consent process or to require a participant advocate to act as a liaison between an Investigator and a research participant, the participant's family, or a participant's legally authorized representative.

When meeting the requirement to attest that informed consent to the California Medical Experiment Act have been satisfied, the consent form is signed and dated by any person other than the subject or the subject's guardian or legally authorized representative who can attest that the requirements for informed consent has been met, as specified in Section 24175 of the California Health and Safety Code. At UCI, the investigator's signature serves this purpose and an impartial witness is not required (see Procedure # 35 A I).

- I. Observation of the consent process by a third party also called a witness is required in the following situations:
 - A. When using the foreign language short form process for participants who do not speak English;
 - B. When obtaining informed consent from a participant (or the participant's guardian or legally authorized representative) who can understand and comprehend the language but is physically unable to talk or write. The participant can be entered into a study if they are competent and able to indicate approval or disapproval by other means.
 - C. When obtaining informed consent from a participant (or the participant's guardian or legally authorized representative) who can speak but is unable to read or write.
 - D. When obtaining informed consent from a participant (or the participant's guardian or legally authorized representative) who is blind.
- II. The IRB may determine those additional protections such as observation of the consent process by an impartial witness or the involvement of a participant advocate in the consent process or throughout the course of the research study are necessary when the research:
 - A. Involves high risk to special or vulnerable populations (cognitively impaired individuals, children, prisoners, adults unable to read);
 - B. Methodology or procedures are ethically sensitive (e.g., donation of embryos for stem cell research); and/or
 - C. Is conducted by researcher who previously has failed to comply with the requirements of the Department of Health and Human Services (DHHS) regulations
 - D. Involves any other situation determined by the IRB to require additional protections.

III. Witness Role

- A. The role of a witness is to observe the consent process in situations required per Federal and State regulations, per UCI IRB policy or per the determination of the IRB.
- B. The witness should remain unbiased regarding the research and the participants. Their role is to assure the conduct of legally effective informed consent.
- C. The role of the witness may be served by a member of the IRB or may be an impartial third party. A witness must be an adult who is not a member of the study team (i.e., is not listed on the protocol narrative) and who is not a family member of the participant.
 - a. Short Form Consent Process: In cases where the interpreter or translator is an impartial third party to an oral / IRB approved short form consent process but is not physically present (e.g., a virtual consent process), the family member of the participant may be allowed to serve as a witness. The family member serving as a witness must be fluent in both English and the language of the participant. The witness must sign and date both the short form written informed consent document and a copy of the IRB approved English version of the consent document.
- D. The IRB Committee may require that the Investigator obtain an impartial witness, or the IRB may appoint an impartial witness.

IV. Participant Advocate Role.

- A. As determined by the IRB, the role of a participant advocate is to assure that the participant receives equitable and ethical treatment during the informed consent process and/or throughout the course of the research study. The advocate could be a single person with an interest in the population studied or a group of people interested in the safety of human research participants, usually within a certain population (e.g., breast cancer patients, patients with schizophrenia, etc.).
- B. The IRB Committee may require, at their discretion, that the Investigator use a participant advocate or provide an advocacy group as a contact to the participants. Moreover, the IRB may appoint a specific participant advocate.

References:

The Belmont Report

45 CFR 46

21 CFR 50

California Health and Safety Code 24170-24179.5

FDA Information Sheets: Frequently Asked Questions: Informed Consent Process, A Guide to Informed Consent

Guideline for Good Clinical Practice: <http://www.ich.org/LOB/media/MEDIA482.pdf>

Procedure Number: 35.A**Title: Procedure for the Role of a Witness and/or Participant Advocate****Procedure:**

This procedure outlines the process for the use of an impartial witness or a participant advocate in assisting the UCI Institutional Review Board (IRB) in the protection of human research participants.

- I. Investigator's Responsibilities.
 - A. To obtain an impartial witness to observe the consent form process when federal and state regulations apply to the research (see IRB Policy # 35, Item I).
 - B. To obtain an impartial witness to observe the informed consent process, per the authority of the IRB.
 - C. To utilize a participant advocate, to assist in the informed consent process and/or oversee the research process in studies where the IRB determined such oversight was required.
 - D. When meeting the requirement to attest that informed consent to the California Medical Experiment Act has been satisfied, the consent form is signed and dated by any person other than the subject or the subject's guardian or legally authorized representative who can attest that the requirements for informed consent have been met. At UCI, the investigator's signature serves this purpose and an impartial witness is not required.
- II. IRB Committee Responsibilities.
 - A. It is the responsibility of the IRB Committees to determine whether an impartial witness, participant advocate or advocacy group are necessary when the research:
 1. Involves high risk to special or vulnerable populations (cognitively impaired individuals, children, prisoners, adults unable to read);
 2. Methodology or procedures are ethically sensitive (e.g., donation of embryos for stem cell research); and/or
 3. Is conducted by researcher who previously has failed to comply with the requirements of the Department of Health and Human Services (DHHS) regulations
 4. Involves any other situation determined by the IRB to require additional protections.
 - B. The IRB Committee may determine that the impartial witness observe the consent process or a participant advocate be involved in specific activities associated with the research, e.g. the informed consent process or throughout the course of the research study.
- III. IRB Administrator Responsibilities.
 - A. The Administrator will conduct a pre-review of the study application and informed consent documents submitted with a new study application to determine the vulnerability of the research participants or the potential for vulnerability of the targeted population. If more information is needed regarding additional protections for inclusion of a vulnerable population, the informed consent process or documentation, the Administrator will

contact the Investigator and request the additional information.

- B. The Administrator will assure the informed consent document contains the proper language for the use of an impartial witness or participant advocate, if applicable.
- C. The Administrator will assist the Investigator in the appointment of an advocate, an advocacy group or an impartial witness, if deemed appropriate by the IRB Committee or requested by the Investigator.

Policy Number: 36

Title: Children

Date of Last Revision: 6/16/08, 11/20/10, 05/01/16, 09/16/22

Policy:

It is the policy of UC Irvine (UCI) Institutional Review Board (IRB) to review, approve, and provide guidance on the special ethical and regulatory considerations when children are involved in human subjects research based on the Federal regulations at 45 CFR 46 Subpart D and in addition to those imposed under other IRB policies, procedures, and other applicable Federal, State, and local laws.

I. Definitions:

- A. **Children:** According to Federal regulations 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 will be conducted.” In California, the legal age is 18.
- B. **Minors:** In California, individuals under the age of 18 years old are considered minors. Because in California some people under 18 years of age can consent for themselves to some research procedures, not all “minors” meet the federal criteria for being “children.”

II. IRB Review and Approval of Research Involving Children

The special vulnerability of children makes consideration of involving them as research participants particularly important. To safeguard their interests and to protect them from harm, special ethical and regulatory considerations apply for reviewing research involving children. Both the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA) afford additional protections for children in research. The IRB may approve research involving children only if those special provisions, as applicable, are met. The IRB must classify research involving children into one of four categories and document their discussions of the risks and benefits of the research study. The four categories of research involving children that may be approved by the IRB Committee are based on the degree of risk and benefit to individual subjects.

III. Categories of Research Involving Children

- A. Research Not Involving Greater than Minimal Risk to Children (45 CFR 46.404, 21 CFR 50.51). When the IRB finds that no greater than minimal risk to children is presented, the IRB may approve the research only if the IRB finds that adequate provisions are made for soliciting the assent of the children and permission of their parents or legal guardians, as set forth below in Section III.
- B. Research Involving Greater than Minimal Risk but Presenting the Prospect of Direct Benefit to the Individual Child (45 CFR 46.405, 21 CFR 50.52). If 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 child, or by a monitoring procedure that is likely to contribute to the child’s well-being, the IRB may approve the research only if the IRB finds that:
 - 1. The risk is justified by the anticipated benefit to the children;

2. The relation of the anticipated benefit to the risk is at least as favorable to the children as that presented by available alternative approaches; and
 3. Adequate provisions are made for soliciting the assent of the children and permission of their parents or legal guardians, as set forth below in Section III.
- C. Research Involving Greater than Minimal Risk and No Prospect of Direct Benefit to the Individual Child, but Likely to Yield Generalizable Knowledge about the Child's Disorder or Condition (45 CFR 46.406, 21 CFR 50.53). If 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 child, or by a monitoring procedure which is not likely to contribute to the well-being of the child, the IRB may approve the research only if the IRB finds that:
1. *The risk represents a minor increase over minimal risk;*
 2. 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;
 3. 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 participants' disorder or condition; and
 4. Adequate provisions are made for soliciting assent of the children and permission of their parents or legal guardians, as set forth below in Section III.
- D. Research Not Otherwise Approvable, which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Children (45 CFR 46.407, 21 CFR 50.54). If the IRB finds the research does not meet the requirements set forth in categories 46.404, 46.405 or 46.406 as described above, the IRB may approve the research only if:
1. 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 children; and
 2. If Federally funded, the Secretary of the Department of Health and Human Services (DHHS), after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following an opportunity for public review and comment, has determined either:
 - a) That the research in fact satisfies the conditions of categories 46.404, 46.405, or 46.406; or
 - b) The following:
 - (1) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
 - (2) The research will be conducted in accordance with sound ethical principles; and
 - (3) Adequate provisions are made for soliciting the assent of children and the permission of their parents or legal guardians, as set forth below in Section III.
 - c) The research can not begin until the IRB has received approval for the research from OHRP and grants final approval.

3. For non-Federally funded research meeting 45 CFR 46.407, see IRB Procedure # 36.B.

IV. **Requirements for Permission by Parents or Legal Guardians and for Assent by Children**

- A. Adequate Provisions for Child's Assent. The IRB must find that adequate provisions are made for soliciting the assent of child participants when in the judgment of the IRB the children are capable of providing assent.
 1. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, for some children, or for each child, as the IRB deems appropriate. The child should be given an explanation of the proposed research procedures in a language that is appropriate to the child's age, experience, maturity, and condition.
 2. Waiver of Assent. If the IRB determines either of the following to be true, then the assent of the children is not a necessary condition for proceeding with the research:
 - a. The capability of some or all of the children is so limited that they cannot reasonably be consulted; or
 - b. 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.
 - (1) Therefore, when the research offers the child the possibility of a direct benefit that is important to the health or well-being of the child and is available only in the context of the research, the IRB may determine that the assent of the child is not necessary.
 - (2) Additionally, in such circumstances, a child's dissent which should normally be respected may be overruled by the child's parents at the IRB's discretion. When research involves the provision of experimental therapies for life-threatening diseases such as cancer, however, the IRB should be sensitive to the fact that parents may wish to try anything, even when the likelihood of success is marginal and the probability of extreme discomfort is high. Should the child not wish to undertake such experimental therapy, difficult decisions may have to be made. In general, if the child is a mature adolescent and death is imminent, the child's wishes should be respected.
 - (3) Finally, even where the IRB determines that the child participants are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived for adults in accordance with IRB Policy # 32 regarding waiver or alteration of informed consent.
- B. Adequate Provisions for Parents' or Legal Guardians' Permission The IRB must find that adequate provisions are made for soliciting the permission of each child's parents or legally authorized representative.
 1. Research not involving greater than minimal risk to children (45 CFR 46.404, 21 CFR 50.51, 21 CFR 50.55). Where parental permission is to be obtained, the IRB must determine whether the permission of one parent is sufficient even if the other parent was alive, known,

competent, reasonably available, and shared legal responsibility for the care and custody of the child; or the permissions of both parents is required unless one parent was deceased, unknown, incompetent, or not reasonably available, or when only one parent had legal responsibility for the care and custody of the child.

2. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child (45 CFR 46.405, 21 CFR 50.52, 21 CFR 50.55). Where parental permission is to be obtained, the IRB must determine whether the permission of one parent is sufficient even if the other parent was alive, known, competent, reasonably available, and shared legal responsibility for the care and custody of the child; or the permissions of both parents is required unless one parent was deceased, unknown, incompetent, or not reasonably available, or when only one parent had legal responsibility for the care and custody of the child.
3. Research involving greater than minimal risk and no prospect of direct benefit to the individual child, but likely to yield generalizable knowledge about the child's disorder or condition (45 CFR 46.406, 21 CFR 50.53, 21 CFR 50.55). When the research is approved under Section III.C. above, and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
4. Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (45 CFR 46.407, 21 CFR 50.54, 21 CFR 50.55). When the research is approved under Section III.D. above and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

C. Waiver of Parental or Legal Guardian Permission - If the IRB determines that a research protocol is designed for conditions or a participant population in which parental or legally authorized representative permission is not a reasonable requirement to protect the participants (for example, neglected or abused children), it may waive the consent requirements described above, provided both:

1. An appropriate mechanism for protecting the children who will participate as subjects in the research is substituted; and
2. The waiver is not inconsistent with Federal, State, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research participants, and their age, maturity, status, and condition.
3. Waiver of Parental Permission may be considered when the:
 - a. Research involves procedures for which adolescents have the legal right to consent on their own behalf, such as prevention, diagnosis and/or treatment of mental health disorders; pregnancy; venereal disease or other infectious or sexually transmitted diseases; alcohol or drug abuse; rape or sexual assault (California Family Code 6920-6929). (See Policy # 29.)
 - b. Research involves self-sufficient minors. (See Policy # 29.)
 - c. Research involves legally emancipated minors. (See Policy # 29.)

- D. Documentation
 - 1. Permission by parents or legal guardians shall be documented in the same manner as required for participants under IRB Policy # 31.
 - 2. When the IRB determines that assent of a child is required, it shall also determine whether and how assent must be documented.
- E. Wards of the State or Other Agency - Children who are wards of the state or any other agency, institution, or entity can be included in research approved under Section III.C. (45 CFR 46.406) and Section III.D. (45 CFR 46.407) only if the IRB finds and documents that 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.
- F. If the research is approved under 45 CFR 46.408(a), the IRB must require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or *in loco parentis*. One individual may serve as advocate for more than one child. The advocate shall 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 Investigators, or the guardian organization.
- G. Pediatric Expertise on IRB Committee. An IRB Committee considering a protocol involving children as participants should:
 - 1. Assess its needs for pediatric expertise among the IRB voting membership to assure that it possesses the professional competence necessary to review the specific research activities; and
 - 2. Include one or more individuals who are knowledgeable about and experienced in working with children. To fulfill this requirement, the IRB Committee may invite a non-voting consultant to assist in the review of issues which require expertise beyond, or in addition to, that available among voting IRB members. If expertise is not available, the IRB will defer review to another meeting.
 - 3. When reviewing research funded by the National Institute on Disability and Rehabilitation Research, should the research purposefully include children with disabilities as research participants, the IRB must include at least one person primarily concerned with the welfare of these research participants.

V. **California Requirements Involving Children**

- A. Consent for Themselves: (California Family Code, Sections 6920-6929): Describes when minors (children) may consent for themselves.
- B. California Requirements for Human Subject Research – Consent of a Minor: Additional Guidance and Requirements:
 - 1. Children - For subjects < 18 years of age, their parents or legal guardians are the legally authorized representatives who may grant permission for their participation in research.
 - 2. Parents - Only the parents may grant permission for their child's participation in research. Assent is to be sought from the child, only after permission has been obtained from the parents. Grandparents and other relatives or caregivers may not grant permission unless they have been granted formal custody of the child by a court. In such cases, the LR must obtain a copy of the court order as evidence of that person's authority to grant permission for participation in research

- on the child's behalf.
3. Children in State Custody - According to the California Department of Children's Services' (DCS) applicable policies by virtue of the court order granting DCS legal custody of certain children (e.g., foster children) that Department is the agency that is authorized to grant permission for participation in research for children in their custody. The decision of whether to grant permission for research is made on a case-by-case basis by DCS. In such cases, the LR must obtain a copy of the court order from DCS.
 4. Mature Minors or Emancipated Minors - In certain limited circumstances, it may be appropriate to allow a mature minor to consent to participation in a research study in the absence of the permission of a parent or legal guardian if the minor has the sufficient capacity to consent to the procedures involved in the research study.
 5. The IRB will determine whether the inclusion of mature minors or emancipated minors in research activities in the absence of the permission of a parent or legal is appropriate. Further, each situation is judged on a case-by-case basis. *For clinical investigations, UCIMC Hospital Administration should be consulted before initiating any research activity including screening.* Documentation of those decisions must be included in the research file.
 6. The following information provides examples of circumstances under which California law combined with federal regulations permits individuals under 18 to enroll in research without permission from parent(s) or guardian(s):
 - (1) Minors may consent for themselves to medical care related to the prevention or treatment of pregnancy, but not necessarily to sterilization or abortion [California Family Code Section 6925; Health and Safety Code Section 123450 for abortion].¹
 - (2) Minors 12 years of age or older have the legal right to consent on their own behalf, for:
 - a) Mental health treatment or counseling on an outpatient basis or residential shelter services (in limited circumstances) [California Family Code Section 6924].
 - b) Medical care related to the diagnosis or treatment of infectious, contagious, or communicable diseases that are required to be reported to the local health officer or a related sexually transmitted disease [California Family Code Section 6926].
 - c) Medical care related to the diagnosis or treatment of the condition and collection of medical evidence about alleged rape or sexual assault [California Family Code Section 6927].
 - d) Medical care and counseling related to the diagnosis and treatment of an alcohol or drug-related problem [California Family Code Section 6929].
 - (3) Self-sufficient minors who are:
 - a) 15 years of age or older;
 - b) living separately from their parents/guardians; and

¹ (highlighting remains intentionally): American Academy of Pediatrics v. Lungren (1997) 16 Cal.4th 307. **A minor may consent to an abortion without parental consent and without court permission.** California Health and Safety Code remains unchanged.

- c) managing their own financial affairs have the legal right to consent on their own behalf to medical or dental care [California Family Code 6922].
- (4) Emancipated minors, those who are:
 - a) married or divorced
 - b) on active duty in the U.S. armed forces **or** emancipated by the court; and
 - c) have the legal right to consent on their own behalf to medical, dental, or mental health treatment. They also have extensive other rights to enter into legal and business arrangements, and so can consent to be included in other research (e.g., interviews, surveys) [California Family Code 7000-7143].
- (5) Capacity to consent depends upon:
 - a) The age, ability, experience, education, training, and degree of maturity and judgment of the minor. A minor between the ages of fourteen (14) and eighteen (18) may have such capacity, but a minor under the age of fourteen (14) would rarely have such capacity;
 - b) The conduct and demeanor at the time consent is to be given;
 - c) The totality of the circumstances;
 - d) The nature of the proposed research procedures and their risks, probable consequences, benefits, and alternatives to the treatment; and
 - e) The minor's ability to appreciate the nature, risks, consequences, benefits, and alternatives of the proposed research procedures.
- C. **Emancipated Minors** (California Family Code, Sections 7000-7002; 7050-7052; 7120-7123): Further defines an emancipated minor and rights of emancipated minors.
- D. **Experimental Use of Drugs and Consent for Minors Provision** (California Health and Safety Code, Sections 111515– 111545): Minor consent is required prior to administering an experimental drug. Parental or legal guardian consent (permission) is required and minor consent (assent) is required for children 7 years of age or older.
- E. **Mandatory Reporting of Child Abuse or Neglect** (California Penal Code, Section 11164 -11174.3) Identifies who is a “mandated reporter” required to report known or reasonably suspected child abuse or neglect.
- F. **Parental Consent for Children to Participate in Research** (California Education Code, Section 51513): For K-12 students - tests, questionnaires, surveys, or examinations containing any questions about the pupil's or the pupil's family's personal beliefs or practices in sex, family life, morality, and religion require written parental consent (permission).

VI. **Department of Education Requirements When Involving Minors in Research**

- A. The Family Educational Rights and Privacy Act (FERPA) (20 U.S.C. § 1232g; 34 CFR Part 99) is a Federal law that protects the privacy of student education records. The law applies to all schools that receive funds under an applicable program of the U.S. Department of Education.
- B. The Protection of Pupil Rights Amendment (PPRA) (20 U.S.C. § 1232h; 34 CFR Part 98) applies to programs that receive funding from the U.S. Department of Education (ED). PPRA is intended to protect the rights of parents and students.
- C. *Children* are persons enrolled in research not above the elementary or secondary education level, who have not reached the age or majority as determined under state law.
- D. No student shall be required, as part of any program specified in 98.1 (a) or (b), to submit without *prior consent* to psychiatric examination, testing, or treatment, or psychological examination, testing, or treatment, in which the primary purpose is to reveal information concerning one or more of the following:
 - a. Political affiliations or beliefs of the student or the student's parent;
 - b. Mental and psychological problems potentially embarrassing to the student or his or her family;
 - c. Sex behavior and attitudes;
 - d. Illegal, anti-social, self-incriminating and demeaning behavior;
 - e. Critical appraisals of other individuals with whom the student has close family relationships;
 - f. Legally recognized privileged and analogous relationships, such as those of lawyers, physicians, and ministers;
 - g. Religious practices, affiliations, or beliefs of the student or student's parent or;
 - h. Income, other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under a program.
- E. Prior Consent means:
 - a. Prior consent of the student, if the student is an adult or emancipated minor; or
 - b. Prior written consent of the parent or guardian, if the student is an unemancipated minor.
- F. For certain types of research projects not directly funded by the United States (U.S.) Department of Education and conducted in a school that receives funding from the U.S. Department of Education, the IRB will ensure compliance with U.S. Department of Education regulations that schools are required to develop and adopt policies in conjunction with parents regarding the following:
 - a. The right of a parent of a student to inspect, upon the request of the parent, a survey created by a third party before the survey is administered or distributed by a school to a student.
 - b. A procedure for granting a request by a parent for reasonable access to such survey within a reasonable period of time after the request is received.
- G. Arrangements to protect study privacy that are provided by the agency in the event of the administration or distribution of a survey to a student containing one or more of the following items (including the right of a parent of a student to inspect, upon the request of the parent, any survey containing one or more of such items);

- a. Political affiliations or beliefs of the student or the student's parent;
 - b. Mental and psychological problems potentially embarrassing to the student or his or her family;
 - c. Sex behavior and attitudes;
 - d. Illegal, anti-social, self-incriminating and demeaning behavior;
 - e. Critical appraisals of other individuals with whom the student has close family relationships;
 - f. Legally recognized privileged and analogous relationships, such as those of lawyers, physicians, and ministers;
 - g. Religious practices, affiliations, or beliefs of the student or student's parent or;
 - h. Income, other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under a program.
 - H. The right of a parent of a student to inspect, upon the request of the parent or guardian, any instructional material to be used as part of the educational curriculum for the student. Instructional material may include teacher's manuals, films, tapes or other supplementary instructional material, which will be used in connection with any research or experimentation program or project.
 - 1. Research or experimentation program or project means any program or project in any research that is designed to explore or develop new or unproven teaching methods or techniques.
 - a. Any applicable procedures for granting a request by a parent for reasonable access to instructional material received.
 - I. The administration of physical examinations or screenings that the school or agency may administer to a student.
 - J. The collection, disclosure or use of personal information collected from students for the purpose of marketing or for selling that information (or otherwise providing that information to others for that purpose), including arrangements to protect student privacy that are provided by the agency in the event of such collection, disclosure or use.
 - a. The right of a parent of a student to inspect, upon the request of the parent, any instrument used in the collection of personal information before the instrument is administered or distributed to a student and
 - b. Any procedure for granting a request by a parent for reasonable access to such instrument within a reasonable period of time after the request is received.
- VII. **Environmental Protection Agency Requirements When Involving Minors in Research**
- A. Research requirements when supported by the EPA:
 - 1. The EPA prohibits research involving the intentional exposure of children to any substance.
 - 2. The EPA requires application of 40 CFR 26 Subpart D to provide additional protections to children as participants in observational research, i.e., research that does not involve intentional exposure to any substance.
 - B. EPA policy requires submission of IRB determinations and approval to the EPA Human Subjects Research Review official for final review and approval before the research can begin.
 - C. Research not supported by any federal agency that has regulations for protecting human research participants and for which the intention of the

research is submission to the EPA, the EPA regulations protecting human research participants apply, including the prohibition of the intentional exposure of children to any substance.

References:

21 CFR 50 Subpart D

40 CFR 26 Subpart D

45 CFR 46 Subpart D

Department of Education 34 CFR 356.3, 34 CFR 98.4

The Protection of Pupil Rights Amendment (PPRA) (20 U.S.C. § 1232h; 34 CFR Part 98)

The Family Educational Rights and Privacy Act (FERPA) (20 U.S.C. § 1232g; 34 CFR Part 99)

OHRP Report 98-03, NIH Policy Guidance on the Inclusion of Children in Research

California Family Code 6920-6929

California Family Code 7000-7143

California Health and Safety Code 111530

HRP Policy # 29

Procedure Number: 36.A**Title: Procedure for Review of Research Involving Children****Procedure:**

This procedure provides guidance on the special ethical and regulatory considerations of children involved in human subjects research under the jurisdiction of the UC Irvine (UCI) Institutional Review Board (IRB).

I. Lead Researcher (LR) Responsibilities

- A. The LR will address specific questions related to the inclusion of children with any new study submission in which children will be a target population for research activities.
- B. When the research is funded by the United States (U.S.) Department of Education or the research is conducted in a school that receives funding from the U.S. Department of Education, the LR will comply with requirements of the FERPA and the PPRA.
- C. For certain types of research projects not directly funded by the United States (U.S.) Department of Education and conducted in a school that receives funding from the U.S. Department of Education, the investigator will obtain a permission letter from an authority of the school (e.g., school principal) or school district that the school complies with requirements of the FERPA and the PPRA and that these requirements are followed in the conduct of the research.
- D. The LR should describe in the protocol narrative if and how assent will be obtained and documented for IRB review and approval.
 1. An LR must take into account the ages, maturity, and psychological state of the children involved when planning methods to obtain and document assent.
 2. In some cases, the IRB may require additional techniques such as the use of larger type, simple schema, and pictures to help boost a child's comprehension of the text.
 3. The UCI IRB recommends the following documentation:
 - a) Parental permission utilizing an informed consent document;
 - b) Ages less than 7 years: An oral script in very simple language appropriate for children less than 7 years of age;
 - c) Ages 7 to 12 years: An assent form written simply and at a comprehension level appropriate for a child 7 years of age; and
 - d) Ages 13 to 17 years: A combination assent/parental permission consent form which may be in the same language as the adult consent document.
 4. The LR should not solicit a child's assent without intending to take his or her wishes seriously. In situations where the potential benefits of the study are such that the physicians and parents will enroll the child regardless of the child's wishes, the child should simply be told what is planned and should not be deceived. In such cases, the LR should request a waiver for assent from the IRB.
 5. Once a waiver of assent has been approved, the Investigator will obtain parental permission unless waiver from parental permission has been granted (See IRB Policy # 32)
 6. The LR may not approach the child to assent to the research study until the parents or legal guardians have given written permission.

II. **IRB Committee Responsibilities**

- A. The IRB Committee must review the proposed research taking into consideration all applicable UCI policies, as well as the degree of risk and discomfort involved in the research in relation to the direct benefits it offers to the child before it can determine whether or not the IRB has authority to approve the study.
- B. When determining whether children are capable of assenting, the IRB shall take into account the age, maturity, and psychological state of the children targeted for the study population. This determination may apply to all children involved in the study, some of the children, none of the children, or on a case-by-case basis, as deemed necessary by the IRB. When the IRB decides that assent is not a requirement of some children, the IRB will determine and document which children are not required to provide assent.
- C. The IRB must determine the appropriate ages for assent and the method of documentation of assent.
- D. The IRB must assure that special protections afforded to children found in 45 CFR 46, Subpart D have been met for this population.
- E. The Committee may not review or make a determination regarding studies involving children, as a target population, unless it has sufficient expertise in pediatric ethical, clinical, and psychosocial issues. Therefore, a Committee member with expertise must be in attendance at the convened meeting or experts who have this knowledge must be consulted by the IRB. When the IRB Committee renders its determination, it will include:
 - 1. The children's category and corresponding rationale under which the proposed research qualifies (e.g., 45 CFR 46.404-46.407); and
 - 2. Adequate provisions for obtaining assent from the children and how such assent will be documented. If assent is waived by the Committee, the rationale for such determination must be provided.
 - 3. Federally-funded studies determined by the IRB Committee to meet 45 CFR 46.407 for children, will be given a "pending approval" status until a determination by the Secretary of the Department of Health and Human Services (DHHS) is received. The Director of Human Research Protections or designee will be promptly notified when the IRB determines a study meets 45 CFR 46.407. Documentation sent to the Secretary includes:
 - a) IRB minutes from the convened meeting documenting the IRB findings;
 - b) The complete IRB application and informed consent documents;
 - c) The relevant protocol and/or grant application; and
 - d) Any supporting material including the Investigator's Brochure, if applicable.
 - 4. If OHRP grants approval under Category 46.407, then the IRB may grant final approval.
 - 5. If OHRP requires changes in the process of approval, or any other changes are made after the IRB "approved pending" revisions, an amendment request must be submitted for review and approved by the IRB Chairperson or his or her designee, unless the IRB Chairperson determines the changes submitted are significant, which require IRB Committee review (See IRB Procedure # 18.A).

6. At any time the Chairperson may refer the study to the IRB Committee for further review.
7. The research can not begin until the IRB has received approval for the research from OHRP and grants final approval.
- F. Non-Federally funded studies determined by the IRB Committee to meet 45 CFR 46.407 for children and meet all criteria for approval under 45 CFR 46.111, will be given a “pending approval” status until the research proposal is reviewed by both an expert panel and a community panel, for recommendations (See IRB Procedure # 36.B).
- G. When children as wards of the State are involved in research under 45 CFR 46.406 and 45 CFR 46.407, the required additional individual acting on behalf of the child as guardian or *in loco parentis* may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interest of the child for the duration of the child’s participation in the research and who is not associated in any way with the Investigators, or the guardian organization (e.g., CASA Volunteer).
- H. For research following Environmental Protection Agency (EPA) regulations and guidance;
 1. When research is conducted or supported by the EPA or when research is intended for submission to the EPA, research involving intentional exposure of pregnant women or children to any substance is prohibited.
 2. The IRB may review and approve observational research involving children that does not involve greater than minimal risk only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians as set forth in §26.406
 3. The IRB may review and approve observational research involving children that involves greater than minimal risk but presenting the prospect of direct benefit to the individual participants if the IRB finds and documents that:
 - a. The intervention or procedure holds out the prospect of direct benefit to the individual subject or is likely to contribute to the subject’s well-being;
 - b. The risk is justified by the anticipated benefit to the subjects;
 - c. The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
 - d. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in §26.406.

III. **IRB Analyst or Higher Responsibilities**

- A. The Analyst will verify that all documentation related to the enrollment of children is complete as part of the initial study documents.
- B. When the research is funded by the U.S. Department of Education or the research is conducted in a school that receives funding from the U.S. Department of Education, the Analyst will confirm that the LR obtained permission from the school to conduct research at the school and the school has verified that it complies with requirements of FERPA and the PPRA and that these requirements are followed in the conduct of the research.

- C. For certain types of research projects not directly funded by the U.S. Department of Education and conducted in a school that receives funding from the U.S. Department of Education the Analyst will confirm that the LR obtained permission from the school to conduct research at the school and the school has verified that it complies with requirements of the FERPA and the PPRA and that these requirements are followed in the conduct of the research.
- D. The Analyst will conduct a pre-review and take into consideration the type of research and verify the appropriate category of research under Subpart D.
- E. The Analyst takes into consideration the age, maturity, and psychological state of the children targeted in the proposed research when pre-reviewing the assent and informed consent documents.
- F. E-mails recommending pre-review changes to the informed consent documents are to be sent to the LR by the Analyst.
- G. Once the pre-review revisions are received from the LR, the Analyst will forward the revised informed consent documents to the assigned Reviewers with appropriate expertise in children and prepare the Reviewer and Committee packets.

References:

45 CFR 46.116

45 CFR 46 Subpart D

OHRP Report 98-03, NIH Policy Guidance on the Inclusion of Children in Research

IRB Guidebook, Chapter 6, Section C, Children and Minors

IRB Procedure 18.A, "Procedure for Modifications to Previously Approved Applications or Claims for Exemption"

IRB Policy 30, "Legally Effective and Prospectively Obtained Informed Consent"

IRB Policy 32, "Waiver of Informed Consent for Human Subjects Research or Exception of Informed Consent Requirements for Emergency Research"

IRB Procedure 36.B, "Review of Non-Federally Funded Research Meeting 45 CFR 46.407"

40 CFR 26.404-.406

Procedure Number: 36.B**Title: Procedure for Review of Non-Federally Funded Research Meeting 45 CFR 46.407****Procedure:**

This procedure outlines the process for reviewing non-federally funded research which meets 45 CFR 46.407 for the protection of children as a vulnerable population.

I. Lead Researcher (LR) Responsibilities

- A. The LR is responsible for providing a written rationale for use of this vulnerable population, including supporting documentation (e.g., literature search) of study design, safety monitoring, and risk/benefit ratio justification.
- B. The LR will provide additional documentation or materials as requested by the IRB in order to support the justification for research under category 45 CFR 46.407.
- C. The LR will, as requested, assist the IRB in preparation for Panel and Committee review by providing any additional materials and documentation required for adequate review.
- D. The LR will be available and may be required to present the proposed study to the Expert Panel.
- E. The LR cannot initiate the research, including screening and recruitment, until all reviews are complete and all requested revisions or recommendations are satisfied and final approval has been granted by the IRB.

II. IRB Committee Responsibilities

- A. The IRB Committee will review the proposed research according to IRB Policy # 36 and determine that the research involving children does not meet the requirements for approval under 45 CFR 46.404 (research not involving greater than minimal risk), 46.405 (research involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects), or 46.406 (research involving greater than minimal risk and no prospect of direct benefit to the individual subjects but likely to yield generalizable knowledge about the subject's disorder or condition), but that the research, not otherwise approvable, presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children.
 - 1. The IRB Committee will provide the rationale and documentation that the research does not meet 45 CFR 46.404, 46.405, or 46.406 for the protection of this vulnerable population.
 - 2. The IRB Committee will provide rationale and documentation that the research would be approvable under 45 CFR 46.407.
- B. The IRB will consult with experts at DHHS, experts in relevant disciplines, and representatives of the community in which the research will be conducted to provide the opportunity for review and comment, before determining whether the proposed research may be conducted under 45 CFR 46.407.
- C. The IRB Committee will determine the composition for both the Expert Review Panel and the Community Review Panel.
 - 1. Expert Review Panel Membership:
 - a) IRB or other neutral Facilitator;
 - b) Between 10 and 15 Members;

- c) IRB Committee Child Representative/Expert;
 - d) Additional IRB Representatives with clinical knowledge;
 - e) Non-affiliated Experts in the field specific to the proposed research;
 - f) Ethicists;
 - g) Community Pediatricians (not involved in research, but appropriate to the study population);
 - h) Pharmacy representatives (if applicable);
 - i) Other applicable Experts (e.g., pediatric social worker, child psychologist, etc.); and
 - j) No person which may be perceived as having a conflict of interest (to avoid possible coercion).
- 2. Community Review Panel Membership:
 - a) Between 10 and 15 Members;
 - b) IRB Committee Community Member;
 - c) Additional IRB Representatives with clinical knowledge and ability to answer questions in lay language;
 - d) Community Representatives that work regularly with the involved population; and/or
 - e) Parent representatives of the target population.
- D. The IRB Committee will identify questions for each panel to address and discuss, utilizing the Reviewer Checklist.
- E. The IRB Committee will determine the information to be provided to each panel for review. Information that may be included in the packet:
 - 1. Expert Review Panel (to meet before the Community Review Panel):
 - a) Cover letter from IRB;
 - b) Reviewer Checklist;
 - c) Belmont Report;
 - d) Regulations, including Subpart D;
 - e) IRB Committee Minutes;
 - f) Complete IRB Application for Human Research including informed consent and assent documents, and the study protocol;
 - g) Ad hoc reviewer comments (if applicable); and/or
 - h) Summary of background information including articles, literature search, and supporting materials.
 - 2. Community Review Panel:
 - a) Cover letter from IRB;
 - b) Reviewer Comment Form;
 - c) Lay Summary of Belmont Report;
 - d) Regulations, including Subpart D and a lay summary;
 - e) Complete IRB Application for Human Research including informed consent and assent documents, and the study protocol;
 - f) Ad hoc reviewer comments (if applicable);
 - g) Summary of background information including articles, literature search, and supporting materials; and/or
 - h) Summary from the Expert Review Panel meeting.
 - 3. The IRB Committee will identify a deadline for completion of the panel reviews.
 - 4. Following completion of both panel reviews, the IRB Committee will review recommendations from the panel meetings and make a determination regarding approval of the research, including any additional study revisions identified by the Expert Review Panel and Community Review Panel.

5. The IRB Committee will recommend any additional compliance guidelines (e.g., increased review frequency, observation of consent and assent process, additional DSMB protections, etc.)

III. **IRB Administrator Responsibilities**

- A. The Administrator will prepare guidance to assist the IRB Committee in making a determination that proposed research meets 45 CFR 46.407 for the IRB Committee.
- B. The Administrator will notify the Director of Human Research Protections or designee of the 45 CFR 46.407 determination by the Committee.
- C. The Administrator will prepare guidance to assist the Expert Review Panel and the Community Review Panel in evaluating the proposed research for approval under 45 CFR 46.407.
- D. Following the determination that a non-federally funded research proposal meets 45 CFR 46.407, the Administrator with the assistance of the Director of Human Research Protections or designee will seek guidance from administration and/or OHRP in the continuation of review under this category.
- E. The Administrator will prepare or request that the LR provide a literature search for supporting documentation of study design, safety monitoring, and risk/benefit ratio justification.
- F. The Administrator with the assistance of others (i.e., IRB Chair, IRB Members, and Director of Human Research Protections or designee) will recruit and coordinate identified Experts for participation on the Expert Review Panel.
- G. The Administrator with the assistance of others (i.e., IRB Chair, IRB Members, and Director of Human Research Protections or designee) will recruit and coordinate identified Community Members for participation on the Community Review Panel.
- H. The Administrator will prepare and obtain confidentiality agreements (Consultant Agreement) from all Community and Expert Panel Members.
- I. The Administrator will prepare and distribute packets to Panel Members for review prior to panel meetings only after a signed and dated Confidentiality Agreement has been received.
- J. The Administrator will coordinate arrangements for Panel Meetings (e.g., location, time, notification of Panel members, etc.)
- K. The Administrator will attend each Panel meeting, documenting minutes from the meeting.
- L. The Administrator will write a summary of the Expert Review Panel meeting for distribution and review by the attendees.
- M. The Administrator will prepare Panel recommendations for IRB Committee review and final determination regarding the study.

IV. **Expert Review Panel and Community Review Panel Responsibilities**

- N. The Community Review Panel may meet for an initial orientation session prior to convening a meeting for formal review of the proposed research to allow for an overview of the research in general.
- O. The Expert Review Panel and the Community Review Panel will review the proposed research and make one of the following recommendations:
 1. The Expert and Community Panels will recommend that the proposed research be disapproved, as it does not meet 45 CFR 46.404, 46.405, 46.406, or 46.407 for the protection of children as a vulnerable population;

2. The Expert and Community Panels will recommend that the proposed research meets 45 CFR 46.404, 46.405, or 46.406 for the protection of children as a vulnerable population; or
3. The Expert and Community Panels will recommend that the proposed research be approved under 45 CFR 46.407, only if the panels determine that:
 - a) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
 - b) The research will be conducted in accordance with sound ethical principles;
 - c) Adequate provisions are made for soliciting the assent of children and the permission of their parents or legal guardians as set forth in 45 CFR 46.408; and
 - d) Any recommendations for revisions (e.g., added protections, etc.) for IRB Committee review and consideration.

V. **IRB Administration Responsibilities**

- A. IRB Administration will assist the IRB Committee members with identification of Panel Members.
- B. IRB Administration will assist with appointing a moderator or facilitator for the Expert and Community Panel Meetings.
- C. IRB Administration will assist with providing compliance support to ensure consistency among HRP teams, IRB Committees, and Panel Meetings and adherence to Federal regulations and institutional policies and procedures.
- D. IRB Administration will assist with oversight of proceedings and processes.

References:

45 CFR 46, Subpart D

21 CFR 50, Subpart D

IRB Policy 36, "Vulnerable Populations: Children"

Policy Number: 37

Title: Prisoners

Date of Last Revision: 10/12/07, 11/21/10, 02/16/11, 09/21/12, 01/28/15, 05/01/16, 05/31/19, 06/03/19, 09/28/20, 04/12/22, 08/17/22

Introduction to Policy:

Prisoners are vulnerable because they are in a restrictive, institutional environment that affords little opportunity for making choices, earning money, communicating with outsiders, or obtaining medical care. Because their autonomy is limited, prisoners may participate only in certain categories of research. Special precautions aim to assure that their consent to participate in the research is both knowing and voluntary.

Applicable Definitions:

45 CFR 46.303 (HHS – Subpart C): Definition of a Prisoner: “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 ([45 CFR 46.303\(c\)](#)). Individuals are prisoners if they are in any kind of penal institution, such as a prison, jail, or juvenile offender facility, and their ability to leave the institution is restricted. Prisoners may be convicted felons or may be untried persons who are detained pending judicial action, for example, arraignment or trial. Common examples of the application of the regulatory definition of prisoner are as follows:

1. Individuals detained in a residential facility for court-ordered substance abuse treatment as a form of sentencing or alternative to incarceration are prisoners.
 - a. Individuals receiving non-residential court-ordered substance abuse treatment and are residing in the community are not prisoners.
2. Individuals with psychiatric illnesses committed involuntarily to an institution as an alternative to a criminal prosecution or incarceration are prisoners.
 - a. Individuals voluntarily admitted to an institution for treatment of a psychiatric illness, or who have been civilly committed to non-penal institutions for treatment because their illness makes them a danger to themselves or others, are not prisoners.
3. Parolees detained in a treatment center as a condition of parole are prisoners.
 - a. Individuals living in the community and sentenced to community-supervised monitoring, including parolees, are not prisoners.
4. Probationers and individuals wearing monitoring devices are generally not prisoners; however, situations of this kind frequently require an analysis of the particular circumstances of the planned participant population. Institutions may consult with OHRP when questions arise about research involving these populations.

Minimal Risk Definition per 45 CFR 46.303(d): *Minimal risk* is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.¹

¹ Differs from 2018 Common Rule Definition of 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.

- I. **UC Irvine (UCI) Institutional Review Board (IRB) Level of Review²**
 - A. **Full Committee Review: At UCI, the *initial review of research that involves an interaction with a prisoner requires full committee review.*** This includes research that qualifies under categories 45 CFR 46.306 (i) and (ii).
 1. Future reviews may occur under the expedited review procedure (subcommittee) **should the *full committee* agree the research involves minimal risk as allowed by the regulations at 45 CFR 46.306.**
 2. The IRB member(s) reviewing the research must include a prisoner or a prisoner representative.
 3. For categories 45 CFR 46.306 (iii) and (iv), full committee review is always required, along with DHHS consultation.
 - B. **Subcommittee / Expedited Review: At UCI, for research that involves access to prisoner data with no interaction or intervention with the prisoner population (that coincide with categories 45 CFR 46.306 (i) and (ii)), initial review may be done at subcommittee.** The IRB member reviewing the research must include a prisoner or a prisoner representative.
 - C. **Subcommittee / Exempt Review:** IRB exemptions do not apply EXCEPT for research aimed at involving a broader subject population that **only incidentally** includes prisoners [45 CFR 46.104(b)(2)].
- II. **Composition of IRB when Prisoners are Involved in Research**
 - A. When an IRB reviews a protocol involving prisoners as subjects, the composition of the IRB must satisfy the following requirements of HHS regulations at 45 CFR 46.304 (a) and (b):
 1. A majority of the IRB (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the IRB; and
 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.
 3. The prisoner representative must have a close working knowledge, understanding and appreciation of prison conditions from the perspective of a prisoner. Suitable individuals could include present or former prisoners; prison chaplains; prison psychologists, prison social workers, or other prison service providers; persons who have conducted advocacy for the rights of prisoners; or any individuals who are qualified to represent the rights and welfare of prisoners by virtue of appropriate background and experience.
- III. **IRB Review and Approval of Research Involving Prisoners – Federal Criteria**
 - A. It is the policy of the UCI IRB to review and approve all research involving prisoners with additional ethical and regulatory considerations applicable to prisoners under 45 CFR 46, Subpart C.
 - B. The UCI IRB must review all research in which prisoners are the target population, the subject is a prisoner at the time of enrollment, or when a currently enrolled participant becomes incarcerated *and research interventions and interactions would occur during the incarceration period or if identifiable private information will be obtained during the incarceration period.*
 - C. **When the IRB is reviewing a protocol in which a prisoner is a participant, the IRB Committee must make, in addition to requirements under 45 CFR 46, Subpart A, seven findings under 45 CFR 46.305(a). See Table 1 – Federal.**

² For reference, the Department of Health and Human Services (DHHS) regulations allow expedited review of research involving prisoners. The Office for Human Research Protections (OHRP) recommends that the full committee IRB review research-involving prisoners as human subjects. If the research is reviewed under the expedited review procedure, OHRP recommends that the IRB member(s) reviewing the research include a prisoner or a prisoner representative.

1. **As part of the seven findings, the first finding requires confirmation of which permissible research category the study represents.**

IV. **IRB Review and Approval of Research Involving Prisoners – California Criteria**

A. **The California Department of Corrections and Rehabilitation (CDCR) must approve research involving state prisoners.** Note that county or local jails may detain state prisoners.

1. **CDCR Link:** <https://www.cdcr.ca.gov/research/research-requests/>
2. **It is the investigator's responsibility to identify and meet these and other related CDCR requirements.**

B. **Committee for the Protection of Human Subjects (CPHS) approval may apply to prisoner research.** CPHS is the institutional review board (IRB) for all of the departments under the California Health and Human Services Agency (CHHSA). CPHS is also the IRB required to review all research-related requests for state personal information to the University of California and non-profit educational institutions. (CPHS must also approve research requests for release of data relating to birth and death certificated from the California Department of Public Health.)

1. **CPHS Link:** <https://www.chhs.ca.gov/cphs/>
2. **It is the investigator's responsibility to identify and meet these and other related CPHS requirements.**

C. **As applicable, researchers must also comply with the additional limitations and requirements in [California Penal Code Sections 3501 – 3523](#).** These provisions limit the types of biomedical research that may be conducted and place additional requirements on other types of research.

1. **It is the Lead Researcher's responsibility to identify and meet CA penal code requirements, as applicable.**
2. **Notable California Considerations:**
 - i. CA Penal Code 3502 prohibits the conduct of biomedical research on prisoners except when a physician treating a prisoner has determined that access to a drug or treatment available only under a treatment protocol or treatment IND is in the best medical interests of the prisoner and the prisoner has provided consent per CA penal Code Section 3521.
 - ii. In addition, per CA Penal Code 3504, any physical or mental injury of a prisoner resulting from the participation in behavioral research, irrespective of causation of such injury, shall be treated promptly and on a continuing basis until the injury is cured.
 - iii. CA Penal Code 3505 states behavioral research shall be limited to studies of the possible causes, effects and processes of incarceration and studies of prisons as institutional structures or of prisoners as incarcerated persons which present minimal or no risk and no more than mere inconvenience to the subjects of the research. Informed consent shall not be required for participation in behavioral research when the California Department of Corrections determines that it would be unnecessary or significantly inhibit the conduct of such research. In the absence of such determination, informed consent shall be required for participation in behavioral research.
 - iv. CA Penal Code 3515 states that in any biomedical or behavioral research, the California Department of Corrections must determine the following:
 1. That the risks to the prisoners consenting to research are outweighed by the sum of benefits to the prisoners and the importance of the knowledge to be gained;

2. That the rights and welfare of the prisoners are adequately protected, including the security of any confidential personal information;
 3. That the procedures for selection of prisoners are equitable and that subjects are not unjustly deprived of the opportunity to participate;
 4. That adequate provisions have been made for compensating research related injury;
 5. That the rate of remuneration is comparable to that received by non-prisoner volunteers in similar research;
 6. That the conduct of the activity will be reviewed at timely intervals; and
 7. That legally effective informed consent will be obtained by adequate and appropriate methods.
- v. CA Penal Code 3521 states that a prisoner shall be deemed to have given their informed consent only if each of the following conditions has been satisfied:
1. Consent is given without duress, coercion, fraud, or undue influence;
 2. The prisoner is informed in writing of the potential risks or benefits, or both, of the proposed research;
 3. The prisoner is informed orally and in writing in the language in which the subject is fluent of each of the following:
 - a. An explanation of the biomedical or behavioral research procedures to be followed and their purposes, including identification of any procedures which are experimental;
 - b. A description of all known attendant discomfort and risks reasonably to be expected;
 - c. A disclosure of any appropriate alternative biomedical or behavioral research procedures that might be advantageous for the subject;
 - d. The nature of the information sought to be gained by the experiment;
 - e. The expected recovery time of the subject after completion of the experiment;
 - f. An offer to answer any inquiries concerning the applicable biomedical or behavioral research procedures; and
 - g. An instruction that the person is free to withdraw their consent and to discontinue participation in the research at any time without prejudice to the subject.
- vi. CA Penal Code 3522 states that at the time the prisoner is informed in writing of the potential risks or benefits, or both, of the proposed research, they must also be given information as to
- a. the amount of remuneration they will receive for the research, and
 - b. the manner in which the prisoner may obtain prompt treatment for any research-related injuries. The amount of remuneration must be comparable to that which is paid to non-prisoner volunteers in similar research.
- vii. CA Penal Code 3508 states behavioral modification techniques shall be used only if such techniques are medically and socially acceptable means by which to modify

- behavior and if such techniques do not inflict permanent physical or psychological injury.
- vii. CA Penal Code 3509 notes that nothing in this title is intended to diminish the authority of any official or agency to adopt and enforce rules pertaining to prisoners, so long as such rules are not inconsistent with this title.
- viii. Informed consent shall not be required for participation in behavioral research when the department determines that it would be unnecessary or significantly inhibit the conduct of such research. In the absence of such determination, informed consent shall be required for participation in behavioral research.
- ix. CA Penal Code 3521 specifies conditions in which informed consent of the prisoner may be satisfied.
- x. *Clarification: Per University of California Office of the President (UCOP) advice, where "Department" is referenced in CA Penal Code 3515, this does not refer to the IRB. Per UCOP "Department" refers to CDCR.*

D. Exception to Biomedical Research: In 2016, California amended state regulations (CA Penal Code 3500-3524) to grant an exception to the existing prohibition on biomedical research on prisoners by permitting records-based biomedical research, *using existing information*. The use or disclosure of individually identifiable records pursuant to this subdivision shall only occur after both of the following requirements have been met:

1. The research advisory committee established pursuant to Section 3369.5 of Title 15 of the California Code of Regulations approves of the use or disclosure.
2. The prisoner provides written authorization for the use or disclosure, or the use or disclosure is permitted by Section 164.512 of Title 45 of the Code of Federal Regulations. (Amended by Stats. 2016, Ch. 197, Sec. 2. (SB 1238) Effective January 1, 2017.)
3. See Section IV A above regarding additional approvals.

V. IRB Review and Approval of Research Involving Prisoners – Department of Health and Human Services Supported Research

- A. **For any HHS conducted or supported research involving prisoners, the institution(s) engaged in the research must certify to the Secretary (through OHRP) that the IRB reviewed the research and made seven findings as required by the regulations (45 CFR 46.305(c) and 46.306(a)(1)).**
- B. The certification request may be sent to OHRP via email.
- C. OHRP then will 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.
- D. Following its review of the certification, OHRP will send the institution a letter authorizing the involvement of prisoners in the proposed research, if OHRP determines that the research involves one of the permissible categories.
- E. OHRP will consult with appropriate experts with respect to certain research that falls under paragraphs (iii) and (iv) of 45 CFR 46.306(a)(2). When applicable, OHRP (on behalf of the Secretary of HHS) also will publish a notice of intent to approve such research in the Federal Register.
- F. If OHRP determines that the proposed research does not involve one of the permissible categories, it will state in the letter to the institution that such research involving prisoners cannot proceed.
- G. The research cannot start until the IRB has received approval for the research from OHRP.

- H. If an Investigator wishes to engage in non-HHS supported research, certification is not required. However, the IRB should apply the standards of this policy and the Federal regulations in reviewing the research.

VI. Waiver of the Applicability of Certain Provisions of DHHS Regulations for the Protection of Human Subjects for DHHS Epidemiologic Research Involving Prisoners as Subjects

- A. For a minimal risk epidemiologic study in which prisoners are not the particular focus and the sole purpose of the study is either:
 - 1. To describe the prevalence or incidence of a disease by identifying all cases; or
 - 2. To study potential risk factor associations for that disease.
- B. The two Subpart C provisions that are waived are:
 - 1. *The requirement that an IRB choose one of the four categories in 45 CFR 46.306(a)(2); and*
 - 2. *The requirement that the Secretary (through OHRP) make the final choice of one of the four categories.*
- C. The institution responsible for the conduct of the research certifies to the Office for Human Research Protections, DHHS, acting on behalf of the Secretary, that
 - 1. The IRB approved the research and fulfilled its duties under 45 CFR 46.305(a)(2)–(7) and
 - 2. Determined and documented that
 - a) The research presents *no more than minimal risk* and no more than inconvenience to the prisoner-subjects, and
 - b) Prisoners are not a particular focus of the research.

VII. When a Current Research Participant Becomes a Prisoner

- A. If a participant becomes a prisoner after enrolling in a research study, the Investigator is responsible for reporting the event in writing to the IRB upon learning of the event. This is not required if the study was previously approved by the IRB for prisoner participation.
- B. If research interactions and interventions or obtaining identifiable private information will not occur during the incarceration IRB review and approval under Subpart C is not required. The participant may stay enrolled.
 - 1. If the incarceration has an effect on the study, and Subpart C review has not yet occurred, proceed as follows:
 - a) Option 1: Consider terminating the enrollment of the participant.
 - (1) The Investigator should consider the risks associated with terminating participation in the study. The Investigator is encouraged to contact the IRB Office to discuss with HRP Staff or the IRB Chair/s.
- C. If the participant cannot be terminated for health or safety reasons:
 - a) Follow requirements for Option 2 (below) or
 - b) Remove the participant from the study and keep the participant on the study intervention under an alternate mechanism such as expanded access. If expanded access applies, follow requirements for Option 2.
 - c) Option 2: Submit a modification to the study requesting that the IRB review the research study under Subpart C for the participant to remain in the study.
- D. If some the requirements of Subpart C cannot be met, but it is in the best interest of the participant to remain in the study, the investigator may keep the participant enrolled and inform the IRB. The IRB will then inform OHRP of the decision along with the justification.
- E. The IRB is to review the current research protocol in which the participant is enrolled, taking into special consideration the additional ethical and regulatory concerns for a prisoner involved in research.

VIII. Additional Approvals: Federal Bureau of Prisons

- A. The Federal Bureau of Prisons places special restrictions on research that takes place within the Bureau of Prisons under [28 CFR 512](#). The provisions under 28 CFR 512 specify additional requirements for prospective researchers (both employees and non-employees) to obtain approval to conduct research within the Bureau of Prisons (Bureau) and responsibilities of Bureau staff in processing proposals and monitoring research projects.
- B. When Human Research is conducted with the Federal Bureau of Prisons the organization relies on the Bureau Research Review Board to ensure compliance with 28 CFR 512.

- IX. **Additional Considerations: Department of Defense**
 - A. **The Department of Defense (DoD) does not allow for an expedited IRB review of prisoner research.**
 - B. The DoD prohibits research with Prisoners of War.
- X. **Additional Considerations: Outside California**
 - A. If research activities under the jurisdiction of the UCI IRB will involve prisoners held outside of California, **the investigator is responsible for identifying and ensuring compliance with the laws and regulations of the applicable jurisdictions.** The UCI Protocol Narrative should specify the jurisdictions involved and measures to ensure compliance.
- XI. **Additional Considerations: Minors**
 - A. When a prisoner is also a minor (e.g., an adolescent detained in a juvenile detention facility is a prisoner), IRB Policy 36 regarding children in research will also apply.

References:

DHHS: [45 CFR 46.111](#)

DOJ: [28 CFR 512](#)

IRB Policy 36, "Vulnerable Populations - Children"

CA Department of Corrections, Prisoners in Biomedical and Behavioral Research, Penal Code 3500-3523

Section 3369.5 of Title 15 of the California Code of Regulations

OHRP Guidance Document: "[OHRP Guidance on Involvement of Prisoners in Research](#)", May 23, 2003

Information on CDCR approval processes can be found in the agency's Operations Manual (Article 19), online at

https://www.cdcr.ca.gov/Regulations/Adult_Operations/docs/DOM/DOM%202019/2019-DOM.pdf and on the agency's website at <https://sites.cdcr.ca.gov/research/>.

<https://oshpd.ca.gov/data-and-reports/data-resources/cphs/>

OHRP "Prisoner Research FAQs": <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/fag/prisoner-research/index.html>

UC Davis Checklist: Prisoners: HRP-415

UCLA Office of the Human Research Protection Program Guidance: Special Subject Populations: Prisoners

Procedure:

This procedure outlines the responsibilities as mandated by the Federal regulations when prisoners are involved as participants in research.

I. Lead Researcher (LR) Responsibilities

- A. The LR will address the criteria for the inclusion of prisoners with any new study or amendment submission in which prisoners will be a target population for research activities.
- B. If the participant population has an increased potential to become prisoners, and the LR will be interacting, intervening, or collecting identifiable private information during the incarceration, the LR may choose to have the proposal reviewed initially by the IRB and OHRP (if necessary) for prisoner participation.
- C. As soon as they are made aware, the LR must report in writing to the IRB when a participant becomes a prisoner after enrollment in research activities if the research was not reviewed and approved by the IRB and OHRP in accordance with 45 CFR 46 Subpart C. All research interactions and interventions with, and obtaining identifiable private information about, the now incarcerated prisoner-participant must cease until the requirements of Subpart C have been satisfied with respect to the relevant research activities.
- D. The IRB Chairperson may determine that the participant may continue to participate in the research until the requirements of Subpart C are satisfied in special circumstances in which the LR asserts that it is in the best interests of the participant to remain in the research study while incarcerated and the provisions of CA Penal Code 3500-3523 have been met.
- E. The LR is responsible for obtaining and providing documentation of approval from the detention or correctional facility involved (i.e., prisons, jails, workhouses, etc.) to the IRB.
- F. The LR will provide any additional documents or materials required for certification to the Secretary (through OHRP) for HHS supported research involving prisoners. The IRB Office will help support this submission process.
- G. The LR may not screen, recruit, or enroll any individual involuntarily confined or detained in a penal institution without written IRB approval (and certification to the Secretary (through OHRP) for HHS supported research involving prisoners).
- H. For research conducted within the Bureau of Prisons,
 - 1. The research must comply with all the additional DOJ requirements under 28 CFR 512. This includes:
 - i. When submitting a research proposal to the Bureau, the applicant must demonstrate academic preparation or experience in the area of study of the proposed research.
 - ii. The applicant must provide a summary which includes the following information:
 - a) A summary which includes: names and current affiliations of the researchers; title of the study; purpose of the study; location of the study; methods to be employed; anticipated results; duration of the study; number of participants (staff or inmates) required and amount of time required from each.
 - b) Indication of risk or discomfort involved as a result of participation.
 - c) A comprehensive statement, which includes: review of related literature; detailed description of the research method; significance of anticipated results and their contribution to the advancement of knowledge.
 - d) Specific resources required from the Bureau of Prisons.

- e) Description of all possible risks, discomforts, and benefits to individual participants or a class of participants, and a discussion of the likelihood that the risks and discomforts will actually occur.
- f) Description of steps taken to minimize any risks.
- g) Description of physical or administrative procedures to be followed to: ensure the security of any individually identifiable data that are being collected for the study; destroy research records or remove individual identifiers from those records when the research has been completed.
- h) Description of any anticipated effects of the research study on organizational programs and operations.
- i) Relevant research materials such as vitae, endorsements, sample consent statements, questionnaires, and interview schedules.
- j) A statement regarding assurances and certification required by 28 CFR 46, if applicable.
- iii. The applicant/researcher must assume responsibility for actions of any person engaged to participate in the research project as an associate, assistant or subcontractor to the researcher.

II. **IRB Committee Responsibilities**

- A. The IRB Committee (full committee or subcommittee) must review the proposed research taking into consideration all applicable UCI policies and procedures, as well as the additional requirements for prisoners to participate in research as described in 45 CFR 46, Subpart C and CA Penal Code 3500 -3523.
- B. The Committee may not review or make determinations regarding studies involving prisoners as a target population unless the Committee has a member who is a prisoner or a prisoner representative with a close working knowledge, understanding and appreciation of prison conditions from the perspective of the prisoner. Documentation of expertise is provided by the curriculum vitae of the prisoner or prisoner representative serving on the IRB. *See Section III for Prisoner Representative Responsibilities.*
- C. The IRB Committee will review the proposed research, consents, and applicable documents to determine whether the study meets criteria 45 CFR 46.111 for approval. Written documentation of these criteria is detailed in the final IRB approved version of the IRB application.
- D. In addition, the IRB will discuss the additional protections necessary for this population as outlined in the federal regulations, Subpart C and State requirements.
- E. When a research participant becomes a prisoner, and the IRB has not previously reviewed the proposal for prisoner populations, the IRB will conduct a review of the research proposal in accordance with Subpart C and make one of the following determinations:
 - 1. If a participant becomes a prisoner after enrolling in a research study, the Investigator is responsible for immediately reporting the event (upon learning of the event) in writing to the IRB. This is not required if the study was previously approved by the IRB for prisoner participation.
 - 2. See Policy 37, Section VII above.
- F. For categories 45 CFR 46.306 (iii) and (iv) (regardless of funding): Research may not begin until DHHS has been notified and has performed their consultation with applicable experts. The IRB Office will help to facilitate this notification and process.
- G. For HHS supported research, the institution must certify to the Secretary (through OHRP) that the IRB designated under its assurance of compliance has made the seven findings required under 45 CFR 46.305(a) and a statement indicating that the IRB chose one of the four permissible categories of research in 45 CFR 46.306(a)(2).
 - 1. In addition to the prisoner certification letter, the following information must also be sent to OHRP:

- i. The IRB application (which includes the protocol narrative and any IRB submission materials including the ICDs); and
 - ii. The grant application (including any grant award updates).
 - iii. IRB Teams may refer to the internal share folder for examples of prior certifications: (\\ad.uci.edu\uci\OR\RA\Files\RP\IRB\Common Files -- IRB\HHS Prisoner Certification)
- H. The IRB may approve the research for non-prisoner populations if all the criteria in Subpart C are satisfied. **UCI prisoner research cannot start until the IRB has received approval for the research from OHRP.**
- I. The IRB must inform the LR in writing that no prisoner-subjects can be enrolled or involved until the IRB/institution receives the approval letter from OHRP.
 - 1. The OHRP approval letter will acknowledge receipt of the prisoner certification and indicates the Secretary's (through OHRP) determination/approval that the proposed research falls within the categories of research permissible under 45 CFR 46.306(a)(2).
 - 2. The OHRP approval letter will be provided to the LR and maintained in IRB records.

III. **Prisoner Representative Responsibilities**

For research involving prisoners reviewed by full committee or subcommittee:

- A. The IRB must include a prisoner or prisoner representative.
- B. The prisoner representative must be a voting member of the IRB. The prisoner representative may be listed as an alternative member who becomes a voting member as needed.
- C. The prisoner representative must review research involving prisoners, focusing on the requirements in Subpart C.
- D. The prisoner representative must receive all review materials pertaining to the research (same documents as the primary reviewer).
- E. *At full committee (convened IRB):*
 - 1. The prisoner representative must be present at the full committee when the research involving prisoners is reviewed. If the prisoner representative is not present, research involving prisoners cannot be reviewed or approved.
 - 2. The prisoner representative may attend the meeting by phone, video-conference or webinar, as long as the representative is able to participate in the meeting.
 - 3. The prisoner representative must present his / her review either orally or in writing at the full committee.

IV. **IRB Administrator Responsibilities**

- A. The Administrator will verify that all requisite sections of the IRB application have been completed by the LR as part of the initial or amended study documents.
- B. The Administrator will conduct a pre-review and take into consideration the requirements under 45 CFR 46, Subpart C and CA Penal Code 3500 -3523, under which prisoners may participate in human participants research.
- C. The Administrator will e-mail the LR with any questions or needed clarification in regard to the prisoner population.
- D. The Administrator will verify that the IRB Member/ Full Committee reviewing the research involving a prisoner includes at least one member who is a prisoner or prisoner representative.
- E. To adequately document the IRB review of the research:
 - 1. The curriculum vitae of the prisoner or prisoner representative serving on the IRB will be on file in the IRB;
 - 2. and
 - 3. The discussion and determinations of the IRB regarding findings required per federal and state regulations and noted in Policy 37 Sections III, IV, V above.
- F. For HHS supported research, the Administrator will assist in preparing documents for the certification letter and prepare a draft certification letter to

Secretary (through OHRP) which will be signed by the appropriate institutional official listed on UCI's FWA.

References:

Department of Health and Human Services (DHHS)

45 CFR 46 Subpart C (DHHS)

Office for Human Research Protections (OHRP) Guidance: "OHRP Guidance on the Involvement of Prisoners in Research," May 23, 2003.

Office for Human Research Protections (OHRP) Guidance: Prisoner Research – FAQs. Office for Human Research Protections (OHRP) Guidance: Prisoner Research Certification.

Department of Justice (DOJ)

28 CFR 46

28 CFR 512

California Code

California Penal Code, Sections 3500-3524

California Code of Regulations, Title 15, Article 9.1, "Research of Inmates/Parolees."

California Department of Corrections and Rehabilitation (CDCR) guidance: Research Involving Wards, Inmates & Staff.

California Department of Corrections and Rehabilitation (CDCR) guidance: Research Project Approval Guidelines.

California Committee for the Protection of Human Subjects

Table 1. Federal Requirements for Prisoner Research³

45CFR 46.305 (a)(1)	45 CFR 46.305 (a)(2)	45 CFR 46.305 (a)(3)	45 CFR 46.305 (a)(4)	45 CFR 46.305 (a)(5)	45 CFR 46.305 (a)(6)	45 CFR 46.305 (a)(7)
<p>The research under review represents one of the four following categories of research permissible under 45 CFR 46.306(a)(2) which are as follows:</p> <ul style="list-style-type: none"> i. Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents <i>no more than minimal risk</i> and no more than inconvenience to the subjects; ii. Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents <i>no more than minimal risk</i> and no more than inconvenience to the subjects; iii. Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction and sexual assaults) provided that <i>the study may proceed only after the Secretary has consulted with appropriate experts including experts in penology medicine and ethics, and published notice, in the FEDERAL REGISTER, of his intent to approve such research; or</i> iv. Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. <i>In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology medicine and ethics, and published notice, in the FEDERAL REGISTER, of his intent to approve such research.</i> 	<p>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;</p>	<p>The risks involved in the research are commensurate with risks that would be accepted by non prisoner volunteers;</p>	<p>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 principal investigator provides to the Board 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 project;</p>	<p>The information is presented in language which is understandable to the subject population;</p>	<p>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</p>	<p>Where the Board finds there may be a need for follow-up examination or care of participants 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 participants of this fact.</p>

³ See Policy 37, Section VI for additional considerations for epidemiologic research. Also: Research that meets the criteria described in an HHS Secretarial waiver that applies to certain epidemiological research ([68 FR 36929, June 20, 2003 \(PDF\) - PDF](#)).

Policy Number 38:

Title: Pregnant Women, Human Fetuses, Neonates, and Fetal Tissue

Date of Last Revision: 10/12/2007, 10/23/2010, 08/22/2017, 09/16/2022

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to review and approve research involving pregnant women, human fetuses, and neonates of uncertain viability or nonviable neonates based on the Federal regulations at 45 CFR 46 Subpart B and in addition to those imposed under other IRB policies, procedures, and other applicable Federal, State, and local laws.

- I. Research involving women who are or may become pregnant should receive special attention from the IRB because of women's additional health concerns during pregnancy and because of the need to avoid unnecessary risk to the fetus. Further, in the case of a pregnant woman, the IRB must determine when informed consent of the father is required for research. Special attention is justified because of the involvement of a third party (the fetus) who may be affected but cannot give consent. Procedural protections beyond the basic requirements for protecting human participants are prescribed in the Federal regulations (Subpart B) for research involving pregnant women.
- II. **§46.204: Research Involving Pregnant Women or Fetuses** - Pregnant women or fetuses may be involved in research if all of the following conditions are met:
 - A. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses; and
 - B. 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; and
 - C. Any risk is the least possible for achieving the objectives of the research; and
 - D. 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, her consent is obtained in accord with the informed consent provisions of 45 CFR 46 Subpart A; and
 - E. 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 informed consent provisions of 45 CFR 46 Subpart A, 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; and
- F. Each individual providing consent under (D) or (E) above, is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate; and
- G. For children as defined in 45 CFR 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of 45 CFR 46 Subpart D (See IRB Policy 36); and
- H. No inducements, monetary or otherwise, will be offered to terminate a pregnancy; and
- I. 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
- J. Individuals engaged in the research will have no part in determining the viability of a neonate.

III. **§46.205: Research Involving Neonates**

- A. 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; and
 2. Each individual providing consent under paragraph B.2 or C.5 of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate; and
 3. Individuals engaged in the research will have no part in determining the viability of the neonate; and
 4. The requirements of paragraph B or C of this section have been met as applicable.
- B. Neonates of uncertain viability. Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this policy unless the following additional conditions have been met:
 1. The IRB must determine 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 biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and
 2. 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 45 CFR 46 Subpart A, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.
- C. Nonviable neonates. After delivery a nonviable neonate may not be involved in research covered by this policy unless all of the following additional conditions are met:
 1. Vital functions of the neonate will not be artificially maintained; and

2. The research will not terminate the heartbeat or respiration of the neonate; and
 3. There will be no added risk to the neonate resulting from the research; and
 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 45 CFR 46 Subpart A, except that the waiver alteration provisions of §46.116(c) and (d) 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 will not suffice to meet the requirements of this paragraph.
- D. Viable neonates. If a neonate is judged viable (i.e. likely to survive to the point of sustaining life independently, given the benefit of available medical therapy), it is then called an infant and should be treated as a child for purpose of research participation. A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of 45 CFR 46 Subparts A and D.

IV. **§46.206: Research Involving, After Delivery, the Placenta, the Dead Fetus, or Fetal Material**

- A. 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.
1. For example, the California Protection of Human Subjects in Medical Experimentation Act makes it unlawful for any person or entity to engage in medical experiments or research without the prior knowledge and consent of the mother.
 2. Additionally, no person or entity may offer or accept money or anything of value for an aborted fetus. Violations of these provisions are punishable as a Class E felony.

V. **§46.207: Research Not Otherwise Approvable Which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Pregnant Women, Fetuses, or Neonates** -

The Secretary of the Department of Health and Human Services (DHHS) will conduct or fund research that the IRB does not believe meets the requirements of 45 CFR 46.204 or 45 CFR 46.205 only if:

- A. 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
- B. The Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following

opportunity for public review and comment, including a public meeting announced in the Federal Register, has determined either:

1. That the research, in fact, satisfies the conditions of §46.204, as applicable; or
2. 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; and
 - b) The research will be conducted in accord with sound ethical principles; and
 - c) Informed consent will be obtained in accord with the informed consent provisions of 45 CFR 46 Subpart A and other applicable subparts of 45 CFR 46.

VI. **Modification or Waiver of Specific Requirements** - Upon the request of the Investigator (with the approval of the IRB), the Secretary of the Department of Health and Human Services may modify or waive any of the above requirements of this policy.

VII. **Studies in Which Pregnancy is Coincidental to Subject Selection**

- A. Any study in which women of childbearing potential are possible subjects may inadvertently include pregnant women. Federal regulations require that, when appropriate, subjects be provided 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 as part of the informed consent process.
 1. The IRB must judge whether the mother's participation would pose any risk to the fetus or nursing infant. In some studies, the IRB may need to assure that nonpregnant subjects are advised to avoid pregnancy or nursing for a time during or following the research. Furthermore, where appropriate, subjects should be advised to notify the Investigator immediately should they become pregnant. In some instances, there may be potential risk sufficient to justify requiring that pregnant women either be specifically excluded from the research or studied separately.

VIII. **Exemption from Review** - Note that with the revision of Subpart B on November 13, 2001, the exemptions from IRB review listed at 45 CFR 46.101(b) may now be applied to research involving pregnant women, human fetuses, and neonates in accordance with 45 CFR 46.201(b).

IX. **Environmental Protection Agency Requirements When Involving Pregnant or Nursing Women in Research**

- A. The EPA prohibits research involving the intentional exposure of pregnant or nursing women to any substance.
- B. The EPA requires application of 40 CFR 26 Subpart B to provide additional protections to pregnant women as participants in observational research, i.e., research that does not involve intentional exposure to any substance.

- C. EPA policy requires submission of IRB determinations and approval to the EPA Human Subjects Research Review official for final review and approval before the research can begin.
 - D. Research not conducted or supported by any federal agency that has regulations for protecting human research participants and for which the intention of the research is submission to the EPA, the EPA regulations protecting human research participants apply, including:
 - 1. The EPA extends the provisions of the 40 CFR 26 to human research involving the intentional exposure of non-pregnant, non-nursing adults to any substance.
 - 2. The EPA prohibits the intentional exposure of pregnant women or nursing women to any substance.
- X. **Research Involving Specimens from the Placenta After Delivery or Postmortem Fetal Tissue**
- A. The University of California (UC) is compliant with California law that permits research using fetal remains, which is defined as a lifeless product of conception regardless of the duration of pregnancy (CA Health and Safety Code 123440).
 - B. If identifying data are associated with the material in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and IRB review and approval is required before such materials are collected or used.
 - C. Research involving the transplantation of human fetal tissue for therapeutic purposes must be conducted in accord with applicable State law and the Secretary may not provide support for such research unless the applicant for assistance agrees to conduct the research. The conduct of such research by the Secretary must be in accord with applicable state and local law. Additional guidance on fetal tissue transplantation research is available on the OHRP website.
 - D. The provisions of section 498B of the Public Health Service Act (42 U.S.C. 298g-2), added by Public Law 103-43, the NIH Revitalization Act of 1993 are summarized as follows:
 - 1. It shall be unlawful for any person to knowingly acquire, receive, or otherwise transfer any human fetal tissue for valuable consideration if the transfer affects interstate commerce.
 - a) Valuable consideration does not include reasonable payment associated with the transportation, implantation, processing, preservation, quality control, or storage of human fetal tissue.
 - 2. It shall be unlawful for any person to solicit or knowingly acquire, receive, or accept a donation of human fetal tissue for the purposes of transplantation of such tissue into another person if:
 - a) The donation effects interstate commerce;
 - b) The tissue will be obtained pursuant to an induced abortion; and:
 - (1) The donation will be or is made pursuant to a promise to the donating individual that the donated tissue will be transplanted into a recipient specified by such individual;
 - (2) The donated tissue will be transplanted into a relative of the donating individual; or

- (3) The person who solicits or knowingly acquires, receives, or accepts the donation has provided valuable consideration for the costs associated with such abortion.
 - (a) Valuable consideration does not include reasonable payments associated with the transplantation, implantation, processing, preservation, quality control or storage of human fetal tissue.)

XI. Research Involving Dried Blood Spots Obtained Through Newborn Screening

- A. NIH funded research using newborn dried blood spots collected on or after March 18, 2015, will be considered to be non-exempt human subjects research, and therefore, must follow the HHS protection of human subjects regulations at 45 CFR part 46.
- B. Grant applications and R&D contract proposals submitted to NIH that will use such materials in research should be designated as non-exempt human subjects research and include a complete human subjects section per relevant NIH instructions including plans for inclusion on the basis of sex/gender, race, ethnicity, and age per the NIH Policies on the Inclusion of Women, Minorities, and Children.
- C. Such applications and proposals that are funded by NIH must comply with all the relevant federal regulatory and NIH policy requirements for human subjects research including the requirement that the awardee institution (and all engaged institutions) have a Federalwide Assurance (FWA) from the Office of Human Research Protections (OHRP) and certification of IRB approval of the proposed research.
- D. Parental permission must have been obtained in order to use newborn dried blood spots collected on or after March 18, 2015, in NIH-funded research. Waiver of parental permission for such research is not permitted under this legislation.
- E. Continuing NIH awards that are conducting research with newborn dried blood spots collected on or after March 18, 2015, will also have to comply with these new requirements. Awardee institutions will need to meet all NIH requirements for human subjects research, including IRB approval, prior to starting such research.
- F. NIH will add a specific term and condition to all new and continuing awards conducting applicable newborn dried blood spot research to ensure compliance with the new legislation.
- G. Non-identifiable newborn dried blood spots collected prior to March 18, 2015, may continue to be used in NIH-funded research without parental permission, and this activity would continue to be considered research that does not involve human subjects under the current human subjects regulations.

References:

40 CFR 26
40 CFR 26.Subpart B
45 CFR 46

45 CFR 46 Subpart B

Office for Human Research Protections Guidance for Investigators and Institutional Review Boards Regarding Research OHRP IRB Guidebook, Chapter 6, "Special Classes of Subjects"

OHRP Guidance Document: "Fetal Tissue Transplantation", February 2003.

The NIH Revitalization Act of 1993 (Public Law 103-43) Section 498B of the Public Health Service Act (42 U.S.C. 298g-1).

Procedure Number: 38.A**Title: Procedure for Review of Research Involving Pregnant Women, Human Fetuses, Neonates, and Fetal Tissue****Procedure:**

The purpose of this procedure is to provide guidance on the requirements for review and approval for pregnant women, human fetuses, neonates, and fetal tissue activities in human subjects research under the UC Irvine (UCI) Institutional Review Board (IRB) jurisdiction.

I. Lead Researcher (LR) Responsibilities

- A. The LR will address requirements to include pregnant women, fetuses, or neonates as part of a New IRB Application or Amendment in which those populations are an enrollment target.
- B. The LR will contact the hSCRO Administrator to obtain the necessary documentation to submit with a new IRB Application or Amendment when the research involves the collection of fetal tissue to derive stem cells.
- C. Once the full IRB Committee approves the study, the LR will obtain informed consent from the mother and father as outlined in IRB Policy Section 30.

II. IRB Committee Responsibilities

- A. The IRB Committee must review the proposed research taking into consideration all applicable IRB policies and the requirements for involvement of pregnant women, fetuses, neonates, and fetal tissue transplantation activities in research.
- B. The IRB Committee will review and approve research in accordance with the Federal regulations at 45 CFR 46 Subpart A.
- C. When reviewing research involving pregnant women, the IRB Committee will include in its composition one or more individuals who are knowledgeable about and experienced in working with pregnant women.
- D. The IRB will discuss the additional protections necessary for this population as outlined in the IRB Application. The Primary and Secondary Reviewers will document these added protections as part of the final IRB approved version of the IRB Application..
- E. The IRB must review the proposed research involving fetal tissue to ensure that all federal and state requirements outlined in IRB Policy 38 are met.
- F. The IRB Committee will review observational research involving pregnant women and fetuses using 40 CFR 26 and 45 CFR 46 Subpart B.
- G. For research following Environmental Protection Agency (EPA) regulations and guidance;
 - 1. When research is conducted or supported by the EPA or when research is intended for submission to the EPA, research involving intentional exposure of pregnant or nursing women, or children to any substance is prohibited.

III. IRB Administrator Responsibilities

- A. The Administrator will verify that the IRB Application has been completed or needs additional clarification or detail.

- B. The Administrator will verify if necessary hSCRO documentation has been completed or needs completion as part of the initial study documents and will inform the Human Stem Cell Oversight Committee (hSCRO) Administrator that the new application requires hSCRO review.
- C. The Administrator will conduct a pre-review and will take into consideration the additional requirements under Subpart B for research activities involving pregnant women, fetuses, neonates, or research involving transplantation of fetal tissue.
- D. E-mails recommending pre-review changes to the IRB Application or any attachment are to be sent to the LR by the Administrator or designee via the electronic IRB submission and management system.
- E. Once the pre-review revisions are received from the LR, the Administrator will ensure that all revised attachments, along with the updated IRB Application, have been made available to the assigned Reviewers with appropriate expertise in pregnant women or children, as applicable.

References:

IRB Policy 38, "Vulnerable Populations: Pregnant Women, Human Fetuses, Neonates and Fetal Tissue"

Policy Number: 39

Title: Individuals with Impaired Decision-Making Capacity

Date of Last Revision: 10/12/07, 10/05/10, 09/16/22, 08/21/24

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to review, provide guidance on and approve, as applicable, research involving individuals with impaired decision-making capacity.

- I. **IRB Review and Approval of Research Involving Individuals with Impaired Decision-making Capacity**
 - A. As individuals with impaired decision-making capacity may have diminished autonomy limiting their capacity to provide consent or their ability to withdraw, the IRB should be particularly cognizant of research involving individuals with impaired decision-making capacity.
 - B. The UCI IRB must review all research in which cognitively impaired individuals will be considered as participants to assure that the Investigator has provided additional safeguards to protect the rights and welfare of this vulnerable population.
 - C. The IRB must consider the degree of decision-making impairment of the participant, the level of risk, and the prospect of benefit to the individual participant.
- II. As a general rule, all adults, regardless of their diagnosis or condition, are presumed competent to consent unless there is evidence of a condition that would impair their reasoning or judgment.
 - A. The IRB may determine additional protections (e.g., decisional capacity assessments) are necessary to ensure that persons with fluctuating/limited decision-making capacity can make a voluntary and informed decision concerning their participation in research.
 - B. The IRB may require, at any level risk research, that the Investigator include a decision-making capacity assessment plan if there are reasons to believe that potential subjects' decision-making capacity may be impaired.
- III. **Requirements for Evaluating Decision Making Capacity of Impaired Individuals**
 - A. The IRB must find that appropriate provisions are made for determining the participant's ability to provide consent or their ability to withdraw, through evidence of one or more of the following pertaining to the individual:
 1. The ability to make a choice;
 2. The ability to understand relevant information;
 3. The ability to appreciate the situation and its likely consequences; and
 4. The ability to manipulate information rationally.

- B. The determination of capacity to consent or ability to withdraw may be made through a standardized measure or consultation with another qualified professional. The IRB must approve the process for making such a determination.
- C. Because the capacity to consent or the ability to withdraw may fluctuate, the IRB must evaluate the process for continued verification of understanding and willingness to participate.
- D. For participants who lack decision-making capacity, the IRB may grant approval to obtain the permission of the individual's surrogate decision maker and the assent of the participant. (See IRB Procedure # 30.C.)
 - 1. Surrogate consent may be considered only in research studies relating to the cognitive impairment, lack of capacity, or serious or life-threatening diseases and conditions of the research subject.
 - 2. In research situations where there is the potential for direct benefit to the participant, the IRB may waive the requirement to obtain assent. However, permission from the surrogate decision maker must be obtained.
 - 3. Even where the IRB determines that the individuals are capable of consenting or withdrawing from the research, the IRB may still waive the consent requirements under the circumstances described in the UCI IRB informed consent policy. (See IRB Policy # 32.)
- E. The IRB must also review and approve the appropriate consent documents with the required elements of consent written in a language understandable to the participant.

IV. **Appropriate Provisions for Legally Authorized Representative Consent**

When it is determined by the Investigator that the participant lacks decision-making capacity; the IRB must find that appropriate provisions are made for soliciting the permission of a surrogate decision maker unless the criteria are met to approve a waiver of informed consent. (See IRB Policy # 32.)

V. **Institutionalized Participants**

- A. Surrogate consent to participate in research under California Health & Safety Code Section 24178 is not permitted for persons on an inpatient psychiatric ward, inpatients of a mental health facility, or persons on psychiatric hold.
- B. The IRB must consider the rationale and justification for involvement of institutionalized participants, including an explanation as to why non-institutionalized individuals could not be used.
- C. Regardless of financial support or funding, the UCI IRB must assure that all performance sites "engaged" in research have approval from the IRB of Record for the proposed research to be conducted at the site.
- D. When performance sites are "not engaged" in research and have an established IRB, the Investigator must obtain approval to conduct the research at the "not engaged" site from the site's IRB or provide documentation that the site's IRB has determined that approval is not necessary for UC Irvine to conduct the proposed research at the site.
- E. When performance sites are "not engaged" in research and the "not engaged" site does not have an established IRB, a letter of cooperation/permission must be obtained demonstrating that the

appropriate institutional officials are permitting the research to be conducted at the performance site.

VI. Composition of the IRB when Individuals with Impaired Decision-making Capacity are Involved in Research

- A. When reviewing research involving individuals with impaired decision-making capacity, the IRB Committee will include in its composition one or more individuals who are knowledgeable about and experienced in working with cognitively impaired individuals.
 - 1. When reviewing research funded by the National Institute on Disability and Rehabilitation Research, should the research purposefully include individuals with mental disabilities as research participants, the IRB must include at least one person primarily concerned with the welfare of these research participants.
- B. When the study requires review by the full IRB Committee, it must meet the special composition requirements when conducting reviews for initial review, continuing review, and significant protocol modifications/amendments.

References:

The Belmont Report

Am J Psychiatry 155:11, November 1998, "Guidelines for Assessing the Decision-Making Capacities of Potential Research Subjects with Cognitive Impairment"

The Office of Human Subjects Research (OHSR), National Institutes of Health, Information Sheet #7, "Research Involving Cognitively Impaired Subjects: A Review of Some Ethical Considerations"

California Health & Safety Code Section 24178

IRB Policy # 30

IRB Policy # 32

34 CFR 356.3

Procedure Number: 39.A**Title: Procedure for Review of Research Involving Individuals with Impaired Decision-Making Capacity****Procedure:**

This procedure provides guidance on the special ethical and regulatory considerations of individuals with impaired decision-making capacity involved in human subjects research under the jurisdiction of the UCI Institutional Review Board (IRB).

I. Lead Researcher (LR) Responsibilities

- A. The LR will submit additional information to address the inclusion of individuals with impaired decision-making capacity with any new study submission or amendment in which cognitively impaired participants will be a target population for research activities.
- B. The research plan should address the following considerations:
 - 1. A rationale as to why is it necessary to include this population;
 - 2. A description of potential benefits to this population;
 - 3. A justification for the use of institutionalized individuals, if applicable;
 - 4. A description of the research as it pertains to the institutionalization, if applicable;
 - 5. A description of the procedure for determining capacity for decision-making of the individuals;
 - 6. A description as to how individuals will be protected in the event they lose their capacity to consent and their capacity to withdraw;
 - 7. A description of the methods for assuring adequate protections for the privacy of the participants and the confidentiality of the information gathered; and
 - 8. A description as to how permission will be obtained and documented from the legally authorized representative, if applicable;
- C. A Lead Researcher should not solicit consent of a participant who lacks decision-making capacity without intending to take their wishes seriously. In situations where the potential benefits of the study are such that the physicians and surrogate decision-maker would enroll the participant regardless, and the participant's capacity is so diminished that he/she could not understand the ramifications of not participating, the participant should simply be told what is planned and should not be deceived.
 - 1. A request of waiver for consent should be submitted to the IRB for determination. (See IRB Procedure # 32.A.)
 - 2. Should a situation exist in which the target population lacks decision-making capacity either through trauma, life-threatening condition, or coma, the LR may submit a request for surrogate consent. (See IRB Policy # 30.)
- D. The LR must present an informed consent document to the IRB for review containing the appropriate amount of information for the participant to make an informed decision. If, in the opinion of the Investigator, a complete informed consent document is not appropriate, a waiver or alteration of informed consent should be requested including a rationale for the alteration.

- E. Once approved, the LR may proceed with consent of the participant and/or surrogate decision-maker as outlined in IRB Policies # 29 and # 30, unless a waiver has been granted.
- F. If the research will involve institutionalized participants and depending on whether the performance site is “engaged in research”, a letter of IRB approval or a letter of cooperation from the institutional official from that site must be submitted to the IRB for review and approval.

II. **IRB Committee Responsibilities**

- A. The IRB Committee must review the proposed research taking into consideration all applicable UCI policies and procedures and California law, as well as the degree of risk and discomfort involved in the research in relation to the direct benefits it offers to the participant. In addition, the IRB must be sure that additional safeguards are in place to protect the rights and welfare of these participants.
- B. When determining whether the participants are capable of providing consent, the IRB shall consider the decision-making capacity of the study population. This determination may apply to all participants to be involved in the study, some participants, or on a case-by-case basis, as deemed necessary by the IRB.
- C. When the IRB evaluates the LR’s proposed plan for assessing the decision-making capacity of study population, the IRB considers such factors as:
 - 1. The criteria that will be used for determining the participants’ capacity for providing informed consent;
 - 2. The appropriateness and adequacy of method(s) by which the prospective participants’ decisional capacity will be evaluated (e.g., whether selected tools for assessing competency to consent are acceptable and appropriate);
 - 3. The qualifications of the proposed individual(s) that will assess the participants’ decision-making capacity.
- D. The IRB may require additional protections to ensure that informed consent from the participant is/has been obtained whenever possible. Examples include, but are not limited to, the following as appropriate:
 - 1. Periodic re-consenting;
 - 2. Use of third-party consent monitors during the recruitment and consent process;
 - 3. Required waiting periods to allow more time for the participant to consider the information that has been presented;
 - 4. Obtaining second opinions, using independent consent observers and/or involving a trusted family member or friend in the disclosure and decision-making process; and/or
 - 5. For participants with limited decision capacity, requiring their assent.
- E. The methods in which the full IRB Committee approves a new IRB Application will be followed.
- F. In addition to determining whether the study meets criteria 45 CFR 46.111 for approval, the Primary and Secondary Reviewers must ensure that appropriate protections are in place for this population.
- G. The Committee may not review or decide on studies involving the cognitively impaired, as a target population, unless it has sufficient expertise in the ethical, clinical, and psychosocial issues impacting this

population. Therefore, a Committee member who is knowledgeable about and experienced in working with these subjects must be in attendance at the convened meeting or an expert consultant who has this knowledge must be consulted by the IRB. When the IRB Committee renders its determination, it will include:

1. Requirements for determining the decision-making capacity of the target population or on a case-by-case basis, or a rationale why this requirement will be waived; and
 2. Appropriate methods for assuring the amount of information contained in the consent document are appropriate for the target population and the surrogate decision-maker, when necessary.
- H. When institutionalized individuals are involved in research, the IRB must verify that the institution has granted approval for the research to take place at that site. Depending on whether the performance site is “engaged in research”, a letter of IRB approval or a letter of cooperation/permission signed by the Institutional Official is required.

III. IRB Analyst or Higher Responsibilities

- A. The Analyst will verify that documentation related to the inclusion of individuals with impaired decision-making capacity and use of surrogate consent is completed as part of the initial study documents.
- B. When applicable, the Analyst will conduct a pre-review and take into consideration the capacity of the participants in the proposed research when pre-reviewing the IRB Application, and informed consent documents.
- C. Communication recommending optional pre-review changes to the IRB Application or informed consent documents are to be sent to the LR by the Analyst.
- D. All documentation is reflected in the online electronic submission and management system.

References:

IRB Policy # 29

IRB Policy # 30

IRB Procedure # 32.A

Policy Number: 40

Title: UCI Students and Employees

Date of Last Revision: 08/10/05, 08/20/10, 04/06/18, 04/12/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to review, approve, and provide guidance on the special ethical considerations when UCI students and employees are involved in human subjects research.

- I. **IRB Review and Approval of Research Involving UCI Students or Employees**
 - A. UCI students and/or employees that are asked to volunteer as participants in research are considered a vulnerable subject population because they may feel some pressure to participate, especially if the requesting Investigator is their supervisor or instructor, or someone who might be in a position to influence their future. Students and employees may volunteer to participate out of a belief that doing so will place them in good favor with the Investigator (e.g., participating will result in receiving better grades, recommendations, employment, and the like), or that failure to participate will negatively affect their relationship with the Investigator.
 - B. To protect against even the appearance of coercion or undue influence, Investigators wishing to include UCI Students or Employees must request IRB approval to include this subject population.
 - C. The IRB carefully evaluates the potential for undue influence or coercion when reviewing protocols that include this subject population and ensures that the protocol includes additional safeguards for voluntary participation in research.
- II. **The Investigator must provide a recruitment plan that includes:**
 - A. The steps that will be taken by the Investigator to avoid even the appearance of pressuring or coercing students and subordinates into enrollment or continued participation in research; and
 - B. The safeguards that will be in place to prevent compromised objectivity and/or confidentiality.
- III. In general, unless approved by the IRB, Investigators may not actively recruit participants from within their own department or classroom. However, this does not preclude members of the Investigator's department or class from freely volunteering to participate. For example, anyone is free to respond to general recruitment advertisements posted around campus or through the Social Sciences Human Subjects Pool.
- IV. The Investigator must assure that any results, performance, or any confidential data will not be given to whoever is evaluating the student or employee.

V. UCI Students

- A. It is unacceptable to require participation in research for course credit. However, instructors who wish to involve students in simulations of human experimentation and course-assigned data collection for educational purposes only (as opposed to research purposes) may require such participation as part of the class requirements.
 - 1. UCI students may earn extra course credit through the Social Sciences Human Subjects Pool if the course instructor includes the extra credit option in the course syllabus.
 - 2. When students participate in research studies for class credit, they must be provided alternative methods of equal or less time and effort for earning that credit.
 - 3. The IRB may require the investigator to include the available alternatives to participation in the informed consent document.
- B. Investigators interested in accessing student records for research purposes must review the UCI Office of the Registrar policy on Confidentiality of Students Records. The disclosure of information from student records is governed in large measure by the Federal Family Educational Rights and Privacy Act of 1974, by the State of California Education Code, and by University policy and procedures implementing these laws. Generally, documentation of informed consent is required to access private student information.

References:

21 CFR 56.111(b)

45 CFR 46.111(b)

OHRP IRB Guidebook, Chapter 6, Special Classes of Subjects, "Students, Employees, and Normal Volunteers."

Procedure Number: 40.A**Title: Procedure for Review of Research Involving the UCI Students and/or Employees****Procedure:**

This procedure provides guidance on the special ethical considerations of students and employees participating in human subjects research under the jurisdiction of the UCI Institutional Review Board (IRB).

I. Lead Researcher (LR) Responsibilities

- A. The LR will submit a IRB Application and address specific questions for any new study or amendment in which UCI students or employees will be a target population for research activities.
- B. The research plan should address the following considerations:
 - 1. A rationale as to why is it necessary to include this population;
 - 2. A description of the recruitment plan including how undue influence or coercion and compromised objectivity will be minimized; and
 - 3. A description of the methods for assuring adequate protections for the privacy of the participants and the confidentiality of the information gathered.
- C. The Investigator must provide an informed consent document to the IRB for review containing the appropriate amount of information for the participant to make an informed decision. If, in the opinion of the Investigator, a complete informed consent document is not appropriate, a waiver or alteration of informed consent should be requested including a rationale for the waiver/alteration.
- D. Once approved, the Investigator may proceed with consent of the participant as outlined in IRB Policy # 30, unless a waiver has been granted.

II. IRB Committee Responsibilities

- A. The IRB Committee must review the proposed research taking into consideration all applicable UCI policies and procedures, as well as the degree of risk and discomfort involved in the research in relation to the direct benefits it offers to the participant. In addition, the IRB must be sure that additional safeguards are in place to protect the rights and welfare of these participants.
- B. The methods in which the full IRB Committee approves a new study submission will be followed. In addition to determining whether the study meets criteria 45 CFR 46.111 for approval, the Primary and Secondary Reviewers must assure that adequate provisions and documentation of such provisions have been made for this population.
- C. The Committee may not review or make a determination regarding studies involving the UCI students and employees, as a target population, unless it has sufficient expertise in the ethical, clinical, and psychosocial issues impacting this population. Therefore, a Committee member who is knowledgeable about and experienced in working with these subjects must be in attendance at the convened meeting or an expert consultant who has this knowledge must be consulted by the IRB.

III. **IRB Analyst or Higher Responsibilities**

- A. The Analyst will verify that the IRB Application is completed as part of the initial study documents.
- B. The Analyst will conduct a pre-review and take into consideration the subject population in the proposed research when pre-reviewing the IRB Application, and informed consent documents.
- C. Communications recommending optional pre-review changes to the protocol or informed consent documents are to be sent to the LR by the Analyst.
- D. The assigned Reviewers have access to the protocol through the electronic IRB submission and management system.

Policy Number: 41

Title: Investigational Drugs, Agents, and Biologics

**Date of Last of Revision: 07/28/2006; 07/22/2010; 04/19/2012; 10/17/2012; 05/01/16;
10/06/17; 04/01/19; 04/12/22**

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) that the use of investigational drugs, agents, and/or biologics be reviewed and approved for use in accordance with the federal regulations (the United States Food and Drug Administration (FDA)) and the Department of Health and Human Services (DHHS)).

I. UCI IRB Requirements for the Use of an Investigational Drug, Agent, or Biologic

- A. The UCI IRB conducts initial approval and on-going monitoring of all investigational drugs, agents, and biologics used in human subjects research under its authority.
- B. Prospective IRB review is required even if a waiver from IRB regulations has been granted by the FDA for use of the investigational drug, agent, or biologic.
- C. Prospective review by the convened IRB is required for the use of an investigational drug, agent, or biologic as part of the Right to Try (RTT) Act.
- D. UCI will not provide investigational devices to patients outside of the FDA's expanded access program.
- E. Research that involves the use of a drug other than a marketed drug in the course of medical practice must have an Investigational new drug (IND) number, unless the protocol meets the five exemptions from the requirement of an IND per 21 CFR 312.2(b).
 - 1. The criteria is as follows:
 - a) Use of the investigational drug, agent, or biologic is not intended to be reported to the FDA in support of a new indication for use nor support any significant change in labeling for the product;
 - b) The use of the investigational drug, agent, or biologic is not intended to support a significant change in the advertising of the product;
 - c) The use of the product does not involve a route of administration, dosage level, and/or use in a subpopulation, or other factors that significantly increase the risks, or decrease the acceptability of the risks associated with the use of the drug, agent, or biologic;
 - d) The use will be conducted in compliance with the IRB approval and informed consent procedures;
 - e) The use will be conducted in compliance with the requirements concerning the promotion and sale of the drug, agent, or biologic as described in FDA regulations 21 CFR Sec. 312.7;

2. It is important to note that the above does not intend to invoke exception from informed consent requirements for emergency use.
- F. FDA regulations allow certain individuals not enrolled in clinical trials to obtain **expanded access** to investigational drugs, agents, or biologics through the following methods:
1. **Compassionate Use:** The term “compassionate use” is erroneously used to refer to the provision of investigational drugs outside of an ongoing clinical trial to a limited number of patients who are desperately ill and for whom no standard alternative therapies are available. The term “compassionate use” does not, however, appear in FDA or DHHS regulations. It is preferable, instead, to use the names of the specific access programs when discussing the use of investigational articles outside of formal clinical trials. Prospective IRB review and approval is required.
 2. **Group C Treatment Investigational New Drug (IND):** The "Group C" treatment IND was established by agreement between the FDA and the National Cancer Institute (NCI). The Group C program is a means for the distribution of investigational agents to oncologists for the treatment of cancer under protocols outside the controlled clinical trial. Group C drugs are generally Phase 3 study drugs that have shown evidence of relative and reproducible efficacy in a specific tumor type. They can generally be administered by properly trained physicians without the need for specialized supportive care facilities. Group C drugs are distributed only by the National Institutes of Health under NCI protocols. Although the FDA typically grants a waiver for most drugs used in Group C Treatment IND protocols, the UCI IRB requires prospective IRB review and approval.
 3. **Open – Label Protocol:** A study designed to obtain additional safety data, typically done when the controlled trial has ended and treatment continues. The purpose of such a study is to allow subjects to continue to receive the benefits of the investigational drug, agent, or biologic until marketing approval is obtained. Prospective IRB review and approval is required.
 4. **Parallel Track:** A method approved by the FDA that expands the availability of investigational drugs, agents, or biologics as quickly as possible to persons with AIDS and other HIV-related diseases. These drugs, agents or biologics are utilized in separate protocols that “parallel” the controlled clinical trials and are essential to establish the safety and effectiveness of these new drugs, agents, or biologics. Although the Secretary of the DHHS may, on a protocol-by-protocol basis, waive the provisions of 45 CFR Part 46 where adequate protections are provided through other mechanisms, prospective IRB review and approval is required by the UCI IRB.
 5. **Treatment IND or Biologics:** A mechanism for providing eligible subjects with investigational drugs (as early in the drug development process as possible) for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. The FDA defines an immediately life-threatening disease as a stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment. The FDA will permit an investigational drug to

be used under a treatment IND after sufficient data have been collected to show that the drug “may be effective” and does not have unreasonable risks. Prospective IRB review and approval is required.

1. There are four requirements that must be met before a treatment IND can be issued:
 - a) The drug is intended to treat a serious or immediately life-threatening disease;
 - b) There is no satisfactory alternative treatment available;
 - c) The drug is already under investigation or trials have been completed; and
 - d) The trial sponsor is actively pursuing marketing approval.
2. The FDA identifies two special considerations when a patient is to be treated under a Treatment IND:
 - a) Informed Consent. Informed consent is especially important in treatment use situations because the subjects are desperately ill and particularly vulnerable. They will be receiving medications which have not been proven either safe or effective in a clinical setting. Both the setting and their desperation may work against their ability to make an informed assessment of the risk involved. Therefore, the IRB ensures that potential subjects are fully aware of the risks involved in participation.
 - b) Charging for Treatment INDs. The FDA permits charging for the drug, agent, or biologic when used in a Treatment IND. Therefore, the IRB Committee pays particular attention to Treatment INDs in which the subjects will be charged for the cost of the drugs. If subjects will be charged for use of the test article, economically disadvantaged persons will likely be excluded from participation. Charging for participation may preclude economically disadvantaged persons as a class from receiving access to test articles. The IRB balances this interest against the possibility that unless the sponsor can charge for the drug, it will not be available for treatment use until it receives full FDA approval.
6. **Single-Patient Use:** The use of an investigational drug outside of a controlled clinical trial for a patient, usually in a desperate situation, who is unresponsive to other therapies or in a situation where no approved or generally recognized treatment is available. There is usually little evidence that the proposed therapy is useful but may be plausible on theoretical grounds or anecdotes of success. Access to investigational drugs for use by a single, identified patient may be gained either through the sponsor under a treatment protocol, or through the FDA, by first obtaining the drug from the sponsor and then submitting a treatment IND to the FDA requesting authorization to use the investigational drug for treatment use. Prospective IRB review and approval by an IRB Chair is required.
7. **Emergency IND:** The emergency use of an unapproved investigational drug, agent, or biologic requires an emergency IND. The FDA has established mechanisms and guidance for obtaining an Emergency IND for the use of investigational drugs, agents, or

biologics. Additional UCI IRB guidance regarding emergency IND is provided in IRB Policy 45.

8. **IND Exemptions in the Treatment of Cancer:** The FDA allows for an Investigational New Drug (IND) exemption of studies of lawfully marketed drug products for the treatment of cancer. When determining if an IND needs to be submitted to study marketed drugs for treating cancer, Researchers must apply the exemption criteria listed in 21 CFR 312.2(b)(1)(i-v). Additionally, planned studies may be considered exempt from the requirements of an IND if the studies involve a new use, dosage, schedule, route of administration, or new combination of marketed cancer products in a patient population with cancer and the following conditions apply:

- a) The studies are not intended to support FDA approval of a new indication or a significant change in the product labeling.
- b) The studies are not intended to support a significant change in the advertising for the product.
- c) Investigators and their IRBs determine that, based on scientific literature and generally known clinical experience, there is no significant increase in the risk associated with the use of the drug product.
- d) The studies are to be conducted in compliance with the IRB and informed consent regulations, pursuant to parts 50 and 56.
- e) The studies will not be used to promote unapproved indications in compliance with 21 CFR 312.7.

- G. Where a protocol is subject to review under more than one department or agency's regulations, the requirements of each set of regulations must be met. This situation may arise, for example, with Treatment Investigational New Drugs where both the FDA and DHHS have jurisdiction over the research. The use of an unapproved investigational drug, agent, and/or biologic requires an FDA IND.

- H. **Right to Try (RTT):** In May 2018, the federal Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 was signed into law, creating a federal framework for patients to access investigational new drugs and biologics outside of clinical trials and outside of the U.S. Food and Drug Administration's (FDA) expanded access program. The Federal Right to Act enables a patient with a "life-threatening" disease or condition to access investigational drugs and biologics that have completed Phase 1 testing under an FDA-approved clinical trial and which are either being actively developed or produced by the manufacturer or not placed on clinical hold. Importantly, the federal law does not address the use of investigational devices.

1. In order to receive an investigational drug or biologic under the federal RTT Act, the patient must:
 - a) Have a life-threatening disease or condition;
 - b) Have exhausted treatment options, as certified by the physician;
 - c) Be unable to participate in a clinical trial involving the investigational drug, as certified by the physician; and

- d) Have given his or her written informed consent (or consent of a legally authorized representative) to the treating physician regarding use of the investigational drug.
2. Use of an investigational drug under the RTT is exempt from FDA requirements for review and authorization, so long as the sponsor or manufacturer of the drug is in compliance with FDA requirements applicable to investigational drugs. Note that the law does not limit compliance to the specific investigational drug that is the subject of the use.
 3. The RTT act does require sponsors and manufacturers who have made their investigational drugs available under RTT to annually report to the FDA the number of doses supplied, the number of patients treated, the uses for which the drug was made available, and any known serious adverse events. In turn, the FDA must make this information publicly available on its website.
 4. Patients may be charged the direct costs of making the investigational drug available for their use.
 5. The federal RTT does incentivizes sponsors and manufacturers to make their investigational drugs available by protecting them against liability with respect to acts and omissions regarding the investigational drug. The Act also protects prescribers, dispensers, and other individuals from liability, unless the act or omission constitutes reckless or willful misconduct, gross negligence, or an international tort under state law. Finally, the Act expressly protects against liability to any person for not providing access to an investigational drug under the Act.
 6. The California RTT Act is similar to the federal Act, though there are notable differences.
 - a) In one respect, the California law is broader than the federal right to try law as it applies to use of investigational drugs, biologics and devices that have successfully completed an FDA-regulated Phase 1 trial and remain under active investigation by the FDA. The federal law does not include devices.
 - b) In most instances, the California law imposes more requirements to obtain access to an investigational drug outside of a clinical trial.
 - c) California RTT limits access to patients with an “immediately life-threatening disease or condition”, whereas the federal law only requires patients have a “life-threatening disease or condition.” Thus, under state law, the patient must be in a stage of disease in which there is a reasonable likelihood death will occur in a matter of months.
 - d) The treating physician and a second consulting physician must both recommend that the patient receive the investigational product, attest to this recommendation, and attest that the patient meets the criteria of the state law.
 - e) Specific informed consent requirements must be met. Like the federal law, a surrogate may consent on behalf of the patient consistent with California law requirements. However, the

consent form must contain the information from the California Health and Safety Code - Section 111548.1(h)(1), and also must meet the requirements set forth in the California Protection of Human Subjects in Medical Experimentation Act.

- f) An IRB must review and approve the protocol and consent form.
 - (1) At UCI a Prospective review by the convened IRB is required per UC Office of the General Counsel Health Sciences Research Advisory guidance.
 - g) Reporting requirements between the federal and California RTT Acts also differ. While federal law requires that the sponsor or manufacturer make information available to the FDA (which the FDA must publicly post), the California law imposes an obligation upon the IRB of record to biannually report information regarding the number of requests made to the IRB for an investigational product, the status of each request, the duration of treatment, the costs of treatment paid by patients, the success or failure of the investigational product in treatment, and adverse events.
 - h) Similar to federal law, California RTT does not impose an obligation upon manufacturers to make an investigational product available to a patient. California RTT also provides that a manufacturer may recover the costs of the manufacture of the product. However, the law removes any liability upon the patient's heirs or the patient's health benefit plan, for any outstanding debt related to the treatment using the investigational product.
 - i) In addition, the CA RTT specifically prohibits the Medical Board of California and the Osteopathic Medical Board of California from taking any disciplinary action against a physician's license to practice medicine based solely upon the physician's recommendation to treat or treatment of a patient with an investigational product, so long as the protocol was approved by an IRB. The Act also provides that any actions taken pursuant to the state law by a manufacturer or any other person or entity involved in caring for the patient cannot serve as the basis for any civil, criminal or disciplinary claim or cause of action under state law.
- 7. Given the stricter California law requirements for using an investigational drug without FDA approval (IRB review and approval is required) and the additional protection the California law affords to physicians regarding licensure, UCI will comply with California's RTT law requirements.
 - 8. Because the federal RTT law does not address the use of investigational devices UCI will not provide investigational devices to patients outside of the FDA's expanded access program.

II. **Use of an Investigational Drug, Agent, or Biologic by a Researcher**

- A. In order for an investigational drug, agent, or biologic to be used in clinical research at UCI, an IND number must be issued by the FDA.

- B. A valid IND number is required (e.g., listed on Sponsor Protocol or a copy of the FDA approval of the IND). The UCI IRB may review research without an IND number but will not grant approval until documentation of an IND number is provided to the IRB.
- C. Researchers provide information regarding the use of investigational drugs, agents, and biologics as required in the IRB Application for human research.
- D. Clinical investigations of a drug, agent, or biologic that is lawfully marketed in the United States are exempt from the requirements of an IND as per 21 CFR 312.2(b).
- E. Research involving combinations of FDA approved drugs, agents, or biologics that are currently approved as single use, do not require an IND. However, use of these drugs, agents, or biologics in clinical research must still be prospectively reviewed and approved by the IRB.
- F. The Investigator administering an investigational drug, agent or biologic must meet the following requirements in order to use an investigational drug, agent, or biologic in research conducted under the jurisdiction of the UCI IRB:
 - 1. The drug, agent, or biologic must be used only in accordance with the plan of investigation as described in the FDA-approved IND application and the IRB- approved protocol;
 - 2. The drug, agent, or biologic may only be used in participants under the LR's supervision or under the supervision of a physician who is a Co-Researcher; and
 - 3. Informed consent from the participant or the participant's surrogate decision-maker is prospectively obtained, unless a waiver of consent has been approved by the UCI IRB.
- G. Investigators using an investigational drug/biologic are required to provide a plan about how the drug/biologic will be managed and controlled in the IRB Application. Investigators are required to:
 - 1. Describe how the Investigator will ensure that the investigational drug/biologic is used only in accordance with the UCI IRB approved protocol.
 - 2. Explain who will access to the drug/biologic and how access will be controlled to secure the drug/biologic.
 - 3. Explain how records for control of the drug/biologic will be recorded. For example, use of the sample Drug/Biologic Accountability Log provided on the Human Research Protections website; use of the Drug/Biologic Log provided by the Sponsor; or no log will be used and the researcher must provide justification.
- H. **Research with the use of an investigational drug, agent, or biologic must be conducted in accordance with all UC, UCI and UCI IRB policies and procedures.**
- I. All initial requests for IRB approval of a study that include the use of an investigational drug, agent, or biologic will be reviewed and approved by the full IRB Committee.

- III. **Use of an Investigational Drug, Agent, or Biologic by an Investigator Assuming the Sponsor Function**
- A. In rare instances, a UCI Investigator will assume the Sponsor function for use of an investigational drug, agent or biologic. A *Sponsor-Investigator* is an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The requirements applicable to a sponsor-investigator under this part include both those applicable to an investigator and a sponsor.
 - B. In addition to the requirements above, the UCI Investigator must submit a copy of the FDA Notice of Claimed Investigational Exemption for a New Drug (IND Application) along with their IRB Application for review. UCI IRB approval will not be granted until documentation of a valid IND number is submitted to the IRB.
 - C. The UCI Investigator must comply with all Sponsor function requirements described in 21 CFR 312.
- IV. **Advertising or Recruitment for Studies Involving Investigational Drugs, Agents, or Biologics (See HRP Policy # 22)**
- A. Advertisements or recruiting tools must not include the term “new treatment”, without explaining that the drug, agent, or biologic is “investigational”, meaning non-FDA approved. A phrase such as “receive new treatment” implies that all study subjects will be receiving newly marketed products of proven worth. It is not a treatment since its effectiveness has not been proven or established. The term “new” is misleading as it gives the participant hope of a new intervention when the outcome is unknown. This could be viewed as coercive.
 - B. Advertisements or recruiting materials must not include the promise of “free medical treatment” when the intent is only to say that participants will not be charged for taking part in the investigation or experimental intervention (e.g., drug, agent, biologic). The use of the word “free” could be viewed as unduly influential as it may entice someone to participate in a study for the perceived benefits.
- V. **Informed Consent in Research that Involves an Investigational Drug, Agent, or Biologic**
- A. Informed consent must meet the requirements outlined in the IRB Informed Consent policies and procedures (See HRP Policy # 30);
 - B. No claims are to be made which state or imply, directly or indirectly, that the investigational drug, agent, or biologic is safe or effective for the purposes under investigation or that the drug is in any way superior to another drug;
 - C. The informed consent document must contain a statement that the drug, agent, or biologic is “investigational” or “experimental”;
 - D. The informed consent document must contain a statement that the FDA may have access to the participant's medical records as they pertain to the study; and
 - E. The researcher must assure that throughout the consenting process and study participation the participant understands that the investigational drug, agent, or biologic is under investigation, and that its benefits for the condition under study are unproven.

References:

21 CFR 50

21 CFR 56

21 CFR 210

21 CFR 211

21 CFR 312

45 CFR 46

U.S. Food and Drug Administration Information Sheet: Investigational Use of Marketed Drugs, Biologics and Medical Devices, 1998.

U.S. Food and Drug Administration: Expanded Access of Investigational Drugs, 1998.

FDA Guidance Sheet: IND Exemptions for Studies of Lawfully Marketed Drug or

Biological Products for the Treatment of Cancer, January 2004

UC Office of the General Counsel Health Sciences Research Advisory: *Clinical Use of Investigational Drugs, Devices and Biologics under Federal and California Law*, November 2018

California Right to Try Act: AB-1668 Investigational drugs, biological products, and devices.

UCI Health Management of Investigational Medications Policy, March 2021

Procedure Number: 41.A**Title: Procedure for Review of Research Involving Investigational Drugs, Agents, and Biologics****Procedure:**

This procedure outlines the review and approval process for use of investigational drugs, agents, and biologics in clinical research.

I. Lead Researcher (LR) Responsibilities

- A. The LR will provide all information regarding the use of investigational drugs, agents, and biologics as required in the UCI IRB Application. This will include the identification of the IND number.
- B. When the LR holds the IND for the investigational drug, agent, or biologic, a copy of the FDA approval letter is required as part of the IRB submission.
- C. The LR must provide justification for each of the conditions required for a drug, agent, or biologic to be exempt from the requirements of an IND (See HRP Policy # 41). The IRB Committee will determine if the justification warrants exemption from IND requirements.
- D. **The Investigator will obtain and manage the drug, agent, or biologic in accordance with the UCI Health Management of Investigational Medications Policy.**
- E. The LR will complete the informed consent process unless a waiver has been granted by the IRB.
- F. The LR will maintain all study case report forms and drug dispensing records as required by the sponsor, Institution, and/or FDA.
- G. The LR will notify the IRB of any modifications, unanticipated problems to participants or others that may occur while conducting the research or follow-up.
- H. The LR will assure that unanticipated problems involving participants or others are reported to the IRB via the UCI New Information Report in accordance with HRP Policy # 19.
- I. The LR will complete and submit renewal applications in accordance with HRP policy at the designated review intervals imposed by the IRB.
- J. The Investigator will notify the FDA and IRB of closure or completion of the study and return all unused products per the sponsor's instructions.
- K. When requesting RTT, the LR will utilize and complete the following additional documents as found on the HRP webpage:
 - 1. The Treating Physician Checklist
 - 2. The Treating Physician Attestation
 - 3. The Consulting Physician Attestation
 - 4. Informed Consent for a Eligible Patient Seeking an Investigational Drug or Biologic Under Right to Try Act
 - i. Once approved by the IRB, within 30 days of beginning treatment, the LR will provide the following to IRB@research.uci.edu:
 - a) Provide a copy of the signed attestation.
 - b) Provide the following status as required to reporting to the State Department of Public Health, the Medical Board of

California, and the Osteopathic Medical Board of California:

1. The duration of the treatment.
2. The costs of the treatment paid by eligible patients.
3. The success or failure of the investigational drug, biological product, or device in treating the immediately life-threatening disease or condition from which the patient suffers.
4. Any adverse event for each investigational drug, biological product, or device.

II. IRB Committee Responsibilities

- A. All initial requests for IRB approval of a study that includes the use of an investigational drug, agent, or biologic will be reviewed and approved by the full IRB Committee.
- B. When research involves a drug with an IND, the IRB Committee, together with the IRB Administrator, should evaluate whether the IND number is valid for the proposed use. The purpose of this verification is to prevent situations where researchers may begin FDA- regulated research that require an IND before the FDA has issued an IND number.
- C. If the LR is requesting the drug, agent, or biologic be exempt from IND requirements, the IRB Committee must discuss each of the conditions for an exemption and determine if the LR's justification meets the criteria for exemption from the IND requirements.
- D. The assigned reviewers of the research protocol involving drugs, agents, or biologics will seek clarification from a UCIMC pharmacy representative of any concerns that may affect the risk/benefit assessment.
- E. The full IRB Committee will review the proposed research, informed consent documents (including notification that the FDA may have access to the participant's study records), the procedure for obtaining informed consent, and additional information, when applicable, to determine whether the study meets criteria 45 CFR 46.111 and 21 CFR 56.111 for approval.
- F. The IRB Committee must first consider whether the protocol is scientifically sound. The following aspects of the study should be considered when making a determination regarding risk/benefit ratio:
 1. Prior reviews by the FDA, other institutions, scientific review committees, funding agencies (e.g., NIH), or others; and
 2. Study design which includes the study population, the trial phase, and mechanisms for data analysis and surveillance.
- G. Submission of amendments, unanticipated problems to participants or others, and renewals will be reviewed at the level for which the criteria are met.
- H. Final IRB approval is evidence that the study meets criteria 45 CFR 46.111 and 21 CFR 56.111 as noted above and is documented in the IRB approval letter.

III. IRB Administrator (or designee – e.g., Senior Analyst) Responsibilities

- A. The Administrator will pre-review and request any necessary revisions for submitted documents for use of investigational drugs, agents, or biologics as outlined for new IRB Applications.

- B. The Administrator will verify that additional documents have been submitted by the LR as required:
 - 1. Any supplemental information regarding the investigational drug, agent, or biologic supplied by the sponsor.
- C. When research involves a drug with an IND, the IRB Committee, together with the IRB Administrator, should evaluate whether the IND number is valid.
 - 1. Validation of an IND can be done by:
 - a) Determining that the IND number in the IRB Application matches the Sponsor Protocol or
 - b) Upon receipt of communication from the Sponsor, which corresponds with the IND number provided in the IRB Application or
 - c) Upon receipt of communication from the FDA, which corresponds with the IND number provided in the IRB Application
 - 2. Validation of an IND *should not* involve:
 - a) Confirmation of the IND number by referencing the Investigator's Brochure (IB). This is because one IB often serves multiple IND's.
- D. Once the LR has met all the requisite requirements, the Administrator will place the new study on the next available Committee agenda.
- E. If the LR is requesting the drug, agent, or biologic be exempt from IND requirements, the Administrator must document the IRB Committee's discussion and determination for each of the conditions required for an exemption from the IND requirements.
- F. The Administrator will assist reviewers in obtaining additional information that may be requested regarding the investigational drug, agent, or biologic from the LR.
- G. **For Investigator Initiated Research, the Administrator will ensure that final IRB approval is not released until the protocol has been reviewed and approved by UCI Investigational Drug Services (IDS).**
 - 1. IDS has administrative access to the electronic IRB submission and management system to help facilitate this process.
- H. The Human Research Protections (HRP) staff will process all requests for amendments, unanticipated problems to participants or others, and continuing reviews per corresponding IRB policies and procedures.
- I. The HRP staff will update and maintain current information in the electronic IRB submission and management system.

Policy Number: 42

Title: Investigational Devices

Date of Last Revision: 06/12/2008; 07/22/2010; 05/29/2013; 05/01/2016; 10/16/2018; 04/20/2022

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) that all investigational device use be reviewed and approved by the IRB in accordance with applicable laws and regulations.

The Investigational Device Exemptions (IDE) regulation 21 CFR 812 describes three types of device studies; Significant risk (SR), Nonsignificant risk (NSR), and Exempt studies.

I. SR vs. NSR Devices

- A. Unless exempt by the IDE regulations, an investigational device must be categorized as either a SR device or a NSR device. The initial risk assessment should be determined by the Sponsor, with the IRB making a formal SR/NSR determination during a convened meeting (*see below*).
- B. The FDA is the final arbiter as to whether an investigational device is SR or NSR device. The FDA is available for consultation.
- C. For SR devices a copy of the FDA approval of an Investigational Device Exemption must be submitted to the IRB before UCI IRB approval will be granted.
- D. Research involving the use of a SR device must be conducted in accordance with the full requirements of the FDA and must have an approved Investigational Device Exemption (IDE) from the FDA.
- E. For NSR devices, if the FDA has made an NSR determination and the research poses no greater than minimal risk, the study may be submitted for expedited review. If the FDA has not previously made a NSR determination, the study must be reviewed during a convened meeting with the IRB making the formal SR/NSR determination.
- F. If the IRB disagrees with a sponsor's NSR determination, the sponsor will be required to secure an IDE or documentation of the FDA's NSR determination.
- G. Research involving the use of a NSR device must be conducted in accordance with the "abbreviated" requirements of the FDA as described in the FDA regulations 21 CFR Sec. 812.2(b). In some cases, the FDA may notify the sponsor that it does not agree with the NSR determination and will require the submission of an IDE. All copies of related correspondence must be submitted to the IRB for review.

II. Exemptions from IDE requirements

- A. A device can be exempt from the IDE requirements. If an exempt study is being conducted to collect data to support either a clinical investigation or a marketing application then the study must comply with 21 CFR 50 and should comply with 21 CFR 56. There are seven exemption categories in 21 CFR 812.2(c) that may be claimed (*see B below*):
1. The first two categories pertain to devices that were either manufactured before 1976 or similar products manufactured after 1976 (referred to as a 510K device).
 2. Categories 3 and 4 are the most commonly applied for exemptions.
 3. Categories 5 and 6 are pertinent to the use of devices in animals.
 4. Category 7 pertains to custom devices and is rarely utilized.
 5. The exemption category most commonly claimed is 21 CFR Sec. 812.2(c)(3).
 6. To qualify for exemption 21 CFR Sec. 812(c)(4), the device testing must not be for the purposes of determining safety and effectiveness and must not put subjects at risk. The device testing must be limited to the following:
 - a) Consumer preference testing;
 - b) Testing of a modification; or
 - c) Testing of a combination of two or more devices in commercial distribution.
 7. It is the sponsor's responsibility to provide sufficient justification to support the exemption category being claimed.
 8. An exemption from the IDE requirement is not an exemption from the requirement for prospective IRB review or informed consent.
- B. *Exempted Device Investigation.*
The following categories of devices do not require an IDE:
1. A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time.
 2. A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence (a 510K device)
 3. A diagnostic device, if the sponsor complies with applicable requirements in § 809.10(c) and if the testing:
 - a) Is noninvasive,
 - b) Does not require an invasive sampling procedure that presents significant risk,
 - c) Does not by design or intention introduce energy into a subject, and
 - d) Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

4. A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk.
5. A device intended solely for veterinary use.
6. A device shipped solely for research on or with laboratory animals and labeled in accordance with § 812.5(c).
7. A custom device as defined in § 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

III. **UCI IRB Approval of the Use of an Investigational Device**

- A. Where a protocol is subject to review under more than one department or agency's regulations, the requirements of each set of regulations must be met. This situation may arise, for example, with IDEs where both the FDA and DHHS have jurisdiction over the research. The use of an unapproved SR device requires an FDA investigational device exemption (IDE).
- B. The IRB must determine whether it is in agreement with the rendering of the decision by the sponsor of the device being a non-significant risk or a significant risk device. If the IRB is in agreement with the sponsor's determination of NSR, no report to the FDA is required until the data are submitted. However, the sponsor must be notified if the IRB disagrees with the sponsor's NSR determination.
- C. The IRB must determine whether the device is exempt, based upon information provided in the IRB Application.
- D. The IRB may approve or disapprove the proposed research based on local context and its responsibilities to protect human subjects in research even when approval of the device has been granted by the FDA.
- E. The LR is responsible for the tracking and oversight of FDA-regulated devices in research and must meet the following requirements in order to use an investigational device in research conducted under the jurisdiction of the UCI IRB:
 1. The investigational device must be used only by the LR or qualified study team member;
 2. The investigational device must be used only as approved by the FDA and as described in the currently approved IRB documents;
 3. The researchers must not supply the investigational device to any persons not authorized under the IDE;
 4. Informed consent from the participant or the participant's LAR must be prospectively obtained, unless waived by the IRB; and
 5. Research with the use of an investigational device must be conducted under all UCI IRB applicable policies and procedures.
- F. Researchers using an investigational device are required to provide a plan in the IRB Application about how the device will be managed and controlled. Researchers are required to:
 1. Describe how the Researcher will ensure that the investigational device is used only in accordance with the UCI IRB approved protocol.
 2. Explain who will access to the device and how access will be controlled to secure the drug/biologic. The investigational device must be used only by the LR or qualified study team member.

3. Explain how records for control of the device will be recorded. For example, use of the sample Device Accountability Log provided on the HRP website; use of the Device Log provided by the Sponsor; or no log will be used and the researcher must provide justification.

IV. **In Vitro Diagnostic Device Studies**

- A. Under FDA regulations, clinical investigations using human tissue specimens conducted in support of premarket submissions to FDA are considered human subject investigations [see 21 CFR 812.3(p)]. Many IVD studies are exempt from IDE requirements, under 21 CFR 812.2(c)(3), however FDA regulations for the protection of human subjects (21 CFR Parts 50 and 56) still apply to all clinical investigations that are regulated by FDA [see 21 CFR 50.1; 21 CFR 56.1] even if the clinical investigation involves unidentified, leftover tissue specimens.
- B. The FDA intends to exercise enforcement discretion as to the requirements for informed consent requirements for clinical investigators and IRBs if an *in vitro* diagnostic device investigation is performed and all of the following are true:
 1. The investigation meets the IDE exemption criteria at 21 CFR 812.2(c) (3).
 2. The study uses leftover specimens, that is, remnants of specimens collected for routine clinical care or analysis that would have been discarded. The study may also use specimens obtained from specimen repositories or leftover specimens that were previously collected for other research purposes.
 3. The specimens are not individually identifiable, i.e., the identity of the subject is not known to and may not readily be ascertained by the investigator or any other individuals associated with the investigation, including the sponsor. If the specimen is coded, it will be considered to be not individually identifiable if neither the investigator(s) nor any other individuals associated with the investigation or the sponsor can link the specimen to the subject from whom the specimen was collected, either directly or indirectly through coding systems.
 4. The specimens may be accompanied by clinical information as long as this information does not make the specimen source identifiable to the investigator or any other individual associated with the investigation, including the sponsor.
 5. The individuals caring for the patients are different from and do not share information about the patient with those conducting the investigation.
 6. The specimens are provided to the investigator(s) without identifiers and the supplier of the specimens has established policies and procedures to prevent the release of personal information.
- C. Studies that do not fall within the intended enforcement discretion include (but are not limited to) studies where any of the following is true:
 1. The study does not meet the IDE exemption criteria at 21 CFR 812.2(c)(3);
 2. The specimens are individually identifiable, i.e., the identity of the subject is known to or may be readily ascertained by the investigator or any other individuals associated with the investigation, including the sponsor.

3. The specimens were collected specifically for the proposed investigation. That is, the specimens are not leftover from routine clinical care or analysis or leftover from other research.
4. The amount of specimen needed for the study is more than would be leftover from what is usually collected for routine clinical analysis or,
5. The test results will be reported to the subject's health care provider.

V. Review Process for SR/NSR Studies

- A. The IRB Committee is responsible for reviewing and determining whether it is in agreement with the sponsor's determination of SR or NSR.
- B. The convened IRB Committee must review the sponsor's SR or NSR determination for every investigational medical device reviewed. There is one exception where expedited review may be appropriate as follows:
 1. If the FDA has already made a NSR determination and the IRB agrees that the use of the device in the investigation poses no greater than minimal risk, expedited review of the study may be appropriate under the applicable expedited category(ies).
 2. The FDA NSR determination letter must be provided as part of the expedited review of the study.
- C. Approval of a SR or NSR device will be documented in the meeting minutes for which the study was reviewed and approved*.
 - a) *Approval of the NSR device through an expedited review will be reported to the convened IRB and the NSR risk determination for the expedited study will be documented in the meeting minutes.
- D. Documentation of SR and NSR will be done at the initial review and for each continuing review and/or each modification as applicable where a change in risk or other change has occurred that may affect the device risk determination.
- E. The risk determination made by the IRB Committee is based on the proposed use of the device in an investigation, and not on the device alone.
- F. In deciding if a study poses a SR, the IRB considers the nature of the harm that may result from the use of the device.
 1. Studies where the potential harm to subjects could be life-threatening, could result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure are considered SR.
 2. If the subject must undergo a procedure as part of the investigational study (e.g., a surgical procedure), the IRB considers the potential harm that could be caused by the procedure in addition to the potential harm caused by the device.
- G. The IRB may consult with the FDA for its opinion.
- H. Once the SR or NSR decision has been reached, the IRB considers whether the study should be approved or not. The criteria for deciding if SR and NSR studies should be approved are the same as any other FDA regulated study.
- I. To assure that the risks to the subject are reasonable in relation to the anticipated benefits, the risks and benefits of the investigation are compared to the risks and benefits of alternative devices or procedures.

1. This differs from the judgment about whether a study poses a SR or NSR, which is based solely upon the seriousness of the harm that may result from the use of the device.
- J. When the sponsor determines the investigational device to be NSR and the IRB disagrees (assuming that documentation of NSR status from the FDA is not available), the proposed research is tabled by the convened IRB Committee.
 1. The IRB notifies the LR and requests that he/she contacts the sponsor and notify them of the Committee's determination.
 2. The sponsor may proceed with submitting a request for an IDE approval from the FDA and, when received, the IRB re-reviews the proposed research. UCI IRB approval cannot be granted until FDA documentation concerning the IDE is provided to IRB.
 3. The sponsor or the researcher may withdraw the study and not submit the investigational device to the FDA for consideration of an IDE.
- K. In the event that the FDA rules that the investigational device is a SR device after the sponsor and the IRB have determined the investigational device to be a NSR device, the IRB will suspend the currently approved study detailing the criteria for suspension.
 1. The study may not reopen until an IDE is granted by the FDA and the study is reviewed by the full Committee with appropriate changes to the IRB application, protocol and/or informed consent documents.
 2. The Committee must direct the LR on the issue of re-consenting participants, if appropriate.
- L. Criteria for Approval of SR and NSR Studies
 1. In making its determination on approval, the IRB considers the following:
 - a) Whether the protocol is scientifically sound;
 - b) The risks and benefits of the medical device compared to the risks and benefits of alternative devices or procedures;
 - c) The risks and benefits of the proposed research, in addition to those associated with the use of the device;
 - d) Consideration of prior reviews by the FDA, other institutions, scientific review committees, funding agencies (e.g., NIH), or others; and
 - e) Study design, which includes the study population, the trial phase, and mechanisms for data analysis and surveillance.
- M. Continuing Review of an Investigational Device.
 1. NSR investigational devices and minimal risk studies may receive expedited review at continuing review.
 2. SR investigational devices, regardless of the risk associated with the study, must be reviewed by the full Committee at continuing review.

- VI. **Use of an Investigational Device by an Investigator Assuming the Sponsor Function**
- A. In rare instances, a UCI Investigator will assume the Sponsor function for use of an investigational device. A *Sponsor-Investigator* is an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The requirements applicable to a sponsor-investigator under this part include both those applicable to an investigator and a sponsor.
 - B. In addition to the requirements above, if the device is a SR device, the UCI Investigator must submit a copy of the FDA Investigation Device Exemption Application (IDE Application) along with their IRB protocol application for review. UCI IRB approval will not be granted until documentation of a valid IDE from the FDA is submitted to IRB.
 - C. The UCI Investigator must comply with all Sponsor function requirements described in 21 CFR 812.
- VII. **Individual Patient Expanded Access of a Device that Involves an IDE**
- A. **For an expanded access (also known as compassionate use) request of an investigational device (with an IDE), IRB Chairperson approval is allowable through an expedited review process.**
- VIII. **Advertising or Recruitment for Studies That Involve an IDE (Also See IRB Policy V.B.)**
- A. Advertisements or recruiting tools must not include the term “new treatment”, without explaining that the IDE is “investigational”, meaning non-FDA approved. A phrase such as “receive new treatment” implies that all study subjects will be receiving newly marketed products of proven worth. It is not a treatment since its effectiveness has not been proven or established. The term “new” is misleading as it gives the participant hope of a new intervention when the outcome is unknown. This could be viewed as coercive.
 - B. Advertisements or recruiting tools must not include the promise of “free medical treatment” when the intent is only to say that participants will not be charged for taking part in the investigation or experimental intervention (e.g., device). The use of the word “free” could be viewed as coercive as it may entice someone to participate in a study for the perceived benefits.
- IX. **Informed Consent in Research that Involves an IDE**
- A. Informed consent must meet the requirements outlined in the IRB Informed Consent policies and procedures (See HRP Policies # 36-40);
 - B. No claims may be made which state or imply, directly or indirectly, that the IDE is safe or effective for the purposes under investigation or that the device is in any way superior to any other device;
 - C. The informed consent document must contain a statement that the IDE is “investigational”;
 - D. The informed consent document must contain a statement that the FDA may have access to the participant’s medical records as they pertain to the study; and
 - E. The researcher must ensure that throughout the consenting process and study participation the participant understands that the IDE is

experimental, and that its benefits for the condition under study are unproven.

X. Additional Reporting Requirements

- A. Devices may have an unanticipated adverse device effect (UADE) to participants or others. The investigational device exemption (IDE) regulations define an UADE as “any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.”

UADEs must be reported by the clinical investigator to the sponsor and the IRB (via the “Unanticipated Problems” (UP) Report), as described below:

1. For device studies, investigators are required to submit a report of a UADE to the sponsor and the reviewing IRB as soon as possible, but in no event later than 5 business days after the investigator first learns of the event (§ 812.150(a)(1)).
 2. Sponsors must immediately conduct an evaluation of a UADE and must report the results of the evaluation to FDA, all reviewing IRBs, and participating investigators within 10 working days after the sponsor first receives notice of the effect (§§ 812.46(b), 812.150(b)(1)).
 - a. A sponsor who determines that an unanticipated adverse device effect presents an unreasonable risk to subjects must terminate or suspend all investigations or parts of investigations presenting that risk as soon as possible. Termination or suspension must occur no later than 5 working days after the sponsor makes this determination and no later than 15 working days after the sponsor first received notice of the effect.
 - b. If the device is a significant risk device, a sponsor may not resume a terminated or suspended investigation without IRB and FDA approval. If the device is not a significant risk device, a sponsor may not resume a terminated or suspended investigation without IRB approval and, if the investigation was terminated or suspended for an unanticipated adverse device effect that presented an unreasonable risk to participants or others, FDA approval.
- B. Should the IRB determine that the new information gained in the adverse effect report changes its risk assessment, the IRB will reconsider its prior NSR decision and ask for FDA review.
- C. Within 3 months after termination or completion of the investigation or the Researcher’s part of the investigation, the Researcher must submit a final closing report to the UCI IRB.

References:

21 CFR 50 and 56

21 CFR 812

21 CFR 814

21 CFR 860

45 CFR 46

FDA Information Sheet Guidance, "Frequently Asked Questions About Medical Devices"- January 2006

FDA Information Sheet Guidance, "Significant Risk and Nonsignificant Risk Medical Device Studies"

Procedure Number: 42.A**Title: Procedure for Review of Research Involving Investigational Devices****Procedure:**

The purpose of this procedure is to provide guidance on the use of investigational devices in human subjects research.

I. Lead Researcher (LR) Responsibilities

- A. The LR will provide all information regarding the use of investigational devices as required in the IRB Application. This will include the identification of the IDE number, if applicable.
- B. When an IDE is required, the LR will also complete the FDA's Investigator's Agreement form for submission to the FDA. A copy of this form must be submitted with the initial IRB application.
- C. The initial submission will also include all correspondence from the sponsor and/or FDA in regard to the determination of the device as being a NSR or SR. If the sponsor considers that a study is NSR, the LR should provide the IRB an explanation of the determination and any other information that may assist the IRB in evaluating the risk of the study.
- D. The LR should provide the IRB with a description of the device, reports of prior investigations with the device, the proposed investigational plan, a description of participant inclusion/exclusion criteria and monitoring plan, as well as any other information that the IRB deems necessary to make its decision. The LR should inform the IRB whether other IRBs have reviewed the proposed study and what determination was made. The LR must also inform the IRB of the FDA's assessment of the device's risk if such an assessment has been made.
- E. The LR is responsible for the submission to the IRB of the sponsor's report of prior investigations for the IDE.
- F. It is the LR's responsibility to notify the Sponsor of the SR decision made by the IRB Committee.
- G. Additionally, the LR will provide a description of the component, ingredient, property, principle of operation and each anticipated change in the device during the course of the research.
- H. The LR will complete the informed consent process, unless a waiver has been granted by the IRB.
- I. The LR will maintain all case report forms and records as required by the sponsor, Institution, and/or FDA.
- J. The LR is responsible for the accountability, storage, dispensing, tracking, and oversight of the FDA-regulated devices in accordance with applicable institutional, State, and Federal laws and regulations.
- K. The LR will complete and submit continuing review applications at the established review intervals imposed by the IRB.
- L. The LR will notify the IRB of any amendments, unanticipated device effects, serious adverse events or unanticipated problems to participants or others that may occur while conducting the research or follow-up.
- M. The LR will assure that adverse device effects or unanticipated problems to participants or others are reported to the IRB via the UCI IRB reporting process in accordance with current policy and HRP Policy # 19.

- N. The LR will assure the device is only used under their direct supervision and will discard or ship all unused devices back to the sponsor as specified by the sponsor.
- O. The LR will notify the IRB of study closure or completion of the study and return all unused products per the sponsor's instructions.
- P. The LR will submit the final closing report to the IRB within three months of termination or completion of study.

II. **IRB Committee Responsibilities**

- A. If the research being conducted is to determine the safety or effectiveness of a device but does not have an IDE issued by the FDA, the IRB will confirm whether the device meets the requirements for an abbreviated investigational device exemption (IDE) (21 CFR §812.2(b)(1)) or the protocol meets one of the five exemptions from the requirement for an IDE (21 CFR §812.2(c)).
- B. When research involves a device with an IDE, the IRB Committee, together with the IRB Administrator, should evaluate whether the IDE number is valid. The purpose of this verification is to prevent situations where researchers may begin FDA- regulated research that require an IDE before the FDA has issued an IDE number.
- C. Device studies that are exempt from the IDE requirement may qualify for expedited review Category 1 (e.g., IVD device studies involving unidentified, leftover tissue specimens). Waiver of consent may also be applicable (See 42 above). Based on the initial expedited review, the IRB reviewer may request the IDE study be sent to an additional reviewer or to full Committee.
- D. The IRB Committee is responsible for reviewing and determining whether it agrees with the sponsor's determination of SR or NSR.
- E. See I.C. above for information to be submitted by the LR that may assist the IRB in evaluating the risk of the study. The IRB may also consult with the FDA for its opinion. The risk determination should be based on the proposed use of the device in an investigation, and not on the device alone. In deciding if a study poses a SR, an IRB must consider the nature of the harm that may result from the use of the device. Studies where the potential harm to subjects could be life-threatening, could result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure should be considered SR. Also, if the subject must undergo a procedure as part of the investigational study, e.g., a surgical procedure, the IRB must consider the potential harm that could be caused by the procedure in addition to the potential harm caused by the device. Two examples follow:
 - 1. The study of a pacemaker that is a modification of a commercially available pacemaker poses a SR because the use of any pacemaker presents a potential for serious harm to the subjects. This is true even though the modified pacemaker may pose less risk, or only slightly greater risk, in comparison to the commercially available model. The amount of potential reduced or increased risk associated with the investigational pacemaker should only be considered (in relation to

- possible decreased or increased benefits) when assessing whether the study can be approved.
2. The study of an extended wear contact lens is considered SR because wearing the lens continuously overnight while sleeping presents a potential for injuries not normally seen with daily wear lenses, which are considered NSR.
- F. Once the SR/NSR decision has been reached, the IRB should consider whether the study should be approved or not. The criteria for deciding if SR and NSR studies should be approved are the same as any other FDA regulated study. To assure that the risks to the subject are reasonable in relation to the anticipated benefits, the risks and benefits of the investigation should be compared to the risks and benefits of alternative devices or procedures. This differs from the judgment about whether a study poses a SR or NSR which is based solely upon the seriousness of the harm that may result from the use of the device.
- G. When the sponsor determines the investigational device to be of a non-significant risk and the UCI IRB disagrees, the proposed research is to be deferred by the convened IRB Committee. The IRB will draft a letter of deferral and request that the LR contact the sponsor and notify them of the Committee's determination.
1. The sponsor may proceed with submitting a request for an IDE approval from the FDA and when received the IRB will re-review the proposed research.
 2. The sponsor or the LR may withdraw the study and not submit the investigational device to the FDA for consideration of an IDE.
- H. In the event that the FDA rules that the investigational device is a significant risk device after the sponsor and the UCI IRB have determined the investigational device to be a non-significant risk device, the IRB will suspend the currently approved study detailing criteria for suspension.
1. The study may not reopen until an IDE is granted by the FDA and the study is reviewed by the full Committee with appropriate changes to the IRB application, protocol and/or informed consent documents.
 2. The Committee must direct the LR on the issue of re-consenting participants, if appropriate.
- I. The Committee will review the proposed research, informed consent documents, and additional information, when appropriate, and determine whether the study meets criteria 45 CFR 46.111 and 21 CFR 56.111 for approval.
1. In making its determination on approval, the IRB must consider whether the protocol is scientifically sound. The IRB should consider the risks and benefits of the medical device compared to the risks and benefits of alternative devices or procedures. The research is to be reviewed with all risks and benefits taken into consideration, not just that of the device. This should include:
 - a) Consideration of prior reviews by the FDA, other institutions, scientific review committees, funding agencies (e.g., NIH), or others; and
 - b) Study design, which includes the study population, the trial phase, and mechanisms for data analysis and surveillance.
 - c) Documentation is provided in the IRB approval letter.

- J. Research vs. Therapy. Throughout clinical trials, the distinction between therapy and research must be maintained. For example, a physician who participates in research by utilizing a new device to consenting patients must assure that the patients understand and remember that the device is experimental, and that its benefits for the condition under study are unproven. Furthermore, whereas the LR's primary allegiance is to the protocol, the physician's allegiance is to the patient. Where an individual is both an Investigator and the participant's treating physician, these two allegiances may conflict. The participant must recognize that the person with whom he or she is dealing may have such conflicting interests. The IRB should consider the need to inform the patient of the potential conflict.
 - K. The Committee will consider whether the investigator has developed an adequate plan to ensure that the investigational device is used only in approved research protocols and under the direction of qualified investigators and that the plan ensures proper handling of investigational test articles in accordance with applicable policies and procedures, State, and Federal regulations.
 - L. Continuing review of an investigational device.
 - 1. Non-significant risk investigational devices and minimal risk studies may receive expedited review at continuing review.
 - 2. Significant risk investigational devices, regardless of the risk associated with the study, must be reviewed by the full IRB Committee at continuing review.
 - M. Submission of modifications or unanticipated problems to participants or others, and continuing reviews will be reviewed at the level for which they qualify.
- III. **IRB Administrator Responsibilities**
- A. The Administrator will pre-review and request any necessary revisions for submitted documents for use of investigational devices as outlined for new application.
 - B. When research involves a device with an IDE, the IRB Committee, together with the IRB Administrator should evaluate whether the IDE number is valid.

Validation of an IDE can be done by:

 - a) Determining that the IDE number listed matches the Sponsor Protocol or
 - b) Upon receipt of communication from the Sponsor, which corresponds with the IDE number provided or
 - c) Upon receipt of communication from the FDA, which corresponds with the IDE number provided

Validation of an IDE should not involve:

 - d) Confirmation of the IDE number by referencing the Investigator's Brochure (IB). This is because one IB often serves multiple IDE's.
 - C. Once the LR has met all the pre-review requirements, the Administrator will place the new study on the next available Committee agenda (unless the study may be considered for expedited review – see above).

- D. The Administrator will assist reviewers in obtaining additional information that may be requested regarding the investigational device use from the LR.
- E. Minutes of IRB meetings must document the rationale for SR and subsequent approval or disapproval decisions for the clinical investigation.
- F. Letters requesting revisions from reviewers, and final approval letters are to be drafted using the appropriate template and provided to the Chairperson or his/her designee for their signature or their authorization for use of electronic signature.
- G. The HRP staff will process all requests for amendments, or unanticipated problems to participants or others, and continuing reviews per corresponding policies and procedures.
- H. Appropriate electronic IRB submission and management system entries are to be completed.

Policy Number: 43

Title: Use of a Placebo

Date of Last Revision: 08/10/2005, 08/05/2010, 05/01/2016, 05/18/2022

Policy:

Per UC Irvine (UCI) Institutional Review Board (IRB) policy, the use of placebo in clinical research must be carefully reviewed and, if approved, used in accordance with the federal regulations (i.e., FDA) and recommended guidelines.

I. Use of Placebo in Clinical Research

- A. For certain drug classes, such as analgesics, antidepressants or anti-anxiety drugs, failure to show superiority to placebo in a given study is common. This is also often seen with antihypertensives, anti-angina drugs, anti-heart failure treatments, antihistamines, and drugs for asthma prophylaxis. In these situations, active-control trials (i.e., recognized effective agent) showing no difference between the new drug and control are of little value as primary evidence of effectiveness and the active-control design (the study design most often proposed as an alternative to use of a placebo) is not credible.
- B. The IRB considers the following when determining whether the use of placebo is appropriate:
 - 1. Whether a standard treatment that has been shown to be effective and/or life prolonging.
 - 2. Whether a placebo-recipient would be substantially more likely to suffer harm.
 - 3. Whether it may be ethically acceptable to use a placebo under the following circumstances:
 - a) The toxicity of the standard treatment is such that individuals refuse treatment.
 - b) A treatment for a minor condition is being tested and the placebo-recipients would not be subject to any additional risk of serious or irreversible harm.
 - c) For compelling and scientifically sound methodological reasons its use is necessary to determine the efficacy or safety of a treatment.
- C. The IRB uses the decision algorithm developed by Amdur and Biddle, 2001 (*see below*) to evaluate the ethical use of a placebo control in clinical investigations.
- D. Continued assignment of participants to placebo is unethical once there is strong evidence to support the efficacy of the treatment. Clinical trials should be stopped or their protocols modified when there is sufficient evidence of either a beneficial therapeutic effect or unacceptable side effects.

II. Use of Treatment Withholding Phase

- A. The purpose of a treatment withholding phase is usually to terminate the effects of any drug the patient may have been taking before entering the clinical trial, so that the effects of the trial drug - and only the trial drug -

- may be observed;
- B. Use of Placebo Washout Phase
 - 1. The purpose of a placebo washout period include:
 - a) Terminating the effects of any drug the subject may have been taking before entering the clinical trial, so that the effects of the study drug - and only the study drug - may be observed;
 - b) Learning whether subjects cooperate with instructions to take drugs ("compliance"); and
 - c) Learning which subjects are "placebo responders," in that they experience a high degree of placebo effect.
- C. In some studies, the researcher may plan to exclude those subjects they find either poorly compliant or highly responsive to the placebo.

III. **Use of Placebo and Informed Consent**

- A. The informed consent document must include the following information:
 - 1. Statement that the study involves a placebo;
 - 2. Lay definition of placebo or placebo-washout, if applicable;
 - 3. Rationale for use of placebo;
 - 4. A description of how participants will be assigned to groups;
 - 5. List of any viable treatment alternatives, if applicable;
 - 6. Explanation of the duration of time that a participant will receive placebo;
 - 7. A statement regarding the degree of discomfort and potential effects of not receiving treatment;
 - 8. Explanation of consequences of delayed treatment must be included, if applicable;
 - 9. Explanation that a placebo-recipient's condition may worsen while on placebo;
 - 10. A statement that a placebo-recipients will not receive the same benefit as those who receive active treatment if that treatment is effective;
 - 11. A explanation of blinding (e.g., single-blind; double-blind), if applicable; and
 - 12. A brief description of the safety monitoring process.

IV. **Methods to Minimize Risks Associated with Use of Placebo**

- A. Exclude subjects with an increased risk of harm from non-response.
- B. Include increased monitoring for subject deterioration and the use of rescue medications.
- C. Build in "early escape" mechanisms and explicit withdrawal criteria so subjects will not undergo prolonged placebo treatment if they are not doing well.
- D. Keep the size of the population placed on placebo smaller than the number in active treatment arms.
- E. Compare placebo and active treatment in an "add-on" method, keeping the subjects on identical maintenance treatments and then adding on the active treatment to one arm and placebo to the other. This design is especially applicable when the available treatment is known to decrease mortality or morbidity.
- F. Shorten treatment periods to reduce the risks associated with delayed treatment.
 - 1. In situations in which long-term placebo treatment would not be acceptable, the use of a placebo group for a short period at the beginning of a trial could establish short-term effects. The trial would

then continue without the placebo group.

- G. Unblinded data review by a Data Safety Monitoring Board (DSMB) with interim analysis of study results and safety issues.

References:

21 CFR 56.111
21 CFR 314.126
45 CFR 46.11

Procedure Number: 43.A**Title: Procedure for the Use of a Placebo****Procedure:**

The purpose of this procedure is to provide guidance on the use of a placebo in research.

I. Lead Researcher (LR) Responsibilities

- A. The Lead Researcher will provide all information regarding the use of a placebo as required in the IRB Application. This will include:
 - 1. A description of how participants will be assigned to groups;
 - 2. Explanation of the duration of time that a participant will receive placebo.
 - 3. Whether a proven standard treatment/therapy exists to treat the disease/condition being studied.
 - 4. Whether the standard treatment/therapy is considered to be effective.
 - 5. Justification for the use of the placebo.
 - 6. Whether standard therapy is given to mitigate permanent harms (e.g., psychological harm, disfigurement or other serious adverse sequelae) or whether it is given to treat symptoms that constitute inconvenience or discomfort only.
 - 7. Whether the disease/condition being treated has the potential to progress to a higher risk condition if not actively treated.
 - 8. Whether the natural fluctuation of the disease/condition is significant enough to necessitate the use of placebo to determine if the observed changes are due to treatment or natural history.
 - 9. Whether subjects in the placebo group would be exposed to an increased risk of death, severe morbidity or disability, severe discomfort, or other long-term negative effects.
 - 10. Description of the safety monitoring process, including withdrawal criteria.
- B. The Lead Researcher will include the following information in the informed consent document:
 - 1. Statement that the study involves a placebo;
 - 2. Lay definition of placebo or placebo-washout, if applicable;
 - 3. Rationale for use of placebo;
 - 4. A description of how participants will be assigned to groups;
 - 5. List of any viable treatment alternatives, if applicable;
 - 6. Explanation of the duration of time that a participant will receive placebo;
 - 7. A statement regarding the degree of discomfort and potential effects of not receiving treatment;
 - 8. Explanation of consequences of delayed treatment must be included, if applicable;
 - 9. Explanation that a placebo-recipient's condition may worsen while on placebo;
 - 10. A statement that a placebo-recipient will not receive the same benefit as those who receive active treatment if that treatment is effective;
 - 11. A explanation of blinding (e.g., single-blind; double-blind), if applicable; and
 - 12. A brief description of the safety monitoring process.

- C. The Lead Researcher will notify the IRB of any amendments, unanticipated problems to participants or others that may occur while conducting the research or follow-up.
- D. The Lead Researcher will assure that unanticipated problems to participants or others are reported to the IRB as soon as possible, but no later than 5 working days after the LR first learns of the effect or problem (See HRP Policy # 19).

II. **IRB Committee Responsibilities**

- A. The Committee will review the proposed research, informed consent documents, and additional information, when appropriate, and determine whether the study meets criteria 45 CFR 46.111 and 21 CFR 56.111 for approval.
 - 1. IRB approval is documented through the IRB approval letter.
 - 2. In making its determination on approval, the IRB must consider whether the protocol is scientifically sound. The IRB should consider the risks and benefits of the use of a placebo compared to the risks and benefits of alternative options. The research is to be reviewed with all risks and benefits taken into consideration, not just the use of a placebo. This should include:
 - a) Consideration of prior reviews by the FDA, other institutions, scientific review committees, funding agencies (e.g., NIH), or others; and
 - b) Study design, which includes the study population, the trial phase, and mechanisms for data analysis and surveillance.
- B. Submission of modifications, unanticipated problems to participants or others, and continuing reviews will be reviewed at the level for which they qualify.

III. **IRB Administrator Responsibilities**

- A. The Administrator may pre-review and request any necessary revisions to the new IRB Application or Amendment.
- B. The Administrator will assist reviewers in obtaining additional information that may be requested regarding the use of placebo from the LR.
- C. The Administrator will document the Committee's rationale for use of placebo in the minutes.
- D. The Administrator will request changes on behalf of the IRB via the electronic IRB submission and management system.
- E. Final approval letters are to be drafted using the appropriate UCI IRB template.
- F. The HRP staff will process all requests for amendments, unanticipated problems to participants or others, and renewals per corresponding policies and procedures.

References:

21 CFR 56.111

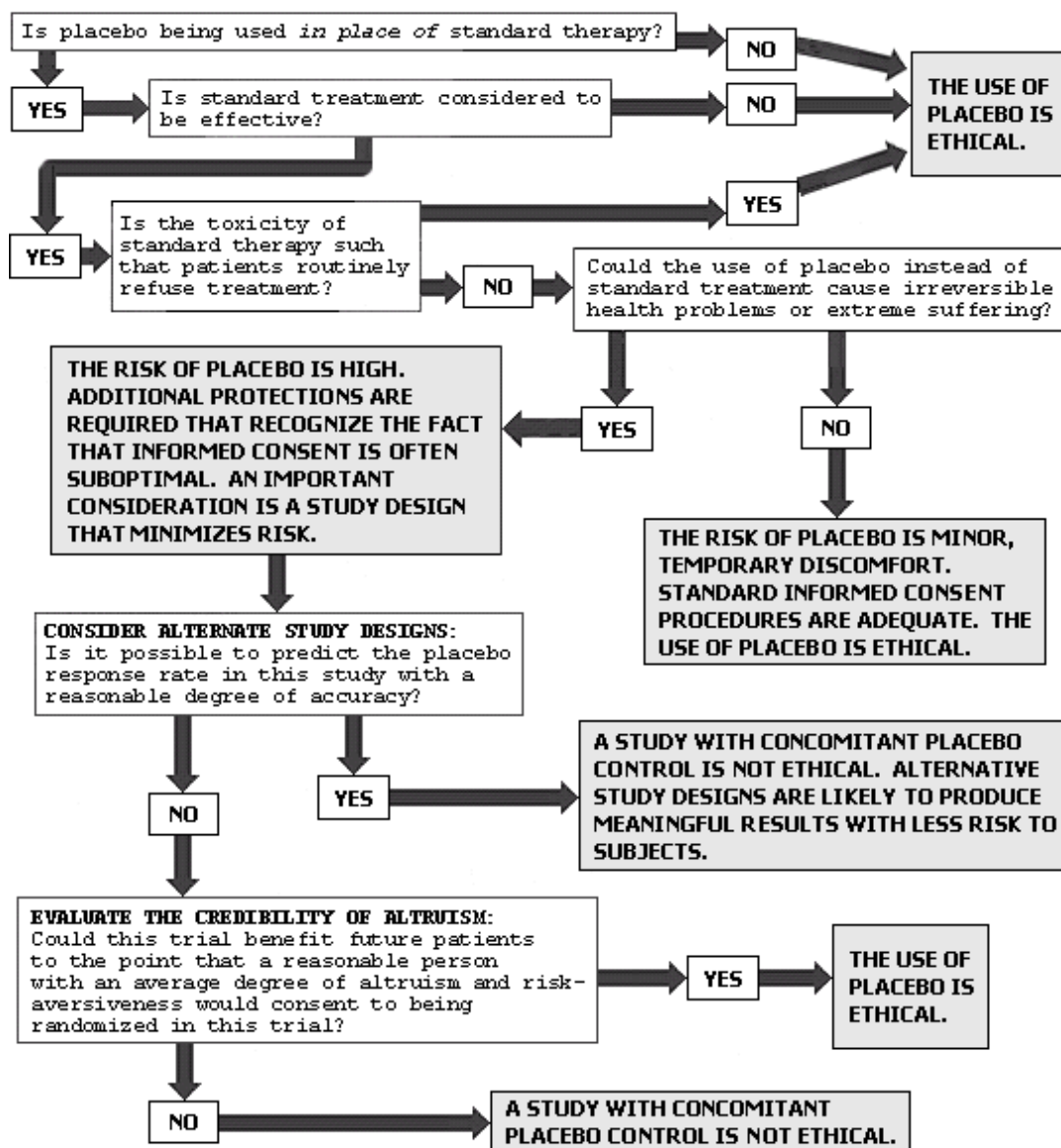
21 CFR 314.126

45 CFR 46.111

Amdur, R.J. and Biddle C., *An Algorithm for Evaluating the Ethics of Placebo-Controlled Clinical Trials*, Radiation Oncology Investigations, (2001), John Wiley and Sons, Inc.

FDA Guidance 1998 Update for Institutional Review Boards and Clinical Investigators

An Algorithm for IRB Evaluation of Studies That Involve Placebo



"An Algorithm for Evaluating the Ethics of Placebo-Controlled Clinical Trials,"
 by Robert J. Amdur, M.D., and Chuck Biddle, C.R.N.A., Ph.D.,
 Radiation Oncology Investigations, copyright © 2001, Wiley-Liss, Inc.,
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Policy Number: 44

Title: Data and Safety Monitoring

Date of Last Revision: 08/10/05; 08/04/10; 05/01/16; 09/28/20, 05/18/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board IRB that clinical investigations¹ involving greater than minimal risk to participants include a plan to assure the safety and welfare of its participants.

In addition, the IRB Chair retains the right to require a monitoring plan for a clinical investigation involving no more than minimal risk, should it be determined appropriate based on the type of risk involved in the study.

- I. **Data and Safety Monitoring** - A Data and Safety Monitoring Plan (DSMP) should be developed based on the size, complexity, and types of potential of risk involved in the research. A DSMP is required when the research meets the definition of a clinical investigation. The IRB has the authority to request a DSMP for other clinical research studies with appropriate justification.

II. **Data and Safety Monitoring Plan**

A detailed plan is required for all clinical investigations involving greater than minimal risk to participants. The level of detail should be based on the research procedures and types of potential risk to the research participants. As noted above, the IRB Chair retains the right to require a monitoring plan for a clinical investigation involving no more than minimal risk, should it be determined appropriate.

All DSMPs must contain at least the following information:

- A. A description of how risks are minimized;
- B. A description of how risks are reasonable in relation to anticipated benefits;
- C. Identification of a Data and Safety Monitor or Data and Safety Monitoring Board (DSMB), if applicable;
- D. A description of the plan to monitor progress and safety;
- E. Depending on the complexity of the research, the plan may include assessments of data quality, timeliness, participant recruitment, accrual and retention.
- F. A description of the plan to assure compliance with reporting of unanticipated problems involving risk to participants or others. This may include:
 - 1. A description of the process for detecting and reporting unanticipated problems involving risk to participants or others;
 - 2. A description of who will be monitoring and collecting unanticipated problems (e.g., LR, Research Coordinator, Research Nurse, etc.);
 - 3. Specification of who will be notified of an unanticipated problems (e.g., IRB, NIH, FDA, LR, etc.);
 - 4. A reporting plan indicating the timing of reports; and

¹ 21 CFR 50.3(c)

- 5. A plan for annual reporting of unanticipated problems if the study will go on longer than one year.
- G. As applicable, an investigator must submit to the sponsor a report of any unanticipated adverse device effect per HRP Policy # 42.

III. **Research Activities that Should Include a DSMB**

- A. The study is intended to provide definitive information about the effectiveness and/or safety of a medical intervention;
- B. Prior data suggests that the intervention under study has the potential to induce a potentially unacceptable toxicity;
- C. The study is evaluating mortality or another major endpoint, such that inferiority of one treatment arm has safety as well as effectiveness implications; or
- D. It would be ethically important for the study to stop early if the primary question addressed has been definitively answered, even if secondary questions or complete safety information were not yet fully addressed.

IV. **DSMB Composition**

- A. The DSMB should have multidisciplinary representation, including physicians from relevant medical specialties and biostatisticians. This may include other experts such as bioethicists, epidemiologists and basic scientists.
- B. The DSMB should have membership limited to individuals free of apparent conflicts of interest, whether they are financial, intellectual, professional, or regulatory in nature.
- C. The appropriate size depends on the type of study and types of expertise needed.

V. **DSMB Responsibilities**

- A. The primary responsibility of the DSMB is to safeguard the interests of study participants. Therefore, the DSM or DSMB will approve the safety measures in the protocol:
 - 1. To preserve the study integrity and credibility; and
 - 2. To facilitate the availability of timely as well as reliable findings to the broader clinical community.
- B. The DSMB will review the progress of the study carefully and diligently.
- C. Each enrolled subject's research chart should be reviewed frequently for side effects and tolerability of the investigational drug.
- D. The DSMB will assure that all unanticipated problems are reported to the IRB according to policies and procedures.

VI. **DSMB Tasks**

Tasks may include, but not be limited to, the following:

- A. Conduct initial review of the proposed research to assure quality study conduct;
- B. Review procedures to assure quality of study conduct including data management and quality control procedures;
- C. Evaluate the quality of ongoing study conduct by evaluating the study accrual, compliance with eligibility, participant adherence to study requirements, and accuracy and completeness of data;
- D. Consider factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on the safety of the participants or the ethics of the study;

- E. Recommend early termination based on efficacy results;
- F. Recommend termination due to unfavorable benefit-to-risk or inability to answer study questions;
- G. Recommend continuation of ongoing studies;
- H. Consideration of overall picture; primary and secondary analysis;
- I. Modify sample sizes based on ongoing assessment of event rates; and
- J. Review final results.

Procedure Number: 44.A**Title: Procedure for Data and Safety Monitoring Plans****Procedure:**

This procedure outlines the use of data and safety plans to assure extra protections and safety in research involving humans.

I. Lead Researcher (LR) Responsibilities

- A. It is the responsibility to address the data and safety plan as part of the initial IRB Application and to provide a copy of the sponsor's DSMP, if applicable.
- B. DSMB reports are to be submitted to the IRB (per HRP Policy # 19) when the report identifies an unanticipated problem involving risk to participants or others. An Amendment referencing the UP report should also be submitted along with the revised documents as applicable (e.g., consent document, recruitment material).
- C. DSMB reports that do not identify new risks or change the risk-benefit profile must be submitted to the IRB at the time of renewal.

II. IRB Committee Responsibilities

- A. The IRB Committee will review the initial IRB Application to assure the adequacy of the DSMP in relationship to the size, complexity, and level of risk of the proposed research.
- B. A DSMP is required when the research meets the definition of a clinical investigation.
- C. The IRB Committee will review the qualifications of the composition of the DSMB including the qualifications of the individual members. The IRB may make recommendations regarding expertise, frequency of meetings, etc., to the Investigator for the enhancement of human participant protections.
- D. The IRB Committee may request additional information or clarification regarding the DSMP or DSMB.
- E. The IRB has the authority to request a DSMP for other clinical research studies with appropriate justification.

III. IRB Administrator Responsibilities

- A. The Administrator may conduct a pre-review of the IRB application.
- B. The Administrator will correspond with the LR if the protocol submitted lacks adequate plans for assuring proper data collection and participant safety, per the findings of the IRB and/ or based on their pre-review.
- C. The Administrator will provide the LR guidance in meeting the IRB requirements for a DSMP, when possible.

21 CFR 56.111(a)(6)

21 CFR 50.3 (c)

45 CFR 46.111(a)(6)

Establishment and Operation of Clinical Trial Data Monitoring Committees Guidance for Clinical Trial Sponsors, March 2006

NIH DSMB Guidelines - Webpage

Policy Number: 45

Title: Emergency Use of a Test Article in a Life-Threatening Situation

Date of Last Revision: 06/06/08; 07/22/10; 03/29/16; 05/01/16; 06/29/17, 09/14/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to recognize the provisions found in the Food and Drug Administration (FDA) regulations for the emergency use of a test article in a life-threatening situation.

Emergency use means the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

- I. FDA regulations exempt research from prior IRB review for the use of a test article in a life-threatening situation in which no standard treatment is available. Physicians must report emergency use to the IRB within 5 working days of use. Any subsequent use of the test article at the institution is subject to IRB review as this would constitute research. Terms such as “interim,” “compassionate,” “temporary,” or other terms for an expedited approval process will not be utilized for requests for emergency use of a test article in a life-threatening¹ situation.
- II. **Criteria for Emergency Use of a Test Article:**
 - A. The patient is in an immediate serious or life-threatening condition that needs immediate treatment;
 - B. No generally acceptable alternative for treating the subject is available; and
 - C. Because of the immediate need to use the drug, agent, or biologic, there is no time to obtain full IRB approval for the use.
 - D. The physician is required to notify the IRB of all emergency uses within five days of the use and to notify the IRB in writing of all exceptions to the requirement for consent within five days of the exception.

Note: The emergency use of an unapproved drug or biologic requires an Emergency IND. The physician must contact the manufacturer of the agent or device to determine if the drug or biologic can be made available for emergency use under the manufacturer’s IND. If the manufacturer does not have an Emergency IND, the physician can contact the FDA directly.

¹ **Life-threatening** means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

- III. Although the emergency use of a test article is exempt from IRB review, it is not exempt from the FDA regulatory requirements to obtain and document consent from the participant or the participant's legally authorized representative. There are situations in which an exception can be made to the requirement to obtain consent. Whenever physicians use a test article on an emergency basis, they need to follow the regulatory requirements for an emergency use of a test article, and either obtain consent in accordance with FDA regulations at 21 CFR 50 or follow the requirements for an exception to the requirement for consent at 21 CFR §50.23(a)-(c).

The use of informed consent is required unless the physician imposing an emergency use situation and another physician not otherwise participating in the clinical investigation certify in writing that all of 21 CFR 50.23(a) have been met:

- A. The human subject is confronted by a life-threatening situation necessitating the use of the test article.
 - B. Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.
 - C. Time is not sufficient to obtain consent from the subject's legal representative.
 - D. There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.
- IV. FDA regulations require IRBs to be notified of all emergency uses within five days of the use and to be notified in writing of all exceptions to the requirement for consent within five days of the exception. The IRB will review these reports at a convened meeting to determine whether the circumstances follow regulatory requirements for the emergency use of a test article, consent was obtained in accordance with FDA regulations at 21 CFR §50, or the circumstances met the exception to the requirement for consent in 21 CFR §50.23(a)-(c).
- V. When following Department of Health and Human Services (DHHS) regulations and guidance, patients receiving a test article that meet the criteria for emergency use as defined by FDA regulations are not considered a research subject. DHHS regulations do not permit data obtained from patients to be classified as human subject research, nor may the outcome of such care be included in any report of research activity subject to DHHS regulations.
- VI. Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care for patients who need such care.
- VII. **Investigational Drugs, Agents, or Biologics (FDA Regulations)**
- A. The emergency use of investigational drugs, agents, or biologics will be handled in accordance with FDA regulations and institutional policies and procedures. Although 21 CFR 56.102(d) allows for an exemption from prior review and approval by the IRB for emergency use, the UCI IRB requests **prior notification** of emergency use of investigational drugs, agents, or biologics. The IRB Chair will review the notification to determine whether the circumstances met the regulatory or legal requirement for the emergency use of a test article.
 - B. FDA regulations at 21 CFR 56.104(c), allows for **one** emergency use of an investigational drug, agent, or biologic without prospective IRB review.

FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval as the subsequent use would constitute research. The only exception to this provision is if the IRB has not had sufficient time to convene a meeting to review the research protocol.

- VIII. Manufacturers or sponsors that agree to allow the use of the investigational drug, agent, biologic or device, but will not ship without “an IRB approval letter”, may be provided a written statement that the IRB is aware of the proposed use and based on the information provided by the physician the proposed use meets the requirements of 21 CFR 56.102(d).
- IX. **Investigational Devices (FDA Regulations)**
- A. The emergency use of investigational medical devices will be handled in accordance with FDA regulations and institutional policies and procedures. Although 21 CFR 56.102(d) allows for an exemption from prior review and approval by the IRB for emergency use, the UCI IRB requests **prior notification** of emergency use of investigational drugs, agents, or biologics. The IRB Chair will review the notification to determine whether the circumstances meet the regulatory or legal requirements for the emergency use of a test article.
 - B. Subsequent emergency use of an investigational medical device may not occur unless the physician or another person obtains approval of an IDE for the device and its use. If an IDE application for subsequent use has been filed with the FDA and the FDA disapproves the IDE application, the device may not be used even if the circumstances constitute an emergency use situation.

References:

FDA 21 CFR 50.23(a)-(c)
FDA 21 CFR 50.24
FDA 21 CFR 50.25(d)
FDA 21 CFR 56.102(d)
FDA 21 CFR 56.104(c)
FDA 21 CFR 812.35(a)
U.S. Food and Drug Administration Device Exemptions Regulation: Frequently Asked Questions about IRB Review of Medical Devices, January 2006.
U.S. Food and Drug Administration IRB Information Sheets: Emergency Use of Unapproved Medical Devices, 1998 Update
U.S. Food and Drug Administration IRB Information Sheets: Emergency Use of an Investigational Drug or Biologic, 1998 Update

Procedure Number 45.A**Title: Procedure for Emergency of a Test Article in a Life-Threatening Situation****Procedure:**

This procedure outlines the process for the emergency use of investigational drugs, agents, biologics, or devices.

I. Physician Responsibilities

- A. Requirements of the emergency use of investigational drugs, agents, or biologics
 - 1. Review the HRP webpage to see whether the investigational drug, agent or biologic has been previously used at UCI. If the test article has previously been used at UCI in a life-threatening situation for emergency use, the physician must obtain IRB approval.
 - 2. The emergency use of an investigational drug, agent, or biologic in a life-threatening situation requires an IND. Therefore, the physician must:
 - a) Contact the manufacturer of the drug, agent, or biologic first to determine if the test article can be made available for the emergency use under the manufacturer's IND; or
 - b) Contact the FDA for an Emergency IND. The FDA may authorize shipment of the test article in advance of the IND submission. Requests for such authorization must be made by the physician to the appropriate department at the FDA.
 - 3. The physician should submit the following information via the electronic IRB submission and management system via a New Application for Expanded Access Single Patient Emergency Use :
 - a) An authorization from the sponsor or manufacturer to allow the emergency use by the Physician of the test article;
 - b) An adequate description of the situation regarding the use of the test article;
 - c) An approved Emergency Use IND or a letter explaining exemption from the FDA;
 - d) The unsigned informed consent document or the certification for the exception from obtaining informed consent; and
 - e) Any other materials that may aid in the understanding the emergency use situation.
 - 4. The IRB Chair, IRB Vice-Chair or medical physician designee will review the electronic IRB submission to determine whether the circumstances met the regulatory requirement for the emergency use of a test article. The criteria are:
 - a) The subject is in an immediate serious or life-threatening condition that needs immediate treatment;
 - b) No generally acceptable alternative for treating the subject is available; and
 - c) Because of the immediate need to use the drug, agent, or biologic, there is no time to obtain full IRB approval for the use.
 - d) The physician is required to notify the IRB of all emergency uses within five days of the use and to notify the IRB in writing of all exceptions to the requirement for consent within five days of the exception.

5. The physician is required to obtain informed consent of the participant or the participant's legally authorized representative unless see #6 below. An Emergency Use informed consent template is available on the HRP website. The informed consent template is to be completed for the specific emergency use situation.
 6. The physician is required to obtain informed consent of the participant or the participant's legally authorized representative unless both the physician imposing the emergency use situation and a physician who is not otherwise participating in the clinical investigation certify in writing (may use an independent physician attestation form available on HRPP website) the following:
 - a) The participant is confronted by a life-threatening situation necessitating the use of the investigational drug, agent, or biologic;
 - b) Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject;
 - c) Time is not sufficient to obtain consent from the participant's legally authorized representative; and
 - d) No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the participant's life.
 7. If, in the Physician's opinion, immediate use of the test article is required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions listed above apply, the physician should make the determination and, within 5 working days after the use, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.
- B. After emergency use procedures for investigational drugs, agents, or biologics
1. The IRB must be notified of all emergency uses within five days of the use and to be notified in writing of all exceptions to the requirement for consent within five days of the exception. The physician is required to complete an amendment to the original application via the electronic IRB submission and management system which should include:
 - a) Name of the investigational drug, agent or biologic;
 - b) Conditions under which the investigational drug, agent or biologic was utilized;
 - c) Date utilized;
 - d) Any unanticipated problems to recipient or others;
 - e) Outcomes, if known; and
 - f) An evaluation of the likelihood of a similar need for the drug, agent, or biologic occurring again. If future use is likely, the physician must immediately initiate efforts to obtain IRB approval and an approved IND for the drug, agent, or biologic's subsequent use.
 2. A copy of the unsigned informed consent document or both the physician imposing the emergency use situation and a physician who is not otherwise participating in the clinical investigation signature certifying in writing that the emergency use situation met the exception to the requirement for consent.

3. Written verification of approval from the IND holder authorizing release of the test article in this emergency use situation. This may have been authorized verbally, but written confirmation should be provided or a letter from the FDA authorizing emergency use of the test article.
- C. Requirements for emergency use of investigational medical devices
1. For investigational devices under an IDE, the IDE regulation permits deviations from the investigational plan without prior approval when necessary to protect the life or physical well-being of a subject in an emergency. An physician may treat a patient with an unapproved medical device in an emergency situation if the following criteria must be met:
 - a) The subject is in a life-threatening condition that needs immediate treatment;
 - b) No generally acceptable alternative for treating the subject is available; and
 - c) Due to the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.
 2. The FDA expects the physician to determine the following:
 - a) Whether the criteria for emergency use have been met;
 - b) To assess the potential for benefits from the unapproved use of the device, and to have substantial reason to believe that benefits will exist; and
 - c) Assure that the decision of the Physician that an “emergency” exists is not based solely on the expectation that IDE approval procedures may require more time than is available.
 3. The physician must assure that the device developer notifies the FDA immediately after an unapproved device is shipped for an emergency use. An unapproved device may not be shipped in anticipation of an emergency.
 4. The physician is expected to follow as many subject protection procedures as possible. These include:
 - a) Concurrence of the IRB Chair, IRB Vice-Chair or medical physician designee;
 - b) Obtaining informed consent from the participant or the participant’s legally authorized representative; or an assessment from a physician who is not participating in the study
 - c) Obtaining a written independent assessment by an uninvolved physician;
 - d) Obtaining authorization from the IDE holder, if an approved IDE for the device exists.
 5. Although the FDA regulations allows for an exemption from prior review and approval by the IRB for emergency use, the UCI IRB requests prior notification of emergency use of investigational device. The physician should submit the following information:
 - a) a New Application for Expanded Access Single Patient Emergency Use via electronic IRB submission and management system
 - b) An authorization from the sponsor or manufacturer to allow the emergency use by the Physician of the test article;
 - c) An adequate description of the situation regarding the use of the test article;

- d) The unsigned informed consent document or the certification for the exception from obtaining informed consent; and
 - e) Any other materials that may aid in the understanding the emergency use situation.
- 6. The IRB Chair, IRB Vice-Chair or medical physician designee will review the Expanded Access Single Patient Emergency Use application to determine whether the circumstances met the regulatory requirement for the emergency use of a test article. The criteria are:
 - a) The subject is in an immediate serious or life-threatening condition that needs immediate treatment;
 - b) No generally acceptable alternative for treating the subject is available; and
 - c) Because of the immediate need to use the device, there is no time to obtain full IRB approval for the use.
 - d) The physician is required to notify the IRB of all emergency uses within five days of the use and to notify the IRB in writing of all exceptions to the requirement for consent within five days of the exception.
- 7. The physician required to obtain informed consent of the participant or the participant's legally authorized representative unless see #8 below. An Emergency Use informed consent template is available on the HRPP website. The informed consent template is to be completed for the specific emergency use situation.
- 8. The physician is required to obtain informed consent of the participant or the participant's legally authorized representative unless both the physician imposing the emergency use situation and a physician who is not otherwise participating in the clinical investigation certify in writing the following:
 - a) The participant is confronted by a life-threatening situation necessitating the use of the investigational (unapproved) medical device.
 - b) Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject;
 - c) Time is not sufficient to obtain consent from the participant's legal representative; and
 - d) No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the participant's life.
- 9. If, in the physician's opinion, immediate use of the test article is required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions listed above apply, the physician should make the determination and, within 5 working days after the use, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.
- D. After emergency use procedures for investigational medical devices
 - 1. The IRB must be notified of all emergency uses within five days of the use and to be notified in writing of all exceptions to the requirement for consent within five days of the exception. The physician is required to complete an amendment to the original application via the electronic IRB submission and management system which should include:

- a) Name of the investigational device;
 - b) Conditions under which the investigational device was utilized;
 - c) Date utilized;
 - d) Any adverse device effects, unanticipated problems to recipient or others;
 - e) Outcomes, if known; and
 - f) An evaluation of the likelihood of a similar need for the device occurring again. If future use is likely, the physician must immediately initiate efforts to obtain IRB approval and an approved IDE for the device's subsequent use.
2. A copy of the unsigned informed consent document or both the physician imposing the emergency use situation and a physician who is not otherwise participating in the clinical investigation signature certifying in writing that the emergency use situation met the exception to the requirement for consent.
 3. Written verification of approval from the IDE holder authorizing release of the test article. This may have been authorized verbally, but written confirmation should be provided.
 4. If an IDE does not exist, the Physician is to notify the FDA of the emergency use and provide the FDA with a written summary of conditions constituting the emergency, subject protection measures, and results.
- E. All submissions are to be made via the online IRB submission and management system.

II. **IRB Committee Responsibilities**

- A. The emergency use of FDA regulated products requires the involvement of an IRB Chair, IRB Vice-Chair or medical physician designee
- B. The IRB Chair, IRB Vice-Chair or medical physician designee will be promptly notified of the Physician's intent for emergency use of an investigational drug, agent, biologic, or device in a life-threatening situation.
- C. The IRB Chair, IRB Vice-Chair or medical physician designee will evaluate the Physician's submission of the Expanded Access Single Patient Emergency Use application and guide the physician in adherence to the FDA regulations and institutional policies and procedures. The IRB Chair, IRB Vice-Chair or medical physician designee will review:
 1. An authorization from the sponsor or manufacturer to allow the emergency use by the Physician of the test article;
 2. An approved IDE;
 3. An adequate description of the situation regarding the use of the test article with an independent physician's certification, if applicable;
 4. The unsigned informed consent document or the certification for the exception from obtaining informed consent; and
 5. Any other materials that may aid in the understanding the emergency use situation.
- D. The IRB Chair, IRB Vice-Chair or medical physician designee may make any of the following decisions:
 1. **Emergency Use Confirmed-CRITERIA MET:** The proposed use meets the emergency use criteria.
 2. **Emergency Use Not Confirmed- CRITERIA NOT MET:** The proposed use does not meet the emergency use criteria. The physician may choose to submit an IRB Application for approval to

conduct human subjects research. Refer to HRP Policy and Procedure # 41.

3. **Emergency Use Not Confirmed – CRITERIA NOT MET: PRIOR INSITUATIONAL USE:** If all the criteria are not met, but the use appears appropriate and there is time for the request to be added to the next IRB agenda and approved prospectively, the physician is referred back to the HRP staff for guidance in submitting the IRB application. In such circumstances, the emergency use would be allowable only if the patient's condition became more urgent while awaiting IRB action.
- E. The IRB will review the completed online Expanded Access Single Patient Emergency Use application and amendment as well as any supporting documentation including the IRB Emergency Use of as Test Article Checklist at a convened meeting to determine whether the circumstances follow regulatory requirements for the emergency use of a test article, consent was obtained in accordance with FDA regulations, or the circumstances met the exception to the requirement for consent. A checklist will be completed by the IRB Chair and a confirmation is sent to the physician for their records.

III. **IRB Administrator Responsibilities**

- A. It is the responsibility of the Administrator to facilitate any inquiries from physicians regarding the emergency use of the FDA regulated product.
- B. The Administrator will contact an IRB Chair, IRB Vice-Chair or medical physician designee to inform him/her of the Physician's notification of emergency use.
- C. The Administrator will promptly notify the Director of Human Research Protections or designee of a physician's notification of an emergency use of a test article in a life-threatening situation.
- D. The Administrator will assist the physician in providing the appropriate documentation prior to the emergency use, if possible, and follow-up with the physician if an adequate written documentation is not received within 5 days following the emergency use of a test article in a life-threatening situation.
- E. The Administrator will update the "Emergency Use" electronic folder and web page accordingly.
- F. The Administrator will add the emergency use of a test article in a life-threatening situation to the upcoming Biomedical IRB Committee Agenda.
- G. The Administrator will provide all IRB members the completed Expanded Access Single Patient Emergency Use application and amendment and any supporting documentation including the IRB Emergency Use of as Test Article Checklist.

Attachments:

FDA Contacts for Obtaining Emergency IND and Guidance on Emergency Use of a Device

Product	Contact
Drug Products	Drug Information Branch (HFD-240) (301) 827-4570
Biological Blood Products	Office of Blood Research and Review (HFM-300) (301) 827-3518
Biological Vaccine Products	Office of Vaccines Research and Review (HFM-400) (301) 827-3070
Biological Therapeutic Products	Office of Therapeutics Research and Review (HFM-500) (301) 594-2860
Nights and Weekends	Division of Emergency and Epidemiological Operations (HFC-160) (301) 443-1240
Devices	Center for Devices and Radiological Health (301) 594-1190

Policy Number: 46

Title: Humanitarian Use Devices

Date of Last Revision: 08/10/2005; 07/22/2010; 05/01/16; 11/21/19, 09/16/22, 08/21/24

Policy

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to review and approve the use of all Humanitarian Use Devices.

I. IRB Review of Humanitarian Use Device (HUD) Use

- A. A HUD is defined as a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year.
- B. In order for a HUD to be used in treatment, diagnosis, or research at UCI, the IRB must approve it. In addition, the FDA must issue a Humanitarian Device Exemption (HDE).
 - 1. The IRB approval must verify that the use of the HUD, as proposed, is in accord with current labeling of the device and does not exceed the scope of the FDA approved indication.
 - 2. The IRB may impose more stringent restrictions for use of the HUD as a means of additional protections, as deemed necessary.
- C. The initial review of a HUD is to be completed by the full IRB Committee. The full Committee may make the determination at initial review that subsequent continuing reviews may go through the expedited review process. Expedited review procedures are appropriate for continuing review since the initial review would have been performed by the full board. The use of the HUD within its approved labeling does not constitute research. Accordingly, an expedited review category does not need to be assigned.
- D. The physician utilizing the HUD for treatment, diagnosis or research must use the HUD only in accordance with the labeling of the device, intended purpose, and in the designated population for which the FDA approved its use.
 - 1. Only the holder of the HUD agreement with the FDA must use the HUD; and
 - 2. Informed consent is required from a patient prior to the use of a HUD when:
 - a) The HUD is the subject of a clinical investigation; or
 - b) The IRB requires use of informed consent.

II. Considerations for Prompt Reporting

- A. Whenever the physician or health care provider receives or otherwise becomes aware of information, from any source, that reasonably suggests that a HUD has or may have caused or contributed to the death or serious injury of a patient, the physician or health care provider must report such findings to the FDA, and the IRB as soon as possible, but no later than 5 working days after the Investigator first learns of the effect or

- problem. IRB reports may be made via the Reportable Event process in the electronic IRB submission and management system (See HRP Policy # 19) .
- B. The physician or health care provider shall promptly report any FDA action(s) regarding the HUD to the IRB.
 - C. Amendments to the HUD or the clinical use of the HUD are to be promptly reported to the UCI IRB in accordance with the IRB policy for modifications.
- III. A HUD may be used off-label in an emergency situation to save the life or protect the physical well-being of a patient. The FDA recommends that the physician and HDE holder follow the same emergency use procedures that govern the use of unapproved devices. Off-label use of a HUD in an emergency situation that cannot wait for IRB review and approval may be handled under the Emergency Use of an Unapproved Drug, Biologic or Device provision provided that the situation meets the FDA criteria under 21 CFR 56.104 (d) and the HUD is not used outside its approved labeling (See IRB Policy # 45).

References:

FDA 21 CFR 814, 803.30

U.S. Food and Drug Administration Device Regulations, June 26, 1996.

HDE Program Guidance for Industry and FDA Staff Information Sheet, September 6, 2019: <https://www.fda.gov/media/74307/download>

<https://www.congress.gov/bill/114th-congress/house-bill/34/text>

A list of approved HDE applications may be found at: <https://www.fda.gov/medical-devices/hde-approvals/listing-cdrh-humanitarian-device-exemptions>

Procedure Number: 46.A**Title: Procedure for Using Humanitarian Use Devices****Procedure:**

This procedure outlines the process for review and approval for use of a Humanitarian Use Device (HUD).

I. Physician Responsibilities

- A. The Investigator will provide all applicable information regarding the use of a HUD in the IRB Application.
- B. A HDE application is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose. The application, however, must contain sufficient information for the FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury, and that the probable benefit to health outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. Additionally, the applicant must demonstrate that no comparable devices are available to treat or diagnose the disease or condition, and that they could not otherwise bring the device to market.
- C. The FDA also recommends that the IRB or appropriate local committee (this is the IRB at UCI) review the following materials, as applicable, during initial review of a request to use a HUD:
 - 1. A copy of the HDE approval order;
 - 2. A description of the device;
 - 3. The product labeling;
 - 4. The patient information packet that may accompany the HUD;
 - 5. A sample consent form for the use of the HUD in clinical care, if required by the IRB or appropriate local committee or by facility policy; and
 - 6. A summary of how the physician proposes to use the device, including a description of any screening procedures, the HUD procedure, and any patient follow-up visits, tests or procedures.
 - 7. A list of approved HDE applications may be found at:
<https://www.fda.gov/medical-devices/hde-approvals/listing-cdrh-humanitarian-device-exemptions> .
- D. An informed consent document will be written, using the IRB consent template, and submitted, when applicable.
- E. The HUD brochure prepared by the manufacturer is to be provided and reviewed with the patient prior to use.
The Physician will fulfill renewal requirements at the designated IRB intervals and in accordance with FDA regulations.
- F. Amendments, serious adverse events or unanticipated problems to participants or others, and renewals are to be reported according to IRB policies and procedures. In addition, these occurrences are to be reported to the FDA and/or manufacturer as outlined in 21 CFR 803.30.
- G. When the use of a HUD is for diagnosis or treatment, and not associated with research or data collection, HIPAA regulations for research are not

applicable. However, HIPAA regulations for hospital medical records per Institutional policy are applicable.

II. IRB Committee Responsibilities

- A. The full IRB Committee will conduct all initial HUD reviews and approvals, including a review of the HDE documents.
- B. The assigned reviewers of the HUD will verify that the provided documents for use of the HUD are congruent with the manufacturing labeling and the approved use under the HDE. The labeling for a HUD must state that the device is a humanitarian use device and that, although the device is authorized by Federal Law, the effectiveness of the device for the specific indication has not been demonstrated.
- C. Based on the information above, the Committee will determine if the HUD request meets the FDA criteria.
- D. Submission of amendments, serious adverse events or unanticipated problems to participants or others, and continuing review will be reviewed at the level for which criteria is met.

III. IRB Administrator Responsibilities

- A. The Administrator or designee will pre-review and request any necessary revisions for submitted documents for the use of the HUD as outlined for new IRB Applications.
- B. The Administrator will verify that a copy of the FDA's Investigator Agreement and any supplemental information regarding the HUD supplied by the manufacturer have been submitted with the initial application as required.
- C. Once the required documentation and revisions are received from the Investigator, the Administrator will place the new study on the next available Committee agenda, assign reviewers, and prepare the reviewer and Committee member packets.
- D. The Administrator will assist reviewers in obtaining additional information that may be requested regarding the HUD from the Investigator.
- E. The Administrator will notify the Physician in writing of the IRB Committee's determinations.
- F. The HRP staff will process all requests for amendments, serious adverse events or unanticipated problems to participants or others, and renewals per corresponding IRB policies and procedures.
- G. Appropriate electronic IRB submission and management system entries are to be completed.

Policy Number: 47:

Title: Billing of Research Participants

Date of Last Revision: 05/01/2006, 08/05/2010, 05/03/2021, 09/16/2022

Policy

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to ensure that research participants or their insurers are not billed for research-related costs unless specifically approved by the FDA.

- I. The IRB has authority to evaluate, on a study-by-study basis as part of the initial review process, whether research-related costs may be billed to subjects who participate in studies where the experimental intervention is thought to be the most appropriate course of treatment for the subjects/patients and where no other funding (e.g., sponsor support) is available to cover such costs.
 - A. Participants or insurers should not be charged for research-related costs associated with participation in:
 1. Phase I studies, except trials in which the experimental intervention(s) is/are considered the most appropriate treatment option;
 2. Phase II, III or IV studies, except trials where the experimental intervention(s) is/are considered the most appropriate treatment option and/or routine and customary care;
 3. Placebo-controlled studies; or
 4. IND or IDE studies, unless charging of subjects is approved by the FDA (*see below for a summary of FDA regulations on IND and IDE standards for subject billing*).
- II. Participants or their insurance carrier (including MediCare/MediCal) should not be billed for an investigational/experimental procedure (i.e., not routine and customary) conducted as a part of a research study that is initiated and sponsored by a private, for-profit entity.
- III. **FDA Regulations on IND and IDE Standards for Subject Billing**
 - A. Charging for Investigational Medical Devices and Radiological Health Products – The IDE regulations allow sponsors to charge for an investigational device, however, the charge should not exceed the amount necessary to recover the costs of manufacture, research, development, and handling of the investigational device.
 1. The FDA generally allows sponsors to charge researchers for investigational devices, and this cost is usually passed on to the subjects.
 2. If charging for the product is permitted, researchers also may charge for related treatment or for services associated with the use of the product.
 - B. Charging for Investigational Drugs and Biologics – Under the IND regulations, the FDA permits a sponsor to charge researchers for an investigational drug or biologic under certain circumstances.
 1. The charge should not exceed an amount that is necessary to recover

- the costs associated with the manufacture, research, development, and handling of the investigational drug or biologic.
2. The FDA may withdraw authorization to charge if the Agency finds that the conditions underlying the authorization are no longer satisfied.
 3. The FDA does not prohibit charging for marketed products that are used in clinical investigations.
 4. If charging for the product is permitted, researchers also may charge for related treatment or for services associated with the use of the product.
- C. Clinical Trials Under an IND
Participants/Insurers should not be charged for an investigational drug or biologic in a clinical trial under an IND without the FDA's prior written approval. In requesting FDA approval, the sponsor must explain why a charge is necessary, i.e., why providing the product without charge should not be considered part of the normal cost of conducting a clinical trial [21 CFR 312.7(d)(1)].
- D. Treatment Protocol or Treatment IND
Participants/Insurers may be charged for an investigational drug or biologic for a treatment use under a treatment protocol or treatment IND, as outlined in 21 CFR 312.34 and 312.35, provided:
1. There is adequate enrollment in the ongoing clinical investigations under the authorized IND;
 2. Charging does not constitute commercial marketing of a new drug for which a marketing application has not been approved;
 3. The drug or biologic is not being commercially promoted or advertised; and
 4. The sponsor is actively pursuing marketing approval with due diligence.
 5. FDA must be notified in writing prior to commencing any such charges. Authorization for charging goes into effect automatically 30 days after receipt of the information by FDA, unless FDA notifies the sponsor to the contrary [21 CFR 312.7(d)(2)].

References:

21 CFR 312.7(d)

21 CFR 812.7(b)

FDA Information Sheets – Guidance for Institutional Review Boards and Clinical Investigators Charging for Investigational Products 1998 Update

Procedure Number: 47.A**Title: Procedure when Requesting Billing of Participants for Research-Related Costs****Procedure:**

This procedure outlines the process for review and approval for billing participants or their insurance for research-related costs.

I. Lead Researcher (LR) Responsibilities

- A. The Lead Researcher will provide all information regarding the billing of research participants or their insurance in the initial IRB Application (including attachments). This will include:
 - 1. Description and estimates all anticipated costs.
 - 2. Justification for billing participants and/or their insurer.
- B. The Lead Researcher will develop a consent form that describes and estimates all anticipated costs for which participants, or their insurers would be responsible.
- C. The Lead Researcher provides documentation that the FDA approved the charging of research participants.
- D. Evidence of cost analysis review must be available in the research record prior to the initiation of the research. The IRB may require cost analysis review prior to IRB review, on a case-by-case basis.

II. IRB Committee Responsibilities

In evaluating whether billing of subjects/insurers for research-related costs may be appropriate, the IRB uses the following guidelines:

- A. Participants or insurers should not be charged for research-related costs associated with participation in:
 - 1. Phase I studies, except trials in which the experimental intervention(s) is/are considered the most appropriate treatment option;
 - 2. Phase II, III or IV studies, except trials where the experimental intervention(s) is/are considered the most appropriate treatment option and/or routine and customary care;
 - 3. Placebo-controlled studies; or
 - 4. IND or IDE studies, unless charging of subjects is approved by the FDA (*see below for a summary of FDA regulations on IND and IDE standards for subject billing*).
- B. Under no circumstances should a participant or his/her insurance carrier (including MediCare/MediCal) be billed for an investigational/experimental procedure (i.e., not routine and customary) conducted as a part of a research study that is initiated and sponsored by a private, for-profit entity.
- C. The IRB may review, on a case-by-case basis, the appropriateness of billing participants/insurers for research-related costs generated by studies that are partially-supported by private sources but which are designed and initiated by University faculty.
 - 1. For purposes of this guidance, "initiated by" means that the design of the experiment originated with the faculty member and was not devised, suggested, proposed or instigated by an outside entity.
- D. For all studies not specifically precluded from billing subjects, the IRB will carefully consider whether requiring participant/insurer billing is

reasonable, ethical, appropriate, fair, and is fully justified in the IRB Protocol.

- E. The consent form must describe and estimate all anticipated costs for which participants/insurers would be responsible.
- F. A participant/insurer should not be billed for treatment of adverse effects, complications, illnesses or injuries suffered as a result of the subject's participation in a research study, unless all three of the following conditions apply:
 - 1. The study is not initiated and sponsored by a private, for-profit entity;
 - 2. The experimental treatment(s) under study is/are considered the most appropriate treatment option or routine/customary care; and
 - 3. Billing the subject/insurer for the experimental procedure(s) that likely caused the illness/injury was determined by the IRB to be permissible.

I. **IRB Administrator Responsibilities**

- A. The Administrator or designee will pre-review the IRB Application and applicable documents and request any necessary revisions.
- B. The Administrator will assist reviewers in obtaining additional information that may be requested regarding the proposed billing practices from the LR.
- C. The Administrator will document the Committee's rationale for the approved billing practices in the minutes.

Policy Number: 48

Title: Education and Training of Lead Researchers and Research Personnel

Date of Last Revision: 08/10/05, 05/26/10, 10/29/10, 01/21/10, 01/28/15, 01/01/17, 05/30/18, 08/21/18, 09/16/22

Policy:

It is the policy of the UC Irvine (UCI) to promote the highest ethical standards in the conduct of research. Lead Researchers and research personnel conducting human subjects research under the jurisdiction of the UCI IRB must complete education and training regarding the protection of human subjects in research. These requirements are designed to ensure that investigators have appropriate knowledge of human subject regulations and procedures, and that they understand the ethical considerations underlying human research protections.

- I. All UCI faculty, staff, and students who serve as lead researchers, co-researchers, or research personnel on a human research study, regardless of the funding source must complete UCI education requirements and provide certification of completion to the UCI IRB.
- II. Faculty sponsors who provide direct oversight of human subjects research must also meet UCI human research protection educational requirement.
- III. Educational Requirements:
 - A. Human Research Tutorials – For individuals engaged in human subject research Human Research Protections (HRP) offers two self-paced, web-based tutorials as follows:
 1. The Collaborative IRB Training Initiative (CITI) Basic [Human Research Protections](#) course (for Biomedical Investigators and for Social & Behavioral Investigators); and
 2. The CITI Research and HIPAA Privacy Protections course.Individuals choose the course that best matches their research activities. These tutorials review core concepts for the responsible conduct of research involving human subjects and guide users through the major principles for conducting research in a way that is consistent with federal and University requirements and with accepted scientific standards. Completion of the tutorials is required of individuals (i.e., Lead Researcher, Co-Investigators, Research Personnel and Faculty Sponsors) who wish to engage in human subject research at UCI before submission of IRB documentation. Additional optional modules are offered via CITI as well.

- B. The learning objectives of the [CITI Human Research Protections Training](#) course are:
1. To provide an understanding of the historical perspectives, ethical principles, associated with the conduct of research with human participants;
 2. To provide a general introduction to the federal regulations and define what constitutes research with human participants; and
 3. To provide a clear understanding of what constitutes informed consent and how it must be applied in research involving humans.
- C. [The Collaborative IRB Training Initiative \(CITI\) Human Research Protections Training](#) course – Refresher course – Lead researchers, co-researchers, faculty sponsors and research personnel are required to complete a CITI refresher course every five years to maintain their knowledge of ethical considerations and regulations regarding human research protections.
1. New researchers who have not completed the Human Research tutorial must complete the CITI basic training for either biomedical or social/behavioral research.
 2. Researchers who have completed the HR tutorial in the last five years must complete the applicable CITI refresher training before their five-year anniversary.
 3. Researchers who have completed a CITI basic training at another institution must access the CITI training program and add UCI as a “Participating Institution” in the CITI Course Registration section and complete applicable CITI refresher courses.
 4. Researchers will receive 90 day notification prior to their five year anniversary of completion of the HR tutorial or CITI training – basic or refresher.
- D. [The CITI Research and HIPAA Privacy Protections](#) course discusses the requirements of the Health Insurance Portability and Accountability Act (HIPAA) and how they supplement the U.S. Department of Health and Human Services (HHS) and U.S. FDA requirements. It also describes situations where full HIPAA privacy protections are required and those that can qualify for waivers, alterations or exemptions with more limited requirements. In addition, it reviews the responsibilities of researchers and institutions for meeting HIPAA privacy requirements and for appropriate data security protections that are necessary to protect privacy.
1. All Researcher and research personnel involved in studies that access, create or disclose Protected Health Information (PHI) must complete the tutorial.
 2. As of July 5, 2017 the CITI Research and HIPAA Privacy Protections course was incorporated as a requirement for all Biomedical Investigators and it was made available to Social & Behavioral Investigators as an optional course.

- E. Good Clinical Practice (GCP) Training for National Institutes of Health (NIH) Research: On September 16, 2016, the NIH issued a new policy that specifies NIH-funded investigators and staff should be trained in GCP. The NIH policy states that all NIH-funded investigators and staff “who are involved in the conduct, oversight, or management of clinical trials should be trained in Good Clinical Practice (GCP), consistent with principles of the International Conference on Harmonisation (ICH) E6 (R2).”
1. HRP offers several CITI courses that meet the NIH requirement.
 2. A refresher course should be completed every three years.
- IV. Lead researchers, co-researchers, faculty sponsors and research personnel who do not complete the requisite Human Research Protections requirements within the required timeframe may be restricted from engaging in research involving human subjects until the requirements are met.
- V. In addition to completing the UCI HRP education requirements noted above, for research involving the Department of Defense (DoD), all personnel who conduct, review, approve, oversee, support, or manage human participant research must *also* meet DoD requirements for research ethics training (see Policy 56). [DoD requirements](#) are also posted at the Human Research Protections Program (HRP) website.
- VI. The Human Research Protections (HRP) website has been created as a resource for all researchers. The website will assist the researchers in navigating the IRB process and adhering to the Federal regulations and IRB policies related to human research protections.
- VII. All investigators and research personnel conducting research involving humans at UCI are encouraged to review the core training materials including the UCI Federalwide Assurance, the UCI IRB policies and procedures, *The Belmont Report*, the Federal regulations including 45 CFR 46, 21 CFR 50 and 56, links to Federal agencies governing human subjects research, and links to other various agencies and resources (e.g., National Institutes of Health, Food and Drug Administration, Office of Human Research Protections, National Bioethics Committee, DoD, etc.) These links are available on the HRP website.
- VIII. The HRP sends e-mail notifications (i.e., Zotmail) to a mailing list of researchers and key study personnel subscribers, to alert them of pertinent IRB issues or decisions that may impact their research. Zotmail messages are then archived and can be accessed via the HRP website.
- IX. Office for Human Research Protections (OHRP) Video Presentations. The HRP website will maintain educational videos developed by the Division of Education and Development at OHRP. Videos provide information on a variety of topics related to the regulations for the protection of human subjects of research described at 45 CFR Part 46. These videos will be posted for the purpose of educating researchers. Each video is approximately 20-25 minutes in length.

- X. IRB Brochure: “Institutional Review Board – Fast Facts” This brochure targets investigators and research personnel to provide basic information about the IRB process including:
- (1) The role of the IRB;
 - (2) Definition of research, human subject, and clinical investigation;
 - (3) Requirements for conducting research involving humans at UCI;
 - (4) UCI IRB Review Process
 - (5) Types of IRB review; and
 - (6) Resources for additional information.
- XI. New researchers, research personnel, and graduate students may request an in-service or “Office Hours” with HRP Staff for the purpose of providing an overview of human research subject regulations and IRB requirements. On-site “Office Hours” are offered by HRP Staff in response to specific requests by the research community regarding human subject research queries. Appointments may be scheduled by emailing HRP Staff.

References:

UC Irvine Human Research Protections Program website:

<https://research.uci.edu/human-research-protections/>

Department of Defense Human Research Protections Program website:

<https://rt.cto.mil/ddre-rt/dd-rtl/hsd/hrp/>

[Policy on Good Clinical Practice Training for NIH Awardees Involved in NIH-funded Clinical Trials; NOT-OD-16-148](#)

Procedure Number: 48.A**Title: Procedure for Education and Training of Lead Researchers and Research Personnel****Procedure:**

This procedure defines the process of meeting the educational requirements for Lead Researchers and research personnel conducting research involving humans under the jurisdiction of the UC Irvine (UCI) Institutional Review Board (IRB).

II. Lead Researcher (LR) and Research Personnel Responsibilities

- A. Initial Training - All Lead Researchers, co-researchers, faculty sponsors and research personnel must complete the Human Research tutorial and HIPAA Research tutorial, if applicable.
 - 1. Effective September 10, 2018: The Lead Researcher will be responsible for confirming that applicable CITI educational tutorials have been completed for UCI undergraduate students serving as research personnel on minimal risk protocols conducted within the state of California. A research personnel log may be used for such purpose. A Human Research Protections (HRP) Research Personnel Log template has been created and is available on the Applications and Forms page: <https://research.uci.edu/wp-content/uploads/study-team-tracking-log.xlsx>. Tutorials may be verified using the [Tutorial Verification Search](#).
- B. The LR will utilize the HRP website to navigate through the IRB process and adhere to the Federal regulations and IRB policies related to human research protections. Additionally, the LR will access the HRP website to view various educational resources. The URL for the HRP website is <https://research.uci.edu/human-research-protections/>.
- C. All Lead researchers, co-researchers, faculty sponsors and research personnel will keep up to date on current events and review the HRP website for current IRB policies and procedures and the Federal regulations, especially those applicable to their area of research. The website includes the following:
 - 1. UCI's Federalwide Assurance;
 - 2. The IRB Review Process;
 - 3. The HRP Staff Contact List;
 - 4. IRB Forms including the Informed Consent Templates;
 - 5. IRB Policies and Procedures;
 - 6. IRB Roles and Responsibilities;
 - 7. Links to various Agencies and Resources on the IRB website:
 - a) National Institutes of Health;
 - b) Food and Drug Administration;
 - c) Office for Human Research Protections; and
 - d) National Bioethics Committee
 - e) Department of Defense (DoD) Requirements
- D. All Lead researchers, co-researchers, faculty sponsors and research personnel are encouraged to view the various educational tools offered on the HRP website and other opportunities offered by UCI throughout the year.

- E. The HRP Education and Quality Improvement Program (EQUIP) as directed by the IRB Committees may provide individualized education to research Investigators and/or their staff in response to deficiencies identified by the Committee. In addition, EQUIP may provide human research protections training at the department's or LR's request.
- F. Other resources are available to Investigators and key study personnel. Researchers and study personnel may access all of the following (including all current and prior versions of the following) via the HRP website.
 - 1. IRB Brochure: "Institutional Review Board – Fast Facts" This brochure targets investigators and research personnel to provide basic information about the IRB process.
 - 2. Zotmail: The HRP will send e-mail notifications (i.e., Zotmail) to a mailing list of researchers and key study personnel subscribers, to alert them of pertinent IRB issues or decisions that may impact their research. Zotmail messages are archived as a resource for the research community.
 - 3. OHRP Video Presentations: These educational videos provide information on a variety of topics related to the regulations for the protection of human subjects of research described at 45 CFR part 46.
 - 4. In-Service or Office Hours: New researchers, research personnel, and graduate students may request an in-service or "Office Hours" with HRP Staff for the purpose of providing an overview of human research subject regulations and IRB requirements. On-site "Office Hours" are offered by HRP Staff in response to specific requests by the research community regarding human subject research queries. These sessions may be scheduled by contacting HRP Staff via email or phone. Contact information for all HRP Staff is maintained on the HRP website.
- H. The Investigator will keep all IRB applications current with Investigator and key study personnel contact information to facilitate the receipt of all mass e-mail notifications alerting them of pertinent IRB issues or decisions that may impact their research.

III. HRP Responsibilities

- A. The HRP will conduct educational sessions throughout the year for all UCI faculty and staff.
 - 1. An example is the quarterly research administration meeting (GRAM).
- B. The HRP will maintain its website with links to Federal, State and institutional resources.
- C. The HRP Staff will maintain active links to the CITI educational tutorials via the website. In addition, current CITI status is provided for the LR and all study team members via the online IRB submission and management system.
- D. The HRP staff is available Monday through Friday 8:00 a.m. – 5:00 p.m. to answer questions and assist lead researchers, co-researchers, faculty sponsors and research personnel with any educational needs.

Policy Number: 49

Title: Education and Training of IRB Members

Date of Last Revision: 01/21/07, 10/29/10, 01/28/15, 09/16/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) that all IRB Committee members complete initial and periodically training in the review and conduct of human research protections.

- I. All new Committee members are required to complete an initial orientation before being assigned as a reviewer. Initial orientation includes:
 - A. An educational session with an IRB Administrator (or designee) detailing: the UCI IRB policies and procedures, The Belmont Report, Federal regulations 45 CFR 46, 21 CFR 50 and 56, and other applicable regulations and guidance (e.g., Department of Defense (DoD)).
 - B. IRB members receive the following materials prior to attending their first IRB meeting:
 1. Original signed copy of the IRB member appointment letter;
 2. IRB Member Standards letter for signature
 3. Conflict of Interest (COI) Disclosure Form (Biomedical IRB Members only)
 4. IRB Member Questionnaire;
 5. Schedule of Committee meetings and IRB submission deadlines;
 6. Roster for respective IRB Committee;
 7. IRB Member Resource e-mail, containing the following materials or links to the following:
 - a) The Nuremberg Code;
 - b) World Medical Association Declaration of Helsinki;
 - c) The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects;
 - d) Exempt and Expedited Categories;
 - e) 45 CFR part 46;
 - f) 21 CFR 312 and 812; 21 CFR parts 11, 50, 54 and 56
 - g) California State Statutes applicable to Human Subjects Protections;
 - h) UCI Human Research Protections Policies and Procedures;
 - i) FDA Information Sheet Guidance;
 - j) FDA Bioresearch Monitoring Compliance Program;
 - k) OHRP Guidance on Unanticipated Problems and Adverse Events;
 - l) DHHS Guidance on HIPAA Privacy in Research;
 - m) IRB Reviewer Checklists
 - C. Collaborative IRB Training Initiative (CITI) Basic Human Research Protections Course for IRB Members: All IRB members are required to complete this tutorial within 3 months of their appointment.
 1. UCI offers two versions of the Basic Human Research Training course: one for Biomedical IRB members and one for Social, Behavioral, Educational IRB members.
 2. A refresher course is required every five years for members to maintain their knowledge of ethical considerations and regulations

- regarding human research protections.
3. For IRB members, the tutorial includes:
 - a) The historical event and ethical principles, associated with the conduct of research with human participants;
 - b) The definition of research with human participants and the federal regulations;
 - c) The informed consent process;
 - d) Vulnerable populations;
 - e) Food and Drug Administration (FDA) considerations;
 - f) Department of Defense (DOD) applicability;
 - g) IRB regulations and the IRB review process;
 - h) Additional training on the role of an IRB member is provided.
 - D. Health Insurance Portability and Accountability Act (HIPAA) Research Tutorial: The internet-based tutorial developed by the UC is designed specifically for researchers involved with Protected (Personal) Health Information (PHI). All IRB members are required to complete the HIPAA Research tutorial within 3 months of their appointment. The learning objectives of the HIPAA Research Tutorial are:
 1. To provide a general introduction to the HIPAA regulations and define what constitutes Protected Health Information; and
 2. To provide a clear understanding of how HIPAA applies to research involving humans.
 - E. Committee Meeting Attendance and Observations: In addition to completing the initial orientation, new IRB Committee members must attend and observe at least one IRB Committee meeting before being assigned as a reviewer.
- II. All IRB members are provided with the training and materials necessary to determine whether a human research study is in compliance with Federal regulations, applicable State laws, UC/ UCI policies, DoD requirements and standards of professional/ethical conduct and practice.
- A. The following opportunities for training are provided to all IRB members:
 1. *Provision of Materials and Presentations during IRB Service:* The HRP staff regularly provides IRB members with relevant educational materials, articles and updates to Federal regulations, State laws and UC/UCI policies. In-service educational presentations by the HRP staff are also regularly provided during IRB meetings on an as needed basis.
 2. *IRB Membership Training:* IRB training is offered on an individual basis or on an as needed basis by the HRP staff. The goal is to keep members up-to-date on Federal regulations, State laws and UC/UCI policies. The IRB members are also given an opportunity to ask questions and to receive assistance by the HRP staff. Group Training is also periodically provided to IRB members by the HRP staff.
 3. *Conferences/External Meetings:* The IRB Chair and/or at least one Committee member for each Committee are encouraged to attend a national or regional human research protections conference.
 4. *ORA Human Research Protections Website:* The HRP website provides public access to IRB guidelines (e.g., difference between exempt, expedited and full committee research, requirements of informed consent, special considerations for vulnerable subject populations, etc.), principles of human subject protection (e.g., the Belmont Report, Nuremberg Code and Declaration of Helsinki),

Federal regulations, State statutes, DoD requirements related to human subject research, UC/UCI policies and UCI procedures. The website also contains a customized web page especially for IRB members, which includes links to frequently used information, links to Office for Human Research Protections (OHRP) videos and other relevant postings that assist IRB members in their role.

References:

UC Irvine Human Research Protections Program website:

<https://research.uci.edu/human-research-protections/>

Department of Defense Human Research Protections Program website:

<https://rt.cto.mil/ddre-rt/dd-rtl/hsd/hrp/>

Procedure Number: 49.A**Title: Procedure for Education and Training of IRB Members****Procedure:**

This procedure outlines the process for completing the human research protections educational requirements for the UC Irvine (UCI) Institutional Review Board (IRB) Committee Member.

I. IRB Committee Member Responsibilities

- A. All IRB Committee members must complete the CITI Basic Human Research Protections Course for IRB Members, including the HIPAA Tutorial, prior to being assigned as a reviewer. All tutorials must be completed within 3 months of appointment.
- B. New IRB Committee members must attend and observe at least one IRB committee meeting prior to before being assigned as a reviewer.
- C. IRB members should review the training and educational materials provided by the HRP staff. These materials aid members in determining whether a human research study is in compliance with Federal regulations, applicable State laws, UC/ UCI policies, DoD requirements and standards of professional/ethical conduct and practice.
- D. IRB members should review the educational resources presented at the IRB Committee meetings.

II. IRB Management and Administator Responsibilities

- A. The IRB Education and Quality Improvement Team (EQUIP), along with IRB Management, and the IRB Administrator are responsible for:
 - 1. Developing, scheduling and conducting the new Committee member's orientation session;
 - 2. Planning and executing monthly education at the IRB Committee meetings; and
 - 3. Planning and executing any additional and periodic training for IRB Committee members.

III. IRB Administrator Responsibilities

- A. The Administrator will assure the Committee member has completed all initial and continuing education requirements as outlined in IRB Policy # 49.

Policy Number: 50

Title: UCI HRP Quality Improvement Program

Date of Last Revision: 08/10/2005, 01/29/09, 12/08/10, 08/08/11, 05/01/16, 03/07/17, 09/20/18, 06/17/20, 09/16/22

Policy:

University of California, Irvine (UCI) Institutional Review Board (IRB) is responsible for ensuring that all human subjects research conducted by faculty, staff, and students at UCI approved sites or using UCI's name is conducted in compliance with federal regulations, state and local law as well as UCI HRP policies, procedures, and UCI's Federalwide Assurance with the Office for Human Research Protections (OHRP), in order to preserve the rights and safety of research subjects, the quality of scholarly work and the integrity of the institution.

- I. To promote accountability and excellence, UCI HRP has developed the Education and Quality Improvement Program (EQUIP). EQUIP monitors and measures the effectiveness, efficiency and quality of UCI's human research protection program.
- II. The primary purpose of the EQUIP is to provide education, training and post-approval monitoring, to assure that all human research protection operations support UCI's mandate to protect the rights and welfare of research participants. This includes compliance with institutional policies and procedures, and applicable federal, state and local laws pertaining to the protection of human subjects in research.
- III. **Components of the Education and Quality Improvement Program (EQUIP)**
 - A. Education (see HRP Policies # 48 and # 49)
 - B. Post-Approval Monitoring – Periodic Quality Improvement Reviews and directed (for cause) investigations of human subjects research.
 - C. Indirect monitoring of research activities through monitoring unanticipated problems involving risk to research participants or others
 - D. Verification from Other Sources
 - E. Ongoing HRP Internal QI Activities
 1. Minutes QI Review
 2. Informed Consent QI Review
 3. Review of IRB Protocols
 4. HRP Benchmarks and Metrics
 5. IRB/HRP Survey
 - F. Participant Outreach and management of participant complaint and concerns
 - G. IRB Member Self-Evaluation
 - H. HRP Staff Performance Evaluation
- IV. **Education**

UCI requires that investigator receive human research training prior to engaging in human subjects research to ensure that investigators have appropriate knowledge of human subject regulations and procedures, and that they

understand the ethical considerations underlying human research protections (See HRP Policies # 48 and # 49 for detailed information regarding education of researchers and IRB members).

V. **Post-Approval Monitoring**

- A. Periodic Quality Improvement Reviews - Periodic compliance audits are conducted using systematic methods to assess investigator and IRB compliance with federal regulations, state and local laws, and UCI HRP policies and procedures. Periodic compliance audits include but are not limited to:
 - 1. Examinations of executed informed consent forms and HIPAA authorizations;
 - 2. Reviews of IRB meeting minutes;
 - 3. Detailed examinations of the protocol in the electronic IRB submission and management system or protocol files as applicable;
 - 4. In-person observations of the informed consent process.
- B. Directed (for cause) reviews/investigations - The IRB or the Director of Human Research Protections may direct the EQUIP Team or other designees to conduct an assessment in response to a particular concern. Concerns that may prompt a for-cause assessment include but are not limited to:
 - 1. Failure of routine audits;
 - 2. Complaints or concerns initiated by a research participant, family member, or research team/workforce member;
 - 3. Reports of serious or continuing non-compliance;
 - 4. Results of audits or monitoring conducted by other UCI components (e.g., ORO, Internal Audit) reported to the EQUIP Team or other HRP staff.
- C. EQUIP or a designee may initiate the periodic compliance reviews and/or conduct the direct audits. Designees include:
 - 1. UCI School of Medicine ORO conducts directed and random periodic compliance reviews of IRB-approved studies when the Lead Researcher is School of Medicine personnel (i.e., faculty, staff, or student) and/or the research is conducted at UCI Medical Center (UCIMC).
 - 2. Internal Audit Services (IAS) is charged with the task of assisting University management and the Board of Regents in the discharge of their oversight, management, and operating responsibilities.
 - 3. The Chao Cancer Center Quality Assurance (QA) Unit conducts post-approval monitoring and faculty and staff education to ensure the Cancer Center maintains compliance with Federal and University regulations for research.
- D. External Sites - Directed audits and periodic compliance reviews may also be conducted by the IRB Education and Quality Improvement Team at non-UCI sites where the UCI IRB serves as their IRB of Record.
- E. External Consultant - The UCI IRB may engage an external consultant with a specific area of expertise to perform or assist with any of the above-defined auditing and reviewing activities.
- F. Reporting of Monitoring Results
 - 1. The results of any monitoring activity or audit activity by the HRP EQUIP team and/or a designee are reported in writing to the

- Director of Human Research Protections or designee.
 2. The Director of Human Research Protections or designee follows the campus policy for resolving allegations of non-compliance in cooperation with the IRB Chair(s) responsible for the review of the research when allegations of or incident(s) of non-compliance are reported.
 3. If the monitoring or auditing activity finds that a human subject participating in a research project has been exposed to unexpected serious harm, the HRP EQUIP team or designee will promptly report such findings to the Director of Human Research Protections or designee.
 4. The Lead Researcher will be required to submit an “Unanticipated Problems” (UP) report and the IRB Chairperson will determine the need for full IRB Committee review.
- G. Suspend or Terminate Research: If the information gained during the monitoring, auditing, or review process indicates that human subjects of a research project were exposed to unexpected serious risk or harm, or that the policies of the IRB were not met, the IRB may suspend or terminate the research (See HRP Policies # 51 and # 52)
- VI. **Indirect monitoring of unanticipated problems involving risk to research participants or others (UPs):** The EQUIP team monitors when potential UPs are reported to the IRB. The HRP staff works closely with the IRB Chair and IRB to manage potential UPs. When an UP may involve noncompliance (See HRP Policy # 52), the EQUIP team works closely with the IRB Chair and IRB to manage the potential UP.
- VII. **Internal HRP QI Activities**
The following activities are performed *quarterly* to ensure compliance with federal regulations and UCI HRP policies:
- A. Minutes QI Review – EQUIP conducts a review of 3 random sets of IRB approved minutes.
 - B. Informed Consent QI Review – Up to 20 IRB approved informed consent documents are reviewed.
 - C. Review of IRB Protocols –Up to 6 random, active studies are reviewed.
 1. EQUIP reviews the last three years of an IRB approved protocol only.
- VIII. **The following activities are performed *monthly or as needed* to ensure compliance with federal regulations and UCI HRP policies:**
- A. HRP Benchmark Targets and Metrics Reports– the HRP has established benchmarks to measure efficiency in all phases of IRB review process. benchmark targets.
 - B. IRB Suggestion In Box (Email)- the HRP Director monitors comments, questions and issues received from the UCI investigators to identify areas for potential improvement in the effectiveness of HRP policies and procedures and for ensuring the protection of human research participants. The HRP Director or designee, will work with the EQUIP team or HRP Staff as necessary to identify and address any programmatic areas of improvement.
- IX. **Verification from Other Sources**
- A. The IRB can require verification that no unapproved changes in an IRB-approved study have occurred since the previous IRB review. The scope

and extent of such an independent assessment is determined on a case-by-case basis.

- B. Sources for such outside information could include:
 - 1. Compliance review from the HRP EQUIP team or designee;
 - 2. Corroboration from School Deans, Department Chairs, Sponsors, other Clinical Research Organizations and other IRBs at collaborating institutions;
 - 3. Copies of FDA audits;
 - 4. Literature searches conducted by clinical librarians;
 - 5. Reports from subjects or study staff; or
 - 6. Directed audit at the request of the IRB Committee or the Director of Human Research Protections or designee.
- C. Examples of when verification from other sources may be requested include, but are not limited to:
 - 1. When the study is complex in design and the project involves unusual types of risk to subjects (e.g., multiple groups, rapid titration schedule to obtain maximum tolerated dose, novel and unique medical device investigations);
 - 2. When the study is conducted by researchers who previously have failed to comply with the requirements of the DHHS regulations or the requirements or determinations of the IRB; or
 - 3. When concerns are raised, based upon information provided in continuing review reports or from other sources, about possible material changes occurring without IRB approval.

X. **Participant Outreach and Management of Complaints and Concerns Regarding Human Subjects Research or the HRP**

- A. To enhance the public's understanding of research, UCI HRP has developed the "For Participants in Human Subject Research" web page which includes frequently asked questions about research participation, quick links to external web-based resources, and the HRP staff contact information. The HRP staff and the IRB Working Group periodically reviews the web page to determine whether additional information can be provided and to verify that the information provided is accurate and up-to-date and the hyperlinks are active.
- B. The HRP staff is responsible for the processing, review and inquiry into all complaints and concerns that are brought to the attention of the IRB/HRP regarding human subjects research conducted at UCI and/or by UCI personnel. Complainants may include, but are not limited to subjects (past, present or potential), subject family members, investigators, other research staff, or any person with concerns (See HRP Policy # 54). When a subject complain may involve noncompliance (See HRP Policy # 52), the EQUIP team works closely with the IRB Chair and IRB to manage the complaint.

XI. **Assessment of IRB Members, IRB Chairs and HRP Staff**

- A. IRB Members are assessed on an annual basis based upon meeting participation, preparedness, quality of review, and knowledge of UCI HRP policies and federal regulations. IRB Members complete the "IRB Member Evaluation" form each July. IRB members receive written or verbal feedback from the IRB Chairs. Individual educational needs are identified and forwarded to the EQUIP or to the Administrator of the Committee.
- B. IRB Chairs receive written or verbal feedback from the Institutional Official

- or designee.
- C. HRP Staff receive annual evaluations, constructive feedback, and individual educational needs are identified with their supervisor.

References:

21 CFR 50

21 CFR 56

45 CFR 46

DOE 0 443. 1A

CA Protection of Human Subjects in Experimentation Act 24173

HRP Policies, 44, 48, 49, 51, 52, 54

Procedure Number: 50.A**Title: Procedure for IRB Compliance Activities****Procedure:**

The purpose of this procedure is to outline the processes for conducting compliance reviews and audits by the UCI IRB Education and Quality Improvement Team.

I. Lead Researcher (LR) Responsibilities

- A. The Lead Researcher will comply with UCI HRP policies and procedures including:
 - 1. Education requirements
 - 2. Reporting Unanticipated Problems Involving Risk to Participants or Others
 - 3. Managing and reporting participant complaints including resolution of the complaint, if applicable.
- B. Periodic Quality Improvement Reviews
 - 1. Lead Researchers will cooperate with the IRB by being available for questions, having documents accessible, and responding to any written requests within the time frame designated by the IRB in association with a compliance review. The preliminary findings will be communicated to the LR to facilitate understanding of the process and collaboration in resolving any outstanding issues/concerns. The LR or designee will be present for a brief exit interview that will occur following each compliance review conducted by the HRP EQUIP team or designee.
 - 2. Lead Researchers will address the recommendations suggested by the UCI HRP EQUIP team or designee and submit responses within a timely manner.
- C. Directed (for cause) Reviews/Investigations
 - 1. LRs will cooperate with the IRB by making him/herself available for questions, having documents accessible, and responding to any written requests within the time frame designated by the IRB in association with a directed audit. Written preliminary audit results will be provided to the LR to facilitate understanding of the process and collaboration in resolving any outstanding issues/concerns. The LR or designee will be present for a brief exit interview that will occur following each directed audit.
 - 2. LRs will abide by all IRB Chairperson or his/her designee and/or full IRB Committee determinations. These determinations may include developing and following a corrective action plan and/or an educational plan and completing it in the time specified by the Committee.
 - 3. The LR may be requested to attend a full IRB Committee meeting to present information addressing any concerns resulting from a directed audit, as well as any determination rendered by the full IRB Committee.

II. IRB Committee Responsibilities

- A. IRB members should comply with UCI HRP policies and procedures including:
 - 1. Education requirements
 - 2. Annual IRB Member Evaluations

- B. Periodic Quality Improvement Reviews
 - 1. The IRB Committee Chair will review a copy of the Compliance Review Report of Findings and may:
 - a) Accept and sign the compliance review report with or without revisions to the currently approved study;
 - b) Impose additional measures for participant safety;
 - c) Mandate education by the HRP EQUIP; and/or
 - d) Refer to full Committee for review and discussion.
- C. Directed (for cause) Reviews/Investigations
 - 1. Directed audits may be requested to assess compliance with local, State, and Federal laws, participant safety, and HRP policies and procedures.
 - 2. Determining the need for such additional supervision or participation by the IRB is made by the IRB on a case-by-case basis during the initial and continuing review, or as new information is presented. Factors to be considered by the IRB in determining whether to undertake such additional supervision or participation may include, but are not limited to:
 - a) Involvement of vulnerable populations;
 - b) Research conducted internationally;
 - c) The involvement of recombinant DNA or other types of gene transfer protocols;
 - d) The use of waiver or alteration of informed consent procedures, (e.g., surrogate consent);
 - e) Research for which subjects would be exposed to additional risks, e.g., breach of confidentiality, Phase 1 studies, disproportionate number or severity of SAEs;
 - f) Previous suspension of the research due to compliance issues, poor record-keeping or other concerns;
 - g) Recommendations from ancillary institutional committees and partners.
 - 3. Upon receipt and review of the directed audit report, the IRB Committee may:
 - a) Accept the audit report with or without revisions to the currently approved study;
 - b) Impose additional measures for participant safety, these may include, but are not limited to:
 - (1) Request status reports after each participant receives intervention;
 - (2) Decrease the continuing review cycle (e.g., 3 months, 6 months, after a specific number of participants are enrolled);
 - (3) Require an independent safety monitor or formation of a DSMB to monitor activities locally, or nationally if UCI is a coordinating center;
 - (4) Request an off-cycle Data Safety and Monitoring Board (DSMB) review and written report;
 - (5) Conduct a follow-up audit by the EQUIP Team;
 - (6) Require oversight/signatures by superior on all research;
 - (7) Replace the LR by a qualified LR who is not subordinate to the LR being replaced;
 - (8) Limit LR's ability to submit new research studies to the IRB; and/or

- (9) Require a subject advocate to participate in or monitor the informed consent process;
- c) Create an education plan recommended by the IRB EQUIP Team, these may include, but are not limited to:
 - (1) One-on-one instruction with the IRB EQUIP Team or an IRB Administrator familiar with study;
 - (2) Attendance of LR and/or research team at IRB Education Sessions;
 - (3) Attendance of LR and/or research team at local, regional or national conferences on human subjects protections;
 - (4) Review of additional regulatory documents or materials (e.g. Belmont Report, 45 CFR 46, HRP policies and procedures, OHRP determination letters);
 - (5) Additional web-based human subjects protection training (e.g. OHRP, NIH, NCI); and/or
 - (6) Completion of pertinent Collaborative Institutional Training Initiative (CITI) human research protections modules.
- d) Accept the audit report and:
 - (1) Request that the LR place the study on voluntary “Administrative Hold”, pending further investigation;
 - (2) Place a “Suspension” on the study, if applicable (See HRP Policies # 51 and # 52).
- 4. The Committee will outline any recommendations in a letter to the LR.
- 5. At the direction of the Director of Human Research Protections or designee, the IRB Chair(s) or the IRB Committee, the IRB may engage an expert consultant to perform or assist with any of the auditing and reviewing activities.

III. **IRB Education and Quality Improvement Team Responsibilities**

- A. The EQUIP teams works with HRP staff and the IRB to monitor unanticipated problems involving risk to research participants or others.
- B. Periodic Quality Improvement (QI) Reviews
 - 1. Periodic QI reviews conducted by the HRP EQUIP team or designee may include, but are not limited to the following:
 - a) Repositories or DNA/Genotyping;
 - b) Research meeting exempt criteria;
 - c) Research meeting expedited criteria;
 - d) Research meeting full IRB Committee reviews;
 - e) Auditing advertisements and other recruiting material as deemed appropriate by the IRB;
 - f) Contact research subjects;
 - g) Observation of the consent process and/or documentation;
 - h) Observation of research interactions or interventions with research participants;
 - i) Non-human research or non-research;
 - j) Self-exempt research;
 - k) Monitoring of the storage and use of investigational devices;
 - l) Review projects to verify from sources other than the LR that no unapproved changes have occurred since previous IRB review; and/or
 - m) Other monitoring activities as deemed appropriate by the IRB.
 - 2. At least half of the periodic QI reviews conducted annually will be conducted on social/behavioral research studies and at least one

periodic compliance reviews will be involve non-UCI sites. Periodic QI reviews conducted on social/behavioral research studies will focus on research that involves greater than minimal risk, research that includes special and/or vulnerable populations, and/or research that involves collection of sensitive personal information.

- a) The LR will be contacted via e-mail using the compliance e-mail template to schedule a site visit.
- b) An exit interview with the study personnel and/or the LR will be conducted at the conclusion of the compliance review to discuss the preliminary findings.
- c) The HRP EQUIP team or designee will draft a review summary, which will include a summary of the findings, as well as specific recommendations. If non-compliance is identified, the HRP EQUIP team will proceed with a report of non-compliance per IRB Policy # 52.

C. Directed (for cause) Reviews/Investigations

1. The HRP EQUIP team or designee will contact the LR to schedule the site visit via e-mail.
2. The HRP EQUIP team or designee will conduct a focused or comprehensive review contingent upon consideration of the request and preliminary evaluation which may include, but is not limited to the following:
 - a) A review of the inclusion/exclusion criteria, participant selection and recruitment methods to verify that subject selection is appropriate;
 - b) A review of the consent process and/or documentation. This may include an observation of the consent process and/or review of the documentation of consent;
 - c) A review of progress reports requested from the LR;
 - d) A review of all study documentation, regulatory documents, presentations, and monitoring reports;
 - e) Monitoring the progress of the activity and intervening as necessary through such steps as visits to the activity site and continuing evaluation to determine if any unanticipated risks to participants or others have arisen; and/or
 - f) Any other related documents as deemed appropriate by the UCI IRB.
3. Conclusion of review activities
 - a) HRP EQUIP team or designee will document the preliminary findings in writing as well as specific recommendations.
 - b) At the conclusion of the directed audit, an exit interview with the LR or his/her designee will be conducted to discuss the preliminary findings to facilitate the LR's understanding of the process and collaborate in resolving any outstanding issues or concerns.
4. Reporting Activities
 - a) A memorandum and a summary of findings will be distributed to the Director of Human Research Protections or designee, the IRB Chairperson of the IRB Committee responsible for the study.
 - b) (Policy # 52)
5. Documentation
 - a) A compliance review electronic file will be created upon initiation of the review activities.

- b) The summary report will be maintained electronically in a secure file.
- D. Off-site Reviews
 - 1. External reviews are conducted by the HRP EQUIP team or designee at non-UCI sites where the UCI IRB serves as the IRB of Record. These reviews will be conducted in accordance with the procedures detailed above. Additionally, assuring proper recruitment, space, facilities, qualified staff, enrollment, and execution of the consenting process may be reviewed.
 - 2. The on-site or remote visits will also entail review of documentation required when applying for a Memorandum of Understanding including but not limited to:
 - a) Verification of up-to-date comprehensive general liability and professional liability for all Investigators and research staff;
 - b) Correct titles and degrees for all research staff;
 - c) Verification of the researcher personnel's qualifications;
 - d) CVs for all research personnel;
 - e) Certificates for all researcher personnel verifying their successful completion of the UCI Human Subjects Training requirements or a comparable Human Research Protections training (e.g., CITI training);
 - f) Documentation of the local research context; and
 - g) Names and phone numbers of the local contacts for each non-UCI site.
- E. Management of participant complaint and concerns
 - 1. To enhance the public's understanding of research, UCI HRP has developed the a web page which includes frequently asked questions about research participation, quick links to external web based resources, and the HRP staff contact information. The HRP staff and the IRB Working Group periodically reviews the web page to determine whether additional information can be provided and to verify that the information provided is accurate and up-to-date and the hyperlinks are active.
 - 2. The HRP staff is responsible for the processing, review and inquiry into all complaints and concerns that are brought to the attention of the IRB/HRP regarding human subjects research conducted at UCI and/or by UCI personnel. Complainants may include, but are not limited to subjects (past, present or potential), subject family members, investigators, other research staff, or any person with concerns. (See HRP Policy # 54). When a subject complaint may involve noncompliance (See HRP Policy # 52), the EQUIP team works closely with the IRB Chair and IRB to manage the complaint.
- F. HRP Internal Quality Improvement (QI) Activities

The following activities are performed *quarterly* to ensure compliance with federal regulations and UCI HRP policies:

 - 1. Minutes QI Review – EQUIP conducts a review of 3 random sets of IRB approved minutes.
 - 2. Informed Consent QI Review – Up to 15 IRB approved informed consent documents are reviewed.
 - 3. Review of IRB Protocols –Up to 6 random, active studies are reviewed.
 - a) EQUIP reviews the last three years of an IRB approved protocol only.

- G. The following activities are performed *monthly or as needed* to ensure compliance with federal regulations and UCI HRP policies:
 - 1. HRP Benchmark Targets and Metrics Reports– the HRP has established benchmarks to measure efficiency in all phases of IRB review process.
 - 2. IRB Suggestion In-Box (Email)- the HRP Director monitors comments, questions and issues received from the UCI investigators to identify areas for potential improvement in the effectiveness of HRP policies and procedures and for ensuring the protection of human research participants. The HRP Director or designee, will work with the EQUIP team or HRP Staff as necessary to identify and address any programmatic areas of improvement.

IV. **General Responsibilities**

- A. If while conducting a directed audit or compliance review the auditor finds an issue that potentially places participants at risk, they will report the findings immediately to the Director of Human Research Protections or designee and the IRB Chairperson of the Committee responsible for the study.
- B. In addition, the auditor will clearly document the reasons for this determination.

Policy Number: 51:

Title: Hold, Suspension, and Termination of IRB Approval

Date of Last Revision: 07/28/06, 09/24/10, 05/01/16, 09/20/18, 09/17/2022

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) that all currently approved research is subject to amendment or change in approval status, as deemed necessary by the UCI IRB. The IRB has the authority to suspend or terminate research for not being conducted in accordance with State and Federal laws/regulations, and/or IRB requirements, policies and procedures; or if it has been associated with unexpected serious harm to subjects. The Investigator also has the option to place the research on administrative hold, while investigating a matter of potential noncompliance or to determine if additional risks are posed to human subjects.

I. Investigator-Imposed Administrative Hold

- A. The Investigator has the option to place some or all research activities on administrative hold pending review by the IRB Chair or the convened IRB and/or until additional information can be provided to the Chair or the IRB to determine if a change in the risk-benefit profile has occurred, if a change in the rights or welfare of the participants has occurred or if potential areas of non-compliance exist in a currently approved study. The Investigator can place an administrative hold on the research if:
 - 1. A complaint is received by the UCI IRB;
 - 2. An allegation of non-compliance is reported to the IRB;
 - 3. A discovery by the Investigator of potential additional risks to subjects; or
 - 4. A potential change in the rights or welfare of the subjects.
- B. The Investigator exercising the option for administrative hold, must submit a Reportable Event [unanticipated problem (UP), serious non-compliance (SNC) or continuing non-compliance (CNC)], or an Amendment to the IRB. The Investigator could place specific activities on hold. For example:
 - 1. Hold on recruitment;
 - 2. Hold on screening/enrollment;
 - 3. Hold on interactions/interventions with subjects; and/or
 - 4. Hold on collection or analysis of private identifiable information about participants.
- C. The Investigator must address the effect of the administrative hold on the rights and welfare of the current subjects.
- D. The investigator must promptly notify the IRB in writing via an amendment submission, of the intention to remove the administrative hold prior to implementing the action.
- E. At any point, the IRB Chair or the IRB can suspend the research and report the suspension in accordance with the UCI HRP Policy on Reporting.
- F. Should the IRB impose a suspension, the IRB suspension will be reported. (See Policy # 53.)

- G. The IRB Chair or their designee, or the IRB Committee may make recommendations for additional education and/or compliance interventions for the Investigator and research personnel.

II. The Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA) both address the suspension and termination of research.

OHRP requires that institutions have written procedures to ensure that the following incidents (see below) related to regulatory requirements pertaining to research conducted under an OHRP- approved assurance are promptly reported to OHRP.

Under FDA regulations at 21 CFR 56.113, an IRB shall have the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, and the Food and Drug Administration.

21 CFR 56.108(b) and 45 CFR 46.103(a) and (b)(5) requires that the IRB follow written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, the FDA, and OHRP of:

- A. Any unanticipated problems involving risks to human subjects or others;
- B. Any instance of serious or continuing noncompliance with these regulations or the requirements or determinations of the IRB; or
- C. Any suspension or termination of IRB approval.

III. FDA, Sponsor, or DSMB-Imposed Holds or Suspensions

- A. Notification of a hold or a suspension by the FDA, a sponsor, or a Data Safety and Monitoring Board (DSMB) unrelated to risk to human subjects (e.g., data analysis) is submitted to the IRB for review and approval as an amendment to previously approved research. Such amendments may be considered minor and may be reviewed by the expedited procedure at subcommittee (See Policy # 17). The IRB will review the amendment to consider if the hold or suspension relates to possible non-compliance.
- B. Notification of a hold or a suspension by the FDA, a sponsor, or a DSMB possibly related to risk to human subjects is submitted to the IRB via the Reportable Event (UP, SNC, CNC) for review by the full Committee for evaluation as a potential unanticipated problems involving risk to participants or others (See Policy # 19). If changes to the protocol and study documents are required as a result of the event, an amendment should also be submitted. Unanticipated Problems determined by the IRB will be reported as per Policy # 53. The IRB will review the report to consider if the hold or suspension relates to possible non-compliance.
- C. The IRB may impose their own suspension of the study, based on their findings. Should the IRB impose a suspension, the IRB suspension will be reported. (See Policy # 53.)

IV. **IRB-Imposed Suspensions**

- A. The IRB Chair or his/her designee, or the full IRB Committee may suspend IRB approval under the following circumstances:
 - 1. Inappropriate involvement of human subjects in research;
 - 2. Inhibition of the rights or welfare of participants;
 - 3. Serious or continuing noncompliance with Federal regulations or IRB policies; or
 - 4. New information regarding increased risk to human participants, etc.
- B. The IRB must consider the effect of the suspension on the rights and welfare of the current participants.
- C. When the IRB Chair suspends a study and the issue is reviewed at the next convened meeting of the IRB.
- D. The IRB reports in writing, all suspensions due to cause, promptly to the Lead Researcher. The letter includes:
 - 1. A statement of the reasons for the IRB's action;
 - 2. A requirement that the Investigator submit to the IRB a proposed script or letter notifying all currently enrolled participants that are affected by the suspension. The IRB Committee reviews the proposed script or letter. If follow-up of subjects for safety reasons is permitted/required by the IRB, participants should be so informed. The IRB may directly contact participants to fulfill this notification; and
 - 3. A requirement that the Investigator report any events to the IRB or sponsor that would have required reporting had the former participants continued to be enrolled in the research. The IRB may mandate oversight or transfer responsibility to another Investigator to ensure implementation of these procedures.
- E. Investigators receiving repetitive suspensions may necessitate institutional actions for serious and continuing non-compliance. (See Policy # 52.)
- F. All suspensions imposed by the IRB will be reported according to Policy # 53.

V. **IRB-Imposed Terminations**

- A. The IRB Committee reviews a study for Termination at a convened IRB meeting.
- B. Only the convened IRB Committee may terminate IRB approval when it is not being conducted in accordance with the IRB's requirements or the Federal regulations or has been associated with unexpected serious harm to participants (See Policy # 19).
- C. The IRB must consider the effect of the termination on the rights and welfare of the current participants.
- D. The IRB reports in writing, all Terminations promptly to the Investigator. The letter includes (as applicable):
 - 1. A statement of the reasons for the IRB's action;
 - 2. A requirement that the researcher submit to the IRB for review proposed procedures for withdrawal of currently enrolled subjects that considers their rights and welfare. Procedures for withdrawal of enrolled participants may include:
 - a) The IRB may mandate oversight or transfer responsibility to another Investigator to assure implementation of these procedures; or
 - b) Arrangements for medical care outside of a research study;

3. A requirement that the Investigator submit to the IRB a proposed script or letter notifying all currently enrolled participants that are affected by the termination;
 - a) The IRB reviews the Investigator's proposed script or letter.
 - b) If follow-up of subjects for safety reasons is permitted/required by the IRB, participants should be so informed.
 - c) The IRB may directly contact participants to fulfill this notification; and
4. A requirement that the Investigator report any events to the IRB or sponsor that would have required reporting had the former participants continued to be enrolled in the research.
 - a) The IRB may mandate oversight or transfer responsibility to another Researcher to ensure implementation of these procedures.
- E. The Investigator is offered an opportunity to respond to the Committee's determinations. The IRB Committee may ask the Investigator to attend the convened meeting to discuss the termination and provide clarification of the issues.
- F. Investigators receiving repetitive Terminations may necessitate additional institutional sanctions for serious and continuing non-compliance. (See Policy # 52.)
- G. All terminations imposed by the IRB are promptly reported according to HRP Reporting Policy. (See Policy # 53.)

VI. **Study Expiration**

- A. If an Investigator fails to provide continuing review information to the IRB or the IRB has not reviewed and approved a research study by the specified continuing review expiration date, the study expires. Enrollment of new participants cannot occur after the expiration date and all research activities must stop.
- B. The IRB notifies the Investigator in writing of protocol expiration. The letter indicates that on or after the expiration date:
 1. Enrollment of new participants must stop;
 2. All research activities must stop; and
 3. Any continuation of research activity is a violation of Federal regulations.
 4. The letter also indicates that the Investigator must immediately submit to the IRB, a list of research participants for whom cessation of the research would cause harm.
- C. Research studies not reviewed and approved within ninety (90) days of the notification of Expiration are administratively closed by the IRB.
- D. Reinstatement of the research generally requires submission of a new IRB Application.

References:

45 CFR 46.103(b)(5)(ii)
 45 CFR 46.113
 42 CFR 50 Subpart A
 21 CFR 56.113
 21 CFR 56.108(b)(3)
 OHRP Guidance Document, "Guidance on Continuing Review" dated July 11, 2002
 HRP Policy 53, "Reporting to the Appropriate Institutional Officials, and the Department or Agency Head(s)"

Procedure Number: 51.A**Title: Procedure for Administrative Hold, Suspension, and Termination of IRB Approval****Procedure:**

This procedure outlines the circumstances and methods in which a study's approval status may be changed and subsequently reinstated.

I. Lead Researcher (LR) Responsibilities**A. Investigator-Imposed Administrative Hold**

1. LR notifies the IRB in writing (via Reportable Events -UP/SNC/CNC; or Amendment) of study activities or recruitment and enrollment activities placed on administrative hold.
2. The LR responds promptly to any requests for additional information from the IRB Committee. In addition, the LR cooperates with the IRB in complying with all recommended education and/or compliance interventions designated by the IRB Committee.
3. The LR contacts the sponsor for any information that they cannot provide to the IRB addressing the possible change in risk-potential benefit profile.
4. During the time in which a study is on administrative hold, unanticipated problems and serious or continuing noncompliance continue to be reported to the IRB.
5. The LR promptly notifies the IRB in writing via an Amendment submission, of the intent to remove the administrative hold prior to implementing.

B. FDA, Sponsor, or DSMB-Imposed Hold or Suspension Unrelated to Potential Risk

1. The notice of hold or suspension or its subsequent removal is forwarded to the IRB as an amendment as soon as possible after the LR first learns of the notice of suspension or its removal.
2. Research activities cease as specified in the hold or suspension notice until the study is re-opened, and the IRB acknowledges the notification by approving the amendment.
3. Unanticipated and serious or continuing noncompliance are still reported to the IRB.

C. FDA, Sponsor, or DSMB-Imposed Hold or Suspension for Potential Risk

1. LRs forward any correspondence indicating a hold or suspension imposed for potential risk, to the IRB via the Reportable Event reporting process as soon as possible, but no later than 5 working days after the LR first learns of the notice of hold or suspension, for full Committee review and approval.
2. Research activities cease as specified in the hold or suspension notice until the study is re-opened by the entity and the full IRB Committee has reviewed and approved the amendment to reinstate the study. Also, the IRB may determine additional criteria for suspension or for re-opening the study.
3. Unanticipated problems and serious or continuing noncompliance are still reported to the IRB.

D. IRB-Imposed Suspensions

1. Research activities cease, as specified in the suspension criteria, until

the LR is notified that the full IRB Committee has granted approval of the study to resume. It is within the authority of the IRB to terminate the study.

2. The LR cooperates with the IRB in complying with all corrective actions as designated by the IRB Committee.
3. The LR notifies the sponsor of the UC Irvine IRB imposed suspension / reinstatement.
4. The LR is responsible for notifying all affected participants of the suspension, as required by the IRB.
5. The LR submits the script or letter to the IRB for approval prior to notification to participants.
6. Unanticipated problems and serious or continuing noncompliance are still reported to the IRB.

E. IRB-Imposed Terminations

1. The LR ceases all study related activities and notifies the sponsor of the termination of UC Irvine IRB approval.
2. The LR is responsible for notifying all affected participants of the termination, as required by the IRB.
3. The LR submits the script or letter to the IRB for approval prior to notification to participants.
4. Unanticipated problems and serious or continuing noncompliance are still reported to the IRB.

F. Study Expiration

1. The LR completes all continuing review requirements promptly.
2. Research activities cease until the IRB has determined continuing review requirements are met and approval is granted.
3. Enrollment of new participants and interaction of already enrolled participants cannot occur after the expiration of IRB approval.
4. The LR may provide justification in writing to the IRB Committee for continuing treatment of participants to avoid additional risk or if the drug is available outside the research study.
5. Unanticipated problems and serious or continuing noncompliance are still reported to the IRB.

II. **IRB Committee Responsibilities**

A. Investigator-Imposed Administrative Hold

1. Once the information requested from the LR has been received and reviewed by the IRB Chair or his/her designee, or the IRB Committee, one of the following determinations occur:
 - a) The IRB Chair or his/her designee can determine that the incident does not require convened IRB review or
 - b) The IRB Chair refers the study to the convened IRB for review and further determination.
2. The IRB Chair or the IRB Committee may require education and/or directed audits be conducted by the IRB Education and Quality Improvement (EQUIP) Team.
3. The IRB Chair or the IRB can suspend the research and report the suspension in accordance with the UCI HRP policy on reporting. (See Policy # 53.)
4. The IRB Chairperson or his/her designee may consult, as needed, with the IRB Working Group (a group made up of other IRB Chairs and Vice Chairs, and some HRP staff) regarding the particular project and/or the LR.

- B. FDA, Sponsor, or DSMB-Imposed Hold or Suspension Unrelated to Potential Risk
 - 1. Notification of a hold or suspension and the reinstatement of research for issues unrelated to risks are reviewed via an amendment by expedited procedures and approved by the IRB Chairperson or his/her designee.
- C. FDA, Sponsor, or DSMB-Imposed Hold or Suspension for Potential Risk
 - 1. Notification of a hold or suspension possibly related to risk is received via the reportable event reporting process is reviewed by the IRB Chair or his/her designee, or the IRB Committee, one of the following determinations occur:
 - a) The IRB Chair or his/her designee can determine that the incident does not require convened IRB review or
 - b) The IRB Chair refers the study to the convened IRB for review and further determination.
 - 2. The IRB Chair or the full IRB Committee may suspend the research. However, the IRB Committee may impose additional restrictions upon research conducted under its jurisdiction.
 - 3. Re-instatement of the research by the FDA, Sponsor, or DSMB is submitted to the IRB as an amendment and approved by the IRB Committee.
 - 4. The IRB notifies the LR in writing of its determinations.
- D. IRB-Imposed Suspensions
 - 1. IRB Chair or his/her designee, or the IRB Committee may suspend at study.
 - 2. The IRB may review a study for Suspension at a full IRB Committee meeting. Examples of these types of circumstances include:
 - a) Failure to comply with prior conditions imposed in writing by the IRB under a Suspension;
 - b) Repeated or deliberate failure to obtain or document informed consent from human participants;
 - c) Repeated or deliberate failure to comply with conditions placed on the study by the University, IRB, Sponsor, or FDA;
 - d) Repeated or deliberate failure to obtain prior review and approval of new protocols and on-going human subjects research by the IRB;
 - e) Repeated or deliberate failure to maintain accurate study records or submit required unanticipated problems involving subjects or others to the IRB;
 - f) Repeated or deliberate falsification or concealment of study records, e.g., by substituting in study records the results of biological samples from participants who met the inclusion criteria for samples of participants who did not meet the inclusion criteria, or by fabricating participants.
 - 3. Prior to presentation at full Committee, the IRB Chair or his/her designee is encouraged to present the details at the IRB Working Group for an open discussion and dialogue to assist the Committee Chairperson in organizing and prioritizing a presentation of the facts for consideration and vote at the next IRB Committee meeting. This promotes consistency and compliance across all IRB Committees.
 - 4. In addition, the Committee may request an ad hoc review from an independent source with expertise in the type of research being conducted or in the specific area of concern.

5. The options for suspension are:
 - a) Suspension of the research; or
 - b) Suspension to recruitment;
 - c) Suspension to screening/enrollment;
 - d) Suspension to interaction/intervention;
 - e) Suspension to analyses with private, identifiable data; and/or
 - f) Suspension to follow-up.
 6. The IRB notifies the LR in writing of its decision to suspend the study for cause and provides a rationale for its actions. This letter includes an opportunity for the LR to respond to the Committee's determinations. The IRB Committee may ask the LR to attend the meeting to discuss the suspension and provide clarification of the issues.
 7. The Committee may request the development of an education plan and/or the completion of a directed audit by the IRB EQUIP Team.
 8. Suspensions for cause are reinstated for approval after corrective actions are completed to the IRB Committee's satisfaction. The Committee may approve the study with or without additional restrictions (e.g., mandating a data and safety monitoring committee to oversee the research at designated intervals, increase in the frequency of IRB Committee review, observation of the consent process, etc.)
- E. IRB-Imposed Terminations
1. The IRB reviews a study for Termination at a full IRB Committee meeting.
 2. Only the IRB Committee can terminate research.
 3. Prior to presentation at full Committee, the IRB Chairperson or his/her designee is encouraged to present the details at the IRB Working Group for an open discussion and dialogue to assist the Committee Chairperson in organizing and prioritizing a presentation of the facts for consideration and vote at the next IRB Committee meeting. This promotes consistency and compliance across all IRB Committees.
 4. In addition, the Committee may request an ad hoc review from an independent source with expertise in the type of research being conducted or in the specific area of concern.
 5. The IRB notifies the LR in writing of the decision to terminate the study for cause and provide a rationale for its actions. This letter includes an opportunity for the LR to respond to the Committee's determinations. The IRB Committee may ask the LR to attend the meeting to discuss the termination and provide clarification of the issues.
- F. Reporting of IRB-Imposed Suspensions or Terminations
1. All IRB-Imposed Suspensions or Terminations for Cause are promptly reported per Policy # 53.
 2. The institution may determine that suspensions or terminations associated with a particular study or an LR are repetitive and warrant action for issues of serious and continuing non-compliance.
- G. Expiration of Approval
1. The IRB notifies the LR in writing of the pending Expiration.
 2. Expired studies may be granted approval after the continuing review requirements are completed and approved at the appropriate level of review for which the study currently qualifies.

3. The IRB Chair or designated Committee Member may review the submitted justification for continuing treatment of participants to avoid additional risk or if the drug is available outside the research study.

III. **Human Research Protections Staff Responsibilities**

A. Investigator-Imposed Administrative Hold

1. The HRP staff (or EQUIP team) notifies the Director of Human Research Protections or designee within 1 working day of any Investigator requests for Administrative Hold.
2. The HRP staff (or EQUIP team) assists the Committee in obtaining any additional information needed for the Chairperson or his/her designee to determine if a change in the risk-potential benefit profile has occurred.
3. The EQUIP Team completes directed audits and/or develops an education plan as deemed appropriate by the IRB Committee. The EQUIP Team is available as a resource to the LR.
4. The HRP staff (or EQUIP team) updates the IRB database accordingly with the current status of the research.

B. FDA, Sponsor, or DSMB-Imposed Hold or Suspension Unrelated to Potential Risk

1. The HRP staff processes the amendment for notification of a hold or a suspension unrelated to risk for administrative acknowledgement. This may occur via expedited review.
2. The HRP staff update the IRB database accordingly with the current status of the research.
3. In the case that the FDA, sponsor, or DSMB has halted enrollment of new subjects, HRP Staff will remove the IRB approved recruitment materials and consent documents from the IRB Database.

C. FDA, Sponsor, or DSMB-Imposed Hold or Suspension for Potential Risk

1. The HRP staff (or EQUIP team) processes the reportable event report and/or amendment for notification of a hold or suspension due to possible risk for full Committee review.
2. The HRP staff (or EQUIP team) notifies the LR in writing of the IRB Committee's determinations.
3. The HRP staff (or EQUIP team) assists the Committee in obtaining any additional information needed for the Chairperson or his/her designee to determine if a change in the risk-benefit profile has occurred.
4. The HRP staff (or EQUIP team) processes the amendment to report reinstatement of the research by the sponsor for full Committee review.
5. The HRP staff (or EQUIP team) updates the IRB database accordingly with the current status of the research.
6. In the case that the FDA, sponsor, or DSMB has halted enrollment of new subjects, HRP Staff (or EQUIP team) will remove the IRB approved recruitment materials and consent documents from the IRB Database.

D. IRB-Imposed Suspensions

1. The HRP Staff (or EQUIP team) notifies the LR in writing of IRB determinations.
2. The HRP Staff (or EQUIP team) assists the Committee in obtaining information from the LR. The HRP Staff and the EQUIP Team keeps

each other apprised of all corrective actions to be taken by the LR and their status.

3. The EQUIP Team completes a directed audit and/or develops an education plan as deemed appropriate by the IRB Committee. The team is available as a resource to the LR.
4. The HRP Staff (or EQUIP team) notifies the Director of Human Research Protections or designee within 1 working day of any Suspensions.
5. The HRP Staff (or EQUIP team) updates the IRB database accordingly with the current status of the research.
6. The Director of Human Research Protections or designees promptly reports the suspension for cause per Policy # 53.
7. In the case that the IRB has halted enrollment of new subjects, HRP Staff (or EQUIP team) will remove the IRB approved recruitment materials and consent documents from the IRB Database.

E. IRB-Imposed Terminations for Cause

1. The HRP Staff (or EQUIP team) notifies the LR in writing of IRB determinations. The letter requires a signature of the Chairperson or his/her designee.
2. The HRP Staff (or EQUIP team) promptly notifies the Director of Human Research Protections or designee within 1 working day of any Terminations.
3. The HRP Staff (or EQUIP team) updates the IRB database accordingly with the current status of the research.
4. The Director of Human Research Protections or designees promptly reports the termination for cause are per Policy # 53.
5. HRP Staff (or EQUIP team) will remove the IRB approved recruitment materials, and consent documents from the IRB Database.

F. Expiration of Approval

1. The HRP Staff assists the Committee in obtaining the additional information required to conduct continuing review of the research.
2. The HRP staff assists the Committee in obtaining a closing report from the LR.

**University of California, Irvine
Human Research Protections
Standard Operating Policies and Procedures**

Policy Number: 52

Title: Research Non-Compliance

Date of Last Revision: 05/01/2006, 07/07/2010, 10/12/2016, 09/01/2017, 12/19/2019, 09/17/2022

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to uphold its role in assuring prompt reporting of any serious or continuing non-compliance with 45 CFR Part 46 or the requirements or determinations of the IRB.

- I. All reports of alleged serious and/or continuing non-compliance or inappropriate involvement of humans in research are investigated. Such reports may come from any source such as an IRB Committee Member, an Investigator, a participant or their family members, institutional personnel, other institutional Committees, UC Irvine Whistleblower Office, UCI Health Affairs Compliance Officer, the media, anonymous sources, or the public. Goals of the IRB, in general, in investigating and managing issues of potential noncompliance include:
 - A. Assuring the safety of human participants;
 - B. Developing action plans to prevent reoccurrence, and promote future compliance;
 - C. Educating research staff to assure the understanding of Food and Drug Administration (FDA) and Office for Human Research Protections (OHRP) guidelines and regulations, and UCI IRB Policy;
 - D. Reporting serious or continuing noncompliance.
- II. Instances meeting the definition of research/scientific misconduct will be reported to the Vice Chancellor for Research.
 - A. Attempts to unduly influence an IRB Committee Member or IRB staff are considered research misconduct.
 - B. IRB members or staff who believe that they have been subject to undue influence must report this to the Assistant Vice Chancellor for Research or utilize the University of California Whistleblower Policy.
 - C. The Assistant Vice Chancellor for Research will report all attempts of undue influence of the IRB process to the Vice Chancellor for Research and the Dean of the Lead Researcher's School.
- III. Definitions of Terms:
 - A. Non-Compliance: Failure to comply with applicable laws, regulations, or institutional policies pertaining to the protection of human subjects, and/or with the requirements or determinations of an IRB.
 - B. Serious Non-Compliance: Failure to comply with applicable laws, regulations, or institutional policies pertaining to the protection of human subjects and/or with the requirements or determinations of an IRB that has a significant adverse impact either on the rights or welfare of participants or on the integrity of the data.
 - C. Continuing Non-Compliance: A pattern of noncompliance that indicates

an inability or unwillingness to comply with applicable laws, regulations, or institutional policies pertaining to the protection of human subjects and/or with the requirements or determinations of an IRB.

References:

45 CFR 46

21 CFR 50 and 56

University of California Policy for Protection of Whistleblowers from Retaliation and Guidelines for Reviewing Retaliation Complaints

IRB Policy 1, "Institutional Oversight of Assurance"

IRB Policy 2, "Activities Subject to IRB Jurisdiction"

IRB Policy 50, "IRB Compliance Activities"

IRB Policy 51, "Administrative Hold, Suspension, or Termination of IRB Approval"

IRB Policy 57, "UCI HRP Policy and Procedure Glossary"

Procedure Number 52.A**Title: Procedure for Investigating and Managing Potential Issues Research Non-Compliance****Procedure:**

This procedure outlines the process for assuring the prompt reporting and management of any serious or continuing non-compliance with 45 CFR Part 46 or the requirements or determinations of the IRB.

I. Lead Researcher (LR) Responsibilities

- A. It is the Lead Researcher's responsibility to adhere to the IRB approved protocol and not to initiate any changes to the protocol prior to IRB review and approval of the change, unless there is an apparent need to minimize risk to the participants. In this case the LR must notify the IRB within 5 working days of the change. (See Policies # 17 and 19.)
- B. The Lead Researcher is responsible for the ethical management, accurate documentation, and the protection of human participants in their research.
- C. The Lead Researcher complies with all requests from the IRB for further information or clarification regarding concerns or issues under investigation.
- D. The Lead Researcher must notify the IRB of potential matters of serious and/or continuing non-compliance.
- E. All incidents of serious and/or continuing noncompliance that occur either at a UCI site, or at a non-UCI site where the UCI IRB is the IRB of record, must be reported to the IRB within 5 business days of the occurrence or within 5 business days from the date in which the LR learned of the occurrence.
- F. If the serious and/or continuing noncompliance meets the definition of an unanticipated problem, the LR must submit a Reportable Event-Unanticipated Problem (UP); otherwise, the LR must submit a Reportable Event-New Information Report (NIR).

II. IRB Committee Responsibilities

- A. When the IRB Committee Chair receives an alleged report of serious and/or continuing non-compliance, the Chair either:
 - 1. Reviews the information, determines the information is not serious and does not meet the definition of continuing non-compliance, the IRB Chair:
 - a) Formulates a corrective action plan;
 - b) Forwards the corrective action plan to the LR; and
 - c) Forwards the information to be included in the IRB agenda as an information item.
 - 2. Reviews the information, determines that more information is needed, and directs an investigation by the HRP Compliance Manager. The LR is notified in writing of the directed investigation (audit); or
 - 3. Reviews the information, determines the information is serious or inhibits the rights or welfare of participants, and forwards the information to the full IRB Committee for review, consideration of

suspension, or consideration of termination. An investigation by the HRP Compliance Manager can occur simultaneously with IRB Committee review for consideration of suspension.

- a) Should the information be forwarded to the full IRB Committee for review, the IRB Chair will present the information to the Committee.
- b) All members of the full IRB Committee will have access to materials related to the issue for their consideration in advance of the scheduled full Committee meeting.
4. If the allegation involved research misconduct, the IRB Chair will report this to the Vice Chancellor for Research.
- B. The IRB Committee reviews the materials provided at a convened meeting, to determine:
 1. There is no issue of non-compliance;
 2. There is noncompliance that is neither serious nor continuing;
 3. There is serious or continuing noncompliance. The IRB office will report this determination according to Policy # 53;
 4. There is insufficient information to make a determination. In this case, the IRB will request additional information from the EQUIP team and defer a determination to a later date.
- C. The IRB Committee considers (required):
 1. Suspension of the research (See Policy # 51)
 2. Termination of the research (See Policy # 51)
 3. Notification of current participants when such information may relate to the participants' willingness to continue to take part in the research
- D. The IRB Committee considers the following added protections (optional, as applicable):
 1. Dismiss the allegation,
 2. Achieve compliance with the cooperation of the Investigator (and report to the appropriate federal Agency when required) via a modification of the protocol or modification of the information disclosed during the consent process,
 3. Providing additional information to past participants
 4. Requiring current participants to re-consent to participation
 5. Modification of the continuing review schedule
 6. Monitoring of the research, including an increase in monitoring of the research activity via a data safety monitor or board and intervention as necessary through steps such as visits to the activity site and continuing evaluation of the site by the IRB Education and Quality Improvement Team;
 7. Monitoring of the consent process
 8. Referral to other organizational entities
 9. Impose sanctions to achieve compliance (and report to the appropriate federal Agency when required), or
 10. Recommend reclassification as possible scientific misconduct.
 11. Verification that participant selection is appropriate and observation of the actual informed consent process by the IRB Education and Quality Improvement Team;
 12. Request an off-cycle data and safety monitor or board review;
 13. Request a directed audit of targeted areas of concern;

14. Request a status report after each participant receives intervention from the LR;
15. Modify the continuing review cycle;
16. Request additional LR and research personnel education focused on human research protections from the IRB Education and Quality Improvement Team or other available sources (e.g., "CITI", OHRP conferences, NIH tutorial, human research protections seminars);

III. **IRB Administrator Responsibilities**

- A. When the HRP Compliance Manager receives a report of alleged serious and/or continuing non-compliance, they verify whether a detailed explanation from the LR accompanies the report.
 1. If a detailed explanation from the LR accompanies the report it is forwarded to the IRB Chair for review.
 2. If a detailed explanation from the LR does not accompany the report the HRP Compliance Manager contacts the LR to request additional information.
 3. If the report contains no explanation from the LR, or comes from a source other than the LR the HRP Compliance Manager forwards the information to the appropriate IRB Chair for review and determination.
- B. If the report contains an explanation from the LR and comes from a source other than the LR, the HRP Compliance Manager forwards the information to the IRB Chair for review.
- C. If the non-compliance is to be reviewed by the convened IRB, the Administrator prepares the following documents for review by all members of the Committee:
 1. The report (investigation report or KR Reportable Event);
 2. The alleged notification of potential noncompliance, if applicable;
 3. The electronic IRB Database Record which, includes the last approved consent document.
 4. Additionally, the assigned IRB Committee member reviews:
 - a) The last approved Investigator's Brochure, if applicable;
 - b) The Grant, if applicable; and
 - c) Any pertinent information (e.g., questionnaires, DSMB reports, etc.)
 - d) All communication between the Lead Researcher and the IRB Committee.
 5. The LR is notified in writing of IRB determinations.
 6. The Administrator maintains and updates the IRB database as applicable with current study information.

Policy Number: 53

Title: Reporting to the Appropriate Institutional Officials, and the Department or Agency Head(s)

Date of Last Revision: 08/10/05, 12/01/10, 01/24/11, 05/01/16, 09/17/2022

Policy:

It is the responsibility of the UCI IRB to assure compliance reporting occurs according to the Federal regulations, institutional policy and UCI IRB policy.

- I. The IRB will maintain written procedures for assuring prompt reporting to the IRB, appropriate institutional officials, and the Department or Agency head of:
 - A. Any unanticipated problems involving risk to participants or others;
 - B. Any serious or continuing non-compliance with this policy or the requirements or determinations of the IRB; and
 - C. Any suspension or termination of IRB approval for cause.
- II. Reporting will take place as soon as possible, but no more than 30 days between the IRB determination or recognition of a reportable event and fulfilling reporting requirements for unanticipated problems involving risk to participants and others. For more serious incidents, a preliminary written report will be provided within five business days with an estimated time for the final report.
- III. Any concerns regarding data integrity or research/scientific misconduct outside of the jurisdiction of the UCI IRB will be referred to the Vice Chancellor for Research for further consideration/action.
- IV. When human subject research involves the Department of Energy (DoE), the UCI IRB will follow DoE regulations and guidance that pertains to ensuring research compliance as per DoE O 443.1A. Specifically, researchers must promptly report the following to the human subject research program manager:
 - A. Any significant adverse events, unanticipated risks; and complaints about the research,
with a description of any corrective actions taken or to be taken
 - B. Any suspension or termination of IRB approval of research
 - C. Any significant non-compliance with HRPP procedures or other requirements
 - D. The time frame for “promptly” is defined as per HRP policy for unanticipated problems. (See Policy # 19.)
 - E. Any compromise of personally identifiable information must be reported immediately
 - F. The time frame for “immediately” is defined as per HRP policy for unanticipated problems. (See Policy # 19.)
- V. When human subject research involves the Department of Defense (DoD), specifically, issues relating to non-compliance, the matter will be referred to the next higher management echelon to take deliberate action for resolution. All

findings of serious non-compliance shall be reported to the Director, Defense and Research Engineering.

- VI. The following shall be reported to the Department of Navy (DoN) Human Research Protection Program (HRPP) Office, as it relates to research involving the DoN and matters of non-compliance:
 - A. All suspensions and terminations of previously approved DoN research protocols.
 - B. The initiation and results of investigations of alleged non-compliance with human subject protections.
 - C. Unanticipated problems involving risks to subjects or others, or serious adverse events in DoN supported research.
 - D. All audits, investigations or inspections of DoN supported research protocols.
 - E. All audits, investigations or inspections of the institution's HRPP conducted by outside entities (e.g. the Food and Drug Administration (FDA), Office for Human Research Protections (OHRP))
 - F. Significant communication between institutions conducting research and other federal departments and agencies regarding compliance and oversight.
 - G. All restrictions, suspensions or terminations of institutions' assurances.
- VII. The Naval command or activity with responsibility for the research will review all allegations of non-compliance with human subject protections and take action, if appropriate. Report the initiation of all investigations and report results, regardless of the findings to the Navy Surgeon General (SG) and appropriate sponsors.
- VIII. Naval IRBs: The primary role of the IRB is to ensure safety and welfare of human research subjects. IRBs make recommendations to the approval authority for research protocols. Naval IRBs report to the Commander, Commanding Officer or Officer in Charge the following:
 - A. All suspensions or terminations of previously approved research protocols,
 - B. The initiation of investigations of alleged non-compliance with human subject protections,
 - C. Unanticipated problems involving risks to subjects or others, or serious adverse events,
 - D. All audits, investigations or inspections of the institution's HRPP conducted by an outside entity (e.g., the FDA of OHRP),
 - E. Significant communication between the institutions conducting research and other federal departments and agencies regarding compliance and oversight.

References:

45 CFR 46.103(b)(5)

21 CFR 56.108(b)

OHRP Guidance on Reporting Incidents to OHRP

DoE O 443.1A

DoD: DoDD 3216.2, para. 4.10

SECNAVINST 3900.39D, para 8d(2), para 8e(6), para 8g(6) and 6k

OHRP Guidance on Reporting Incidents to OHRP

Procedure Number: 53.A**Title: Procedure for Reporting to the Appropriate Institutional Officials, and the Department or Agency Head(s)****Procedure:**

This procedure describes how compliance reporting occurs according to the Federal regulations, institutional policy and UCI IRB policy.

I. IRB Responsibilities

- A. The IRB Chair will report to the Director of Human Research Protections or designee:
 - 1. Any event determined by the IRB to represent any unanticipated problems involving risk to participants or others;
 - 2. Any non-compliance determined by the IRB to be serious or continuing non-compliance; and
 - 3. Any action of the IRB to suspend or terminate its approval for cause.

II. HRP Administration Responsibilities

- A. The Director of Human Research Protections or designee prepares a letter that outlines:
 - 1. The nature of the event;
 - 2. The findings of the organization and IRB;
 - 3. Actions taken by the organization or IRB;
 - 4. Reasons for the organization's or IRB's actions; and
 - 5. Plans for continued investigation or action.
- B. The letter is sent to the following people for review and approval:
 - 1. The Associate Vice Chancellor for Research; and
 - 2. The IRB Chair of the Committee that made the determination.
- C. The letter is signed by the Institutional Official (Vice Chancellor for Research).
- D. The Director of Human Research Protections or designee sends a copy of the letter to:
 - 1. IRB Members of the applicable Committee (as an information item on the convened IRB agenda)
 - 2. OHRP when the study is covered by DHHS regulations.
 - 3. FDA, when the research is FDA-regulated;
 - 4. Other federal agencies when the research is overseen by those agencies, and they require prompt reporting separate from that to OHRP.
 - 5. Study sponsor, if the research is sponsored (this includes NIH, NSF, and industry sponsors);
 - 6. UCI Medical Center IDS pharmacist, if the protocol is suspended or terminated and the research involves investigational drugs;
 - 7. Sponsored Projects, if the research involves a grant or contract for all determinations involving faculty, staff, or students whose primary affiliation is with UC Irvine;
 - 8. The School Dean, Department Chair, Supervisor, and Faculty Sponsor of the Lead Researcher, if applicable;
 - 9. The Associate Vice Chancellor of Research
 - 10. The Associate Dean of Research (School of Medicine)

11. Institutional officials at external sites where the research is conducted and UCI serves as their IRB of record;
12. The appropriate HRP electronic folder, if applicable;
13. Legal Counsel, if appropriate; and/or
14. Risk Management, if appropriate.

Policy Number: 54

Title: Concerns and Complaints Regarding Human Subjects Research

Date of Last Revision: 01/21/2007; 11/08/2010; 05/01/16; 09/17/2022

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to investigate all concerns or complaints received regarding human subjects research conducted under its jurisdiction.

- I. The Director of Human Research Protections or designee must investigate all concerns or complaints received regarding human subjects in research under UCI IRB's jurisdiction. The level of investigation will depend on the seriousness of the situation and the potential risk to participants. Concerns or complaints may come from any source including IRB Committee members, Investigators, participants and their families, Institutional personnel, other Institutional Committees, UCI Whistleblower Office, the media, anonymous sources, or the public.
- II. Concerns or complaints may come from any category of research reviewed and may include anyone involved or not directly involved in the research process/study
- III. Investigations should result in finding a suitable resolution and response to the complainant in a timely manner.
- IV. All concerns and complaints will be handled in a confidential manner. This includes any individual involved in notifying the UCI IRB of an alleged violation of Investigator compliance.
- V. Concerns or complaints that are substantiated will be further investigated through a directed audit conducted by the IRB Education and Quality Improvement Team, and actions will be taken as deemed appropriate by the IRB. The IRB Committee may involve a Subject Advocate or UCI Medical Center Patient Affairs, if applicable.
- VI. Concerns or complaints of a sensitive nature may be brought to the IRB Working Group meeting for discussion and recommendation.
- VII. Human Research Protections provides a suggestion box on its website to allow individuals to voice any suggestions, concerns or complaints. If any concerns are emergent in nature or are such that a participant may potentially be placed at risk, the suggestion box states to please call the IRB directly at (949) 824-8170 or via email at IRB@research.uci.edu.

References:

Institutional Review Board Management and Function; Bankert, E. Gordon, B, Hurley, E, and Shriver, S ; 2022 Jones and Bartlett Publishers, Inc.

Procedure Number: 54.A**Title: Procedure for Concerns and Complaints Regarding Human Subjects Research****Procedure:**

The purpose of this procedure is to outline the actions of the UC Irvine (UCI) Institutional Review Board (IRB) in managing a concern or complaint received regarding human subjects research.

I. Lead Researcher (LR) Responsibilities

- A. It is the responsibility of the LR to notify the IRB via the AE/UP Reporting process of any complaint by a subject that indicates an unexpected risk or which cannot be resolved by the UCI LR. The reporting timeframe is within 10 working days of the researcher becoming aware of the problem. (See HRP Policy # 19.)
- B. It is the responsibility of the LR to report to the IRB at the time of continuing review any complaint made by a participant that was resolved and did not involve an unexpected risk (e.g., a participant complains that he/she did not receive compensation in a timely manner).
- C. Lead Researchers are to cooperate with the IRB by making documents accessible, responding to written requests within the designated time frame, and being available for questions by the IRB.

II. IRB Committee Responsibilities

- A. Initial Concern or Complaint
 - 1. The assigned IRB Chair or his/her designee will be notified by the HRP staff member conducting the investigation or directed audit of planned activities.
 - 2. The IRB Chair or his/her designee may request revisions or additions to the planned investigation or directed audit activities.
- B. Committee Review
 - 1. At the completion of the investigation or directed audit, the findings (if warranted) will be taken to full Committee for review.
 - 2. A determination will be made by the Committee of any further actions that are to be taken.

III. IRB Administrator Responsibilities

- A. Initial concern or complaint
 - 1. When an IRB staff member receives a verbal concern or complaint, he/she will collect as much information as possible while completing the IRB Complaint Information Form.
 - 2. All written concerns or complaints and completed complaint forms are to be forwarded to the Director of Research Protections or designee for investigation into the nature of the concern or complaint.
- B. Review and Follow-up
 - 1. When a concern or complaint is substantiated, the Director of Research Protections or designee will forward the complaint to the IRB Education and Quality Improvement Team for further investigation or a directed audit.

2. When the concern or complaint involves sensitive issues, the complaint may be forwarded to the IRB Working Group for discussion and recommendations prior to initiating any activity.
 3. The results of the investigation will be reported to the Director of Research Protections or designee. If the concern or complaint is study-related, the appropriate IRB Committee will also be notified of the results. If warranted, the results of the investigation will be forwarded to the IRB full Committee for further determinations and/or recommendations.
 4. The Administrator will forward Committee determinations and/or recommendations regarding the investigation to the Executive Director of Research Protections or designee.
 5. If warranted, the Director of Research Protections or designee will notify the Vice Chancellor for Research of the investigation or directed audit outcomes. (See HRP Policy # 53.)
 6. The Administrator will update the IRB database accordingly.
 7. Records of the concern or complaint and subsequent investigation will be kept in a separate encrypted electronic location on the HRP intranet.
- C. Results from the IRB Surveys are monitored for HRP feedback and suggestions, as well as any concerns or complaints that require investigation.

Policy Number: 55

Title: Protocol Deviations and Violations

Date of Last Revision: 01/21/2007, 11/02/2016, 09/01/2017, 12/10/2019, 09/17/2022

Policy:

This policy applies for all events that occur at a UCI site (UCI Main Campus, UCIMC, including UCIMC satellite clinics) or occurs at a non-UCI site where the UCI IRB is the IRB of record:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) that only those protocol deviations and violations that meet the definition of an unanticipated problem involving risk to participants or others must be reported as per Policy # 19 or that involve serious and/or continuing noncompliance be reported per Policy # 52. Protocol deviations and violations that do not constitute an unanticipated problem involving risk to participants or others or do not involve noncompliance are generally not reportable to the UCI IRB.

I. Deviations

- A. Per Policy # 57, a Protocol Deviation is defined as: *Accidental or unintentional changes to, or a planned deviation from the IRB-approved protocol that does not increase risk or decrease benefit or; does not have a significant effect on the subject's rights, safety or welfare; and/or on the integrity of the research. Deviations may result from the action of the participant, researcher, or research staff.*
- B. There are three types of deviations:
 - 1. Emergency deviations - involves a departure from the approved protocol to avoid an immediate hazard to the participant. In such instances there is often not time to seek IRB approval. The LR must notify the sponsor and IRB as soon as possible after the emergency situation occurred per Policy # 19.
 - 2. Major, non-emergency deviations - planned deviations that are non-emergent and represent a major change in the approved protocol. These deviations are changes that the IRB must approve via submission of a modification request or a prospective deviation request prior to implementation of the proposed change (See Policy # 17). NOTE: If a planned major, non-emergency deviation occurs without prior IRB approval, the event is non-compliance which must be reported promptly to the IRB. A LR's failure to report promptly any major, non-emergency deviation for which the LR did not obtain prior IRB approval is itself an incident of non-compliance.
 - 3. Minor or administrative deviations – deviations that do not affect the risk/benefits of the study or do not significantly affect the subject's rights, safety or welfare; and/or on the integrity of the data. LRs may choose to report these deviations at the time of continuing review, although this is not required. Examples of minor or administrative deviations include: follow up visits occurring outside the protocol required time frame because of the participant's schedule, or blood samples being obtained at times close to but not precisely at the time

points specified in the protocol. Minor deviations may occur due to an intentional change made by the LR, the subject's lack of adherence to the protocol or other external factors outside of the Investigator's control (e.g. weather conditions, holidays, etc.) that impact the conduct of the protocol.

- C. Should the Investigator need to deviate from the protocol for no more than 3 subjects, the Investigator may complete the Reportable Event - Prospective Deviation Request prior to implementation of the deviation. The request will be reviewed by the IRB Chair for acceptance of the deviation.
- D. Protocol deviations that meet the definition of an unanticipated problem involving risk to participants or others must be reported to the UCI IRB as per Policy # 19, Investigators should therefore assess each deviation carefully.
- E. In instances where serious and/or continuing noncompliance may be involved, per Policy # 52 a Reportable Event - New Information Report must be submitted within 5 business days of the occurrence or within 5 business days from the date in which the LR learned of the occurrence. The report will be reviewed by the IRB Chair.
- F. Sponsored research agreements may require the PI to notify the sponsor of all unplanned deviations or departures from IRB approved protocol procedures. Sponsor reporting requirements for deviations may differ from UCI IRB reporting requirements. It is the LR's responsibility to comply with the reporting requirements outlined in the signed contract. If investigators have any questions regarding a sponsor's specific deviation reporting requirements, they should check with the sponsor and obtain clarification before the study enrollment begins.
- G. Many sponsors require investigators to follow Good Clinical Practice (GCP) guidelines. The GCP Guidance for Industry states:
"The investigator should not implement any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documented approval/favorable opinion from the IRB...of an amendment, except where necessary to eliminate an immediate hazard(s) to trial subjects, or when the change(s) involves only logistical or administrative aspects of the trial (e.g., change in monitor(s), change of telephone number(s))."

II. Violations

- A. Per policy # 57, a Protocol Violation is defined as: *Accidental or unintentional changes to, or non-compliance with the IRB approved protocol without prior sponsor and IRB approval. Violations generally increase risk or decrease benefit, affect the subject's rights, safety, or welfare, and/or affect the integrity of the research.*
- B. Protocol violations that meet the definition of an unanticipated problem involving risk to participants or others must be reported to the UCI IRB as per Policy # 19 or as noncompliance. Accordingly, Investigators should assess each violation carefully.
- C. Instances of serious and/or continuing noncompliance, according to Policy # 52 must be reported using the Reportable Event - New Information Report within 5 business days of the occurrence or within 5 business days from the date in which the LR learned of the occurrence. The report will be reviewed by the IRB Chair.

References:

45 CFR 46.103

21 CFR 56.108

SACHRP's Recommendations on Protocol Deviations, 2012

Procedure Number: 55.A**Title: Procedure for Protocol Deviations and Violations****Procedure:**

This procedure provides guidance in the reporting requirements and responsibilities of the Investigator and the UC Irvine (UCI) Institutional Review Board (IRB) regarding protocol deviations and/or violations.

I. Lead Researcher (LR) Responsibilities

- A. The LR submits any changes in the protocol prior to implementation to the IRB for review and approval as required by the Federal regulations using the Amendment Application.
- B. The LR monitors research activities for adherence to the protocol and to determine if protocol deviations or violations have occurred.
- C. The LR considers whether or not a deviation or violation meets the definition of an unanticipated problem involving risk to participants or others, as appropriate per Policy # 19.
- D. The LR considers whether or not a deviation or violation involves serious and/or continuing noncompliance, per Policy # 52.
- E. Should the Investigator need to deviate from the protocol for no more than 3 subjects, the Investigator may complete the Reportable Event - Prospective Deviation Request. The request will be reviewed by the IRB Chair for acceptance of the deviation.
- F. Investigators may notify the IRB of deviations by submitting the "Deviation Tracking Log" at the time of continuing renewal. The form will be reviewed by the IRB Chair.
- G. All deviations whether reportable to the UCI IRB or not are to be maintained by the LR.

II. IRB Committee Responsibilities

- A. The IRB will review the Reportable Event - Prospective Deviation Request per current Policy.
- B. The IRB will review all unanticipated problems involving risk to participants or others, as appropriate per Policy # 19.

III. IRB Analyst or Higher Responsibilities

- A. The Analyst will receive deviations or violations submitted by the LR via the Reportable Event - Prospective Deviation Request.
- B. The IRB will review the documentation.
- C. A determination will be made by the Committee of any further actions that are to be taken.

Policy Number: 56

Title: Department of Defense Supported Research

Date of Last Revision: 12/09/2010, 01/21/2011, 05/01/2013, 05/01/2016, 09/23/2020, 09/17/2022

Policy:

In 2006, the Department of the Defense (DoD) enhanced its human subject protection requirements, including the application of those requirements to extramural performers. UCI has signed an assurance with the DoD which requires that UCI apply DoD regulations and policies for the protection of human research participants when conducting, reviewing, approving, overseeing, supporting or managing DoD supported human subject research.

- I. The addendum is recognized by all components of the DoD including the Navy, Army and Air Force. Each branch of the DoD may have their own specific requirements for reviewing research that they support, and these requirements must be followed.
- II. Department of Defense Directive (DoDD) 3216.02 provides the definition of “research” and “experimental subject” including “An activity, for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction.” (32 CFR 219.102(f), reference (c))
- III. Human Subject Research involves the DoD when any of the following apply:
 - A. The research is funded by a component of DoD (e.g.; Navy, Army, Air Force)
 - B. The research involves cooperation, collaboration, or other type of agreement with a component of DoD
 - C. The research uses property, facilities, or assets of a component of DoD
 - D. The subject population will intentionally include personnel (military or civilian) from a component of DoD

DoD policies and requirements do not apply when DoD personnel incidentally participate as subjects in research that is not supported by DoD, and DoD personnel are not an intended population of the research.

- IV. **Application Supplement Form:** Researchers conducting DoD supported research must complete and submit to the IRB the DoD Supplement Form in addition to the protocol materials submitted to the IRB for initial review. The DoD Supplement Form can be found on the Office of Research (OR), Human Research Protection (HRP) Website at: <https://research.uci.edu/human-research-protections/irb-forms/>

- V. **Education**
- A. In addition to completing the UCI HRP education requirements, for research involving the DoD, all personnel who conduct, review, approve, oversee, support, or manage human participant research must *also* meet DoD requirements for research ethics training (initial and continuing education). It is the researcher's responsibility to comply with the DoD requirement.
 - B. Researchers should contact their DoD Liaison for specific information about education requirements.
- VI. **International Research:** When DoD-sponsored research is to be conducted outside of the U.S. or its territories and involves participants who are not United States (U.S.) citizens or DoD personnel, it requires the permission of the host country. The laws, customs, regulations and practices of the host country and those required by UCI, must be followed. An ethics review by the host country, or local DoD IRB with host country representation, is required. Evidence of permission to conduct the research in the host country by certification or local ethics review must be submitted to the UCI IRB prior to initiation of the project.
- VII. **Investigational Drugs, Biologics & Devices** – Certain DoD requirements may not apply when investigational drugs, biologics or devices are used for Force Health Protection in accordance with DoD Directive 6200.2 – Use of Investigational New Drugs for Force Health Protection (Aug. 1, 2000). [See SECNAVINST 3900.39D Para. 4b (5)].
- VIII. **Multisite Research**
- A. For DoD -supported multi-site research, a written agreement must be in place among UCI and the other sites. In the case of an Army supported project, the Army will generate this agreement as a contract. For other DoD components, UCI will work with the researcher to generate the agreement.
 - B. The DoD supplement form must clearly detail the roles and responsibilities of each party, at each site involved in the research.
- IX. **Planned Emergency Research** – For DoD supported research, the Secretary of Defense must waive the requirement of informed consent for planned emergency research.

- X. **Prohibition of Research with Prisoners of War**
 - A. Research involving POWs is prohibited (those persons captured, detained or held under the control of DoD personnel).
 - B. The definition of a “prisoner of war” for the DoD component granting the addendum.
 - 1. Army definition: A prisoner of war is a combatant captured by the enemy and interned until the end of the current conflict.
 - 2. Navy definition: A prisoner of war is a detained person as defined in Articles 4 and 5 of the Geneva Convention Relative to the Treatment of Prisoners of War of August 12, 1949. In particular, one who, while engaged in combat under orders of his government, is captured by the armed forces of the enemy.
- XI. **Reporting Requirements:** Any findings of serious and/or continuing non-compliance will be reported to the appropriate DoD official within 30 days of the determination.
- XII. **Research Involving Human Subjects for Testing of Chemical or Biological Agents** – Research in this category is generally prohibited with narrow exceptions for research for prophylactic, protective or other peaceful purposes that is conducted in accordance with 50 U.S.C. Section 1520a. [See DoD Directive 3216.2 Para. 4.4.5].
- XIII. **Research Related Injury:** DoD supported research requires the research site to make arrangements for the provision of treatment for research related injuries and some DoD components require that participants not bear any costs related to such treatment. Researchers should contact their DoD funding unit’s liaison to determine specific requirements. Also see See HRP Policy and Procedure # 26.
- XIV. **Research/Medical Monitor**
 - A. For research involving more than minimal risk to subjects, an independent medical monitor must be named. Medical monitors should be physicians, dentists, psychologists, nurses or other healthcare providers capable of overseeing the progress of research protocols, especially issues of individual subject / patient management and safety. Medical monitors shall be independent of the investigative team and shall possess sufficient educational and professional experience to serve as the subject advocate.
 - B. The definition of minimal risk based on the phrase “ordinarily encountered in daily life or during the performance of routine physical or physiological examination or tests” shall not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life.
 - i. For example the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).
 - C. The IRB may require that the medical monitor discuss the research progress with the principal investigator, interview subjects, consult on individual cases

or evaluate adverse event reports. Medical monitors must promptly report discrepancies or problems to the IRB.

- D. Medical monitors have the authority to stop a research study in progress, remove individual subjects from a study and take whatever steps are necessary to protect the safety and well-being of research subjects until the IRB can access the medical monitor's report.

XV. Scientific Merit Review

- A. For studies that involve DoD supported research with human subjects, new IRB Applications and substantive modifications to approved research must undergo scientific merit review prior to IRB review.
- B. Independent scientific review requirements are different depending on the branch of the DoD as follows:
 - 1. Navy: Independent scientific review is required per the Secretary of the Navy Instruction 3900.39D
 - 2. For other branch requirements, researchers should contact their program officer.
- C. Scientific review and approval by the Chao Family Comprehensive Cancer Center (CFCCC) Protocol Review and Monitoring Committee (PRMC) and by the IRB in conjunction with the Scientific Review (Statistical Methods) (SR) **does** suffice for this requirement but must occur prior to IRB review.
- D. In the absence of an external review or an established internal review mechanism, researchers should make arrangements with their chair or dean for an *ad hoc* scientific review.

XVI. Special Populations

- A. DoD supported research that affects vulnerable classes of subjects (e.g., fetuses, pregnant women, human in vitro fertilization, prisoners or children) shall meet the protections of 45 CFR Part 46, Subparts B, C, and D.
- B. Researchers must ensure additional protections for military research subjects to minimize undue influence.
- C. If research involves cognitively impaired adults, there must be a direct benefit to the subject.
- D. Researchers must comply with DoD limitations on research when consent by a legally authorized representative is proposed.

XVII. Studies Involving DoD Personnel

- A. When research involves U.S. military personnel, policies and procedures require limitations on dual compensation as follows:
 - 1. Prohibit an individual from receiving pay from more than one position for more than 40 hours of work in one calendar week;
 - 2. The policy includes temporary, part-time, and intermittent appointments.
 - 3. Individuals may receive compensation for research activities if the research activities take place outside of scheduled work hours.
- B. When research involves U.S. military personnel policies and procedures include additional protections for military research participants to minimize undue influence as follows:
 - 1. Officers are not permitted to influence the decision of their subordinates;

2. Officers and senior non-commissioned officers may not be present at the time of recruitment;
3. Officers and senior non-commissioned officers have a separate opportunity to participate;
4. When recruitment involves a percentage of a unit, an independent ombudsman is present.

XVIII. Studies Involving DoD Personnel and the Use of Surveys

- A. Surveys involving DoD personnel, including U.S. military personnel, typically require DoD survey review and approval. When appropriate, the research project is reviewed and approval by the IRB prior to DoD approval. This includes:
 1. Research where DoD personnel and civilian personnel (working with the DoD) are asked to complete surveys; but not when researchers funded by the DoD are conducting survey on non-DoD personnel.
 2. Specific DoD component requirements are as follows:
 - a. Army: Researchers must request approval via the [“Request for Approval for Approval to Survey Department of Army Form”](#)
 - b. Navy: Researchers must refer to the [Navy Survey Policy](#).
 - c. Researchers should contact their program officer for Air Force requirements.
 - d. DoD- Wide Research: Researcher must follow the [DoD Instruction on Surveys of Military Personnel \(surveys across branches of the DoD\)](#).

- XIX. Waiver of Informed Consent:** If the research subject meets the definition of “experimental subject”, a waiver of the consent process is prohibited unless a waiver is obtained from the Secretary of Defense.

References:

32 CFR 219

DoD: SECNAVINST 3900.39D, para 8c(6)

DoDD 3216.02, Sect. 4.4.3, 4.4.3.2.

DoD Instruction 3210.7

DoD Instruction 6200.02

AFRL Instruction 40-402

Reference for Researchers: [Obtaining Approval for a Survey of U.S. Army Personnel](#)

Procedure Number: 56.A**Title: Procedure for Researchers Submitting an IRB Application that Involves DoD****Procedure:**

The purpose of this procedure is to provide guidance for compliance with Department of the Defense (DoD) enhanced human subject protection requirements.

I. Lead Researcher (LR) Responsibilities

- A. New IRB Applications and substantive Amendments to approved research must undergo scientific merit review prior to IRB review.
- B. Submission Documentation
 - 1. Investigators conducting, DoD supported research with human subjects (including research that qualifies for exempt status) must complete and submit the following documents with their application:
 - a. Completion of Education and Training
 - b. Independent Scientific Review
 - c. UCI IRB Department of Defense Supplement Form
 - d. Lead Researcher and Co-investigator CVs
 - e. Data Collection Forms/Case Report Forms
 - f. FDA letter for IND or IDE (as applicable)
 - g. FDA Form 1571 and FDA Form 1572 (as applicable)
 - h. Survey research requirements (as applicable)
 - i. A waiver of consent (as applicable) obtained from the Secretary of Defense.
- C. Researchers must follow UCI policies and procedures for addressing financial and other conflicts of interest. (See HRP Policy # 25.)
- D. Post-Approval Instructions
 - 1. Documentation: Principal Investigators (PIs) and the UCI HRP are responsible for maintaining certain documentation in their files. PIs are also responsible for submitting documentation to DoD prior to starting an IRB-approved study and upon subsequent reviews by the IRB (addenda, continuing reviews, etc.). DoD uses such documentation to conduct a “headquarters-level administrative review.” DoD HRPP requires certain IRB documentation that is not maintained by the PI (such as IRB meeting minutes). These items will be sent directly from the UCI HRP to DoD. UCI HRP will notify the PI when these documents are sent.
 - 2. Department of Navy (DoN) documentation requirements:
 - a. Office of Naval Research (ONR)
 - b. Department of the Navy Human Research Protections Program (DON HRPP)
- E. Contracts and Awards - In addition to requirements set for the by the funding agency, researchers conducting human subject research supported by the DoD or its components must comply with contracting requirements and processes required by UCI Sponsored Projects Administration.

- F. The contact information for submission to ONR is provided at the ONR website above. The contact information for submission to the DoN HRPP is:

Department of Navy Human Research Protection Program (DON HRPP)

Phone: 703-681-9269

E-Mail: usn.ncr.bumedfchva.mbx.don-hrpp@mail.mil

- G. Continuing Education
1. The DoD requires researchers to complete continuing human subject protections training every 3 years.
- H. Amendments to Approved Research
1. When submitting amendments to previously approved research, researchers should review the Defense Supplement to ensure that it still accurately reflects the research. A revised supplement should be submitted (and any additional documentation) if necessary.
 2. If the amendment involves substantive changes (e.g., new procedures, a new subject population), evidence of scientific review and approval is required prior to IRB review.

II. IRB Committee Responsibilities

- A. The materials listed in the Lead Researcher's section of this policy will be reviewed by the IRB at subcommittee or at a convened IRB meeting depending on the level of risk to participants.
- B. In addition to the above materials Committee member reviewers must provide their determinations to the HRP team.
- C. Written determination by a designated institutional official (other than investigators) whether research meets criteria for exemption.
- D. The IRB determines the review interval appropriate to the degree of risk, but not less than once per year.
- E. The IRB reviewer(s) may request that the study be approved, minor modifications required, tabled for re-review by subcommittee, tabled for review by full Committee.
- F. When revisions are requested, the modified documents are re-reviewed and, if acceptable, approval is granted.
- G. The Chairperson or his/her Designee verifies and signs the Approval Letter.

III. HRP Staff Responsibilities

- A. The Administrator will pre-review the DoD Supplement Form and request any necessary revisions and/or documentation to meet the DoD requirements.
- B. The HRP team prepares relevant documents and LR responses to pre-review concerns during the administrative review process.
- C. The Administrator will assist reviewers in obtaining additional information that may be requested regarding the DoD requirements from the LR.
- D. Letters requesting revisions from the Reviewer and approval letters are drafted using the appropriate template which includes a citation to the specific permissible category or categories justifying the expedited review.
- E. New approvals, amendments, and renewals are processed according to

corresponding IRB policies and procedures.

- F. Appropriate database entries are completed in the electronic IRB database.
- G. Approved documents are processed.

Policy Number: 57

Title: Veterans Affairs Supported Research

Date of Last Revision: 08/21/24 – NEW POLICY!

Policy:

Within the Department of Veterans Affairs (VA) is the Veterans Health Administration (VHA). The VHA is America's largest integrated health system, providing care at over 1,300 health facilities. The VHA is also the only organizational component of the VA that can conduct human subject research. The VHA Office of Research and Development (ORD) is responsible for the creation of human research policies. This policy addresses the human subject research protections considerations when the UCI IRB reviews a human subject research protocol supported by the VHA.

I. Human Research Protections

- A. The VHA has the ability to fund veteran-centric research led by VA investigators. To serve as a VA investigator, one must be a VA employee.
- B. The VHA Directive 1200.05(3): Provides the requirements for the protection of human research subjects. This is generally aligned with Office for Human Research Protections (OHRP) guidance.
- C. The VA also aligns with the 2018 Common Rule at 38 CFR 16. The 2018 Common Rule applies to VA research regardless of funding.
- D. The VA follows the Privacy Rule (Health Insurance Portability and Accountability Act of 1996)
- E. The VA Long Beach Healthcare System (VALBHS) Medical Center Director is the individual legally authorized as a Signatory Official to commit VALBHS to an Assurance.

II. UCI Responsibilities

- A. If the UCI-IRB determines a given VALBHS project does not constitute research, does not constitute human subjects research, or that a particular site is not engaged in human subjects research pertaining to that project, the UCI PI will provide written correspondence concerning its decision to the VALBHS Principal Investigator (PI) via the IRB electronic submission system.
- B. The UCI-IRB Research Office will seek feedback from the VALBHS PIs, and VALBHS on the efficiency and effectiveness of UCI-IRB operations as part of a continuous quality improvement process.
- C. If UCI obtains accreditation of the Human Research Protection Program (HRPP) from an accrediting body but fails to maintain accreditation, UCI will notify the VALBHS and ORD in writing within ten (10) business days.
- D. The UCI-IRB Research Office and UCI-IRB will maintain all VALBHS project documentation, membership documents, and other relevant records in accordance with UCI-IRB SOPs, and all VA and other Local, State, and Federal requirements.

III. **Required Ancillary Reviews**

- A. The VA requires both an initial privacy and information security review, prior to IRB review.
- B. A final privacy and information security review occurs prior to VA Research and Development Committee (R&D) review.
- C. The VA facility is responsible for ancillary reviews, including Conflict of Interest, and an assessment of the Principal Investigator and Study Team (e.g., expertise, training, including human subject training, credentialed, etc.) not the reviewing IRB.

IV. **Single IRB**

- A. The VA is agreeable to single IRB; Prior to the 2018 Common Rule, the VA created a central IRB for ORD-funded multi-site studies.
- B. Exceptions from single IRB may be requested from the ORD by VA facility research leadership (i.e., not the investigator).
- C. The VA IRB cannot serve as the IRB of record for any non-VA site.
- D. Collaborative research involving non-VA institutions may not be undertaken without a signed written agreement (e.g., a Cooperative Research and Development Agreement [CRADA] or a Data Use Agreement) that addresses such issues as the responsibilities of each party, the ownership of the data, and the reuse of the data for other research. Any use or reuse of data must be consistent with the protocol, the informed consent document, and the Health Insurance Portability and Accountability Act (HIPAA) authorization.

V. **Greater than Minimal Risk Research**

- A. Human research protocols involving greater than minimal risk must include a Data Safety Monitoring Board or Committee. The meeting frequency, as well as the scope of the Board or Committee must be described in the protocol.
- B. Any minutes, reports or records related to the Data Safety Monitoring Board or Committee will be accessible to the VA.

VI. **Informed Consent Considerations**

- A. Informed consent documents must be both signed and dated by the subject or the subject's legally authorized representative.
- B. Electronic consent is allowable should the process confirm to VA requirements for use of electronic signatures. The VA requirements for use of electronic signatures must meet governmental requirements for authenticity and identification.
- C. Broad consent can only be used when identifiable data or biospecimens are collected solely for *research* purposes in accordance with the requirements in section 17.f of the VHA Directive 1200.05.¹
- D. Use of the VA ICF template is highly recommended to ensure all the VA mandate elements and boiler plate language is in place.

¹ The VA Long Beach does not allow for the use of Broad Consent.

VII. **Required Consent Language**

A. ORD Policy mandates the following consent language, as applicable:

1. A statement that the VA will provide treatment for research related injury.
2. A statement that informs VA research subjects that their insurance will not be charged for any costs related to the research. Note: co-payments for standard medical care or services not part of the research procedures may still apply.
3. When photos, video and/ or audio recordings are taken or obtained exclusively for research purposes:
 - i. A description of any photographs, video, and / or audio recordings to be taken or obtained for research purposes;
 - ii. How the photographs, video, and / or audio recordings will be used for the research; and
 - iii. Whether the photographs, video, and / or audio recordings will be disclosed outside of the VA
4. When the VA conducts a study protected by a Certificate of Confidentiality (CoC):
 - i. When information about the subject's participation will be included in the VHA medical record, information must be given to the prospective subjects as part of the informed consent process that informs them of this research component.
 - ii. For studies that mandate informed consent, the consent document approved by the IRB must include the statement that a study has a CoC.

B. Recruitment:

1. If prospective participants are being contacted by telephone, the study team must make initial contact in person or by letter prior to any telephone contact and refer to those prior contacts when phoning the participant unless there is written documentation that the subject is willing to be contacted by telephone about the study in question or a specific kind of research.
2. The initial contact must provide a telephone number or other means that the potential participant can use to verify the study constitutes VA research.
3. Later Contact – the research team may use telephone calls to the participant by referring to previous contacts and when applicable, the information provided in the informed consent form.
4. The scope of telephone contacts with the participant is limited to topics outlined in IRB-approved protocols and informed consent forms.

VIII. **HIPAA**

- A. The VHA is a covered entity under HIPAA.
- B. The VA will handle the review of any HIPPA human subject research considerations.
- C. VA Form 10-0493 must be used; a standalone HIPAA authorization document is required. The HIPAA authorization must not be combined with the consent document.
- D. The VA facility must ensure the HIPAA authorization language is valid.
- E. For collaborative research that involves both UCI and the VA, the VA will serve as the privacy board for the VA site. The VALBHS Privacy Officer (PO) and Information System Security Officer (ISSO) Representatives will perform the required privacy and information security reviews and provide these reviews to the IRB with submissions.

IX. **Reportable Events**

- A. Reviewing serious adverse events, unanticipated problems involving risks to subjects or others, protocol deviations, complaints, Research Compliance Officer (RCO) audit reports, and any audit reports from sponsors, VA oversight bodies or other oversight agencies, regarding projects for which the UCI-IRB is serving as the IRB of record, in accordance with VHA Directive 1058.01 and VHA Directive 1200.05.
- B. Reportable events must be reported to OHRP even if not supported by an agency signed onto the Common Rule. Due to their Federalwide Assurance (FWA), reportable events that occur on non-exempt human subject research mandate reporting.
- C. UCI Principal Investigator (PI) will provide timely written notice, usually within seven (7) calendar days, to VALBHS PI of UCI-IRB determinations involving the conduct of a research project at VALBHS. This includes contingent approvals and requested amendments, etc.
- D. The VA has specific reporting requirements as follows:
 - 1. Death/s at local site/s, both unanticipated and related to the research must be reported to the IRB "immediately."
 - 2. All local reportable events and unanticipated serious adverse device effects must be reported to the IRB within 5 business days.
 - 3. Protocol deviations and other non-reportable events must be noted in the research file.
 - 4. Local breaches of confidentiality and security must be reported to the IRB within 1 hour, as well as to the necessary privacy offices at the VA.
- E. It is noted that UCI IRB however requires the submission of those events that appear reportable per federal regulations (e.g., unanticipated problems, serious and continuing noncompliance, suspension and terminations of research).

X. **Application Supplement Forms:**

- A. **General DoD:** Researchers conducting DoD supported research must complete and submit to the IRB the DoD Supplement Form in addition to the protocol materials submitted to the IRB for initial review. The DoD Supplement Form can be found on the Office of Research (OR), Human Research Protection (HRP) Website at: <https://research.uci.edu/human-research-protections/irb-forms/> <https://research.uci.edu/wp-content/uploads/WCG-405-Worksheet-Addl-Criteria-DOD.pdf>
- B. **Investigational Drugs:** VA Form10-9012, Investigational Drug Information Record is to be provided at initial application when investigational drugs are involved.

References:

A special thank you to Karen Jeans, Director for Regulatory Affairs for the Office of Research Protections, Policy and Education, Department of Veteran Affairs, whose Smart IRB presentation from March 2024 has been heavily referenced in the creation of this policy.

38 CFR 16

38 CFR 17.85

VHA Directive 1200.05(3) Requirement for the Protection of Human Subjects in Research: <https://www.va.gov/vhapublications/>

VHA Directive 1200.05(3), Paragraph 17.d.(10)

VHA Directive 1200.05(3), Paragraph 17.e.(10)

VHA Directive 1200.05(3), Paragraph 17.k.(10)

VHA Directive 1200-01(1) R&D Committee: <https://www.va.gov/vhapublications/>
<https://grants.nih.gov/faqs>

https://www.research.va.gov/programs/orppe/irb_relationships.cfm

<https://www.research.va.gov/programs/orppe/Checklist-for-VA-Facilities-Using-Independent-Commercial-IRBs-ICDs-and-Combined-ICD-HIPAA-Authorization.docx>

<https://www.research.va.gov/programs/orppe/VA-HIPAA-Authorization-Requirements-When-Using-an-Independent-Commercial-IRB.docx>

<https://www.research.va.gov/programs/orppe/VA-Specific-and-Selected-2018-Common-Rule-Informed-Consent-Requirements-When-Using-an-Independent-Commercial-IRB.docx>

<https://www.research.va.gov/programs/orppe/ORD-IRB-Reliance-Request-Form.docx>

Policy Number: 58

Title: UCI HRP Policy and Procedure Glossary

Date of Last Revision: 10/12/2007; 07/22/2010; 08/08/2011; 01/11/2013; 05/01/2013; 06/18/2013; 10/12/2016; 12/10/2019; 09/17/2022; 08/21/2024

The HRP policy and procedure glossary is an alphabetized listing of specialized terms with their meanings. This glossary will assist the reader to understand new or uncommon vocabulary and specialized terms used in the UCI HRP Policies and Procedures.

1. **Administrative Hold**: An action initiated by the Researcher in response to an IRB request to place specific research activities on hold temporarily pending additional information.
2. **Administrative Review**: The purpose of an Administrative Review is to determine whether the allegation of regulatory non-compliance can be substantiated and whether it requires further review by a regulatory oversight committee. An Administrative Review is initiated when an allegation is received from an individual; it is deemed by the Office of the VCR or the Chair of a regulatory oversight committee that a review is necessary, or when informal or formal monitoring activities reveal potential regulatory non-compliance.
3. **Adverse Event (AE)**: An untoward or undesirable experience associated with research.
4. **Advertising**: A public announcement usually by a printed notice or voice or data broadcast that describes a research study including contact information. Typically this is used for recruitment purposes for a research study.
5. **Amendment**: Any change to an IRB-approved study protocol regardless of the level of review it receives initially.
6. **Anonymous Data**: Information that was previously recorded or collected without any of the 18 identifiers as defined by HIPAA, and no code is assigned which would allow data to be traced to an individual.
7. **Assent**: An individual's affirmative agreement to participate in research obtained in conjunction with permission from the individual's parents or legally authorized representative. Mere failure to object should not, absent affirmative agreement, be construed as assent.
8. **Assurance**: A contract or agreement that establishes standards for human subjects research as approved by the Office for Human Research Protections (OHRP).
9. **Belmont Report**: A statement of basic ethical principles governing research involving human subjects issued by the National Commission for the Protection of Human Subjects in 1978.
10. **Benefit**: A valued or desired outcome; an advantage.
11. **Bonus Payment**: Compensation tied to the rate or timing of recruitment. Examples of bonus payments include but are not limited to the following: The sponsor announces that the highest enrolling site in the nation will receive a \$10,000 bonus; The sponsor offers to pay an additional \$10,000 to any site that enrolls five participants within a week; The sponsor offers to pay an additional \$10,000 to any site that fulfills its recruitment target by the end of the month; The sponsor offers to pay an additional \$1,000 for any subject who agrees to enroll within one day of initial contact.
12. **Cannabis Research Review Committee (CRRC)**: A UCI Committee charged with reviewing marijuana research or industrial hemp, or research that is sponsored by the marijuana industry. CRRC review is recommended before clinical research procedures are initiated. CRRC review will assess the feasibility of study conduct and help to ensure compliance related to research involving cannabis.
13. **Certificate of Confidentiality**: An advance grant of confidentiality issued by the NIH that provides protection against compulsory disclosure, such as a subpoena, for research data in studies that involve data collection about sensitive issues (such as illegal behavior, alcohol or

drug use, or sexual practices or preferences) that require protection of confidentiality beyond preventing accidental disclosures.

14. **Child**: Person who has 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. In California, the individual that meets this definition is a person under 18 years of age.
15. **Children**: According to Federal regulations 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 will be conducted.” According to California law, the legal age of consent is 18 years of age.
16. **Clinical Engineering**: A UCI Committee charged with reviewing the use of medical equipment in an area that operates under the hospital's license and/or equipment used on the hospital's patients and research subjects. Securing CE approval is the responsibility of the LR and is required before clinical research procedures can be initiated.
17. **Clinical Investigation**: Any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the FDA under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or is not subject to requirements for prior submission to the FDA under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.
18. **Coded Information/Data**: For the purposes of this policy, identifying information that would enable the Investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof and a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.
19. **Cognitively Impaired**: Having a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorder), an organic impairment (e.g., dementia) or a developmental disorder (e.g., mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Others, including individuals under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and individuals with severely disabling physical handicaps, may also have diminished ability to make decisions in their best interest.
20. **Compensation for injury**: Payment or medical care provided to participants injured in research; this does not refer to payment (remuneration) for participation in research.
21. **Competent**: Term used to denote capacity to act on one's own behalf; the ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice.
22. **Confidentiality**: Pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others without permission in ways that are inconsistent with the understanding of the original disclosure.
23. **Conflict of Interest**: A situation where an investigator's or IRB member's outside financial interest(s) or obligation(s) bias or has the potential to bias a research project.
24. **Conflict of Interest Oversight Committee (COIOC)**: A Committee mandated by State, Federal and University requirements. The COIOC is charged with ensuring that an investigator's personal interest in, or commitment to, entities outside the University's purview does not compromise or appear to compromise his/her objectivity in performing a research project, in mentoring students involved in a research project or in reporting the results of a research project conducted under the aegis of the UC. COIOC recommends action to the Vice Chancellor for Research (VCR).
25. **Continuing Non-compliance**: A pattern of noncompliance that indicates an inability or unwillingness to comply with applicable laws, regulations, or institutional policies pertaining to the protection of human subjects and/or with the requirements or determinations of an IRB.

26. **Continuing Review:** Periodic review of research activities necessary to determine whether the risk/benefit ratio has changed, whether there are unanticipated findings involving risks to participants or others, whether any new information regarding the risks and benefits should be provided to participants, and to ensure that the protocol remains in compliance with all federal regulations, state laws and UC/UCI policies and procedures.
27. **Cooperative Research:** (45 CFR 46.114 (a)): Cooperative research projects are those projects covered by this policy that involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy.
28. **Coordinating Center:** An institution, department, or center, which agrees to be responsible for the conduct, administrative, or coordinating functions of a multi-center research project.
29. **Covered Entity:** A health plan, a health care clearinghouse, or a health care provider who transmits health information and is therefore subject to the HIPAA regulations. For the purpose of this policy, the University of California is a hybrid Covered Entity with both covered and non-covered functions. All UC covered entities constitute a single health care component (SHCC). Research at the University of California is not a covered function under the HIPAA Privacy Rule. UC's employees/workforce members, when acting solely in their capacity as researchers, are not considered a part of the SHCC. When a UC researcher is also a health care provider or a member of a medical center's workforce, the Privacy Rule applies to the researcher's activities; thus the UC researcher must comply with all requirements of the Privacy Rule.
30. **DHHS:** The Department of Health and Human Services.
31. **Data and Safety Monitor (DSM):** An individual assigned to conduct interim monitoring of accumulating data from research activities to assure the continuing safety of research participants, relevance of the study question, appropriateness of the study, and integrity of the accumulating data. The individual should have expertise in the relevant medical, ethical, safety and scientific issues.
32. **Data and Safety Monitoring:** A plan to oversee the implementation of a study protocol for compliance monitoring.
33. **Data and Safety Monitoring Board/Committee (DSMB or DSMC):** A formally appointed independent group consisting of at least three (3) members assigned to conduct interim monitoring of accumulating data from research activities to assure the continuing safety of research participants, relevance of the study question, appropriateness of the study, and integrity of the accumulating data. Membership should include expertise in the relevant field of study, statistics, and research study design.
34. **Data and Safety Monitoring Plan (DSMP):** A DSMP describes how the LR plans to oversee the research participant's safety and welfare and how adverse events will be characterized and reported. The intensity and frequency of monitoring should be tailored to fit the expected risk level, complexity, and size of the particular study.
35. **Data Use Agreement:** An agreement between UCI and the recipient of the PHI. This agreement establishes who is permitted to use or receive the limited data set; and provides that the limited data set recipient will:
- Not use or further disclose the information other than as permitted by the data use agreement or as otherwise required by law;
 - Use appropriate safeguards to prevent use or disclosure of the information other than as provided for by the data use agreement;
 - Report to the covered entity any use or disclosure of the information not provided for by its data use agreement of which it becomes aware;
 - Ensure that any agents, including a subcontractor, to whom it provides the limited data set agrees to the same restrictions and conditions that apply to the limited data set recipient with respect to such information; and
 - Not identify the information or contact the individuals.
36. **De-identified Health Information:** Health information that has been stripped of all 18

identifiers as defined by HIPAA (See Appendix A), so that the information could not be traced back to an individual. De-identified data also pertains to health information that has been assigned and retains a code or other means of identification provided that:

- a. The code is not derived from or related to the information about the individual;
- b. The code could not be translated to identify the individual; and
- c. The covered entity (as described above) does not use or disclose the code for other purposes or disclose the mechanism for re-identification.

37. **Department of Health and Human Services (DHHS):** The United States government's agency for protecting the health of all Americans and providing essential human services, especially for those who are least able to help themselves.
38. **Deviation:** Accidental or unintentional change to the research protocol that does not increase risk or decrease benefit or have a significant effect on the participant's rights, safety or welfare, or on the integrity of the data. Deviations may result from the action of the participant, researcher, or staff. *This definition may not match the Principal Investigator's or Sponsor's definition.* Examples: a rescheduled study visit, an omitted routine safety lab for a participant with previously normal values; or failure to collect an ancillary self-report questionnaire data (e.g., quality of life).
39. **Directed Audit:** These audits are conducted by the IRB Compliance Team to assess the Investigator's compliance with federal regulations, state and local laws, and UCI IRB policies and procedures. These audits of IRB approved research studies are in response to identified concern(s). Concerns may be identified by an IRB Committee, an external source (e.g. OHRP, FDA or Sponsor), or an internal source (e.g. participant, family member, or Institutional personnel).
40. **Disclosable Financial Interests:**
 - a. Ownership interest, stock, stock options, or other financial interest related to the research, unless it meets all four tests:
 1. Less than \$10,000 when aggregated for the immediate family and
 2. Publicly traded on a stock exchange and
 3. Value will not be affected by the outcome of the research and
 4. Less than 5% interest in any one single entity.
 - b. Compensation related to the research, including salary, consultant payments, honoraria, royalty payments, dividends, loans, or any other payments or consideration with value, including payments made to the University Health Sciences Compensation Plan, unless it meets both of the following tests:
 1. Less than \$10,000 in the past year when aggregated for the immediate family and the
 2. Amount will not be affected by the outcome of the research.
 - c. Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright or licensing agreement.
 - d. Board or executive relationship (e.g., director, officer, partner, or trustee) related to the research, regardless of compensation.
41. **Dissent:** An individual's negative expressions, verbal and/or non-verbal, that they object to participation in the research or research activities.
42. **Dual Use Research Committee (DURC):** Research yielding new technologies or information with the potential for both benevolent and malevolent applications is referred to as "dual use research." The Institutional Review Entity (IRE) is charged with oversight of, and education on, life sciences research involving the use of potential DURC agents at UCI. The Committee advises and reports to the Chancellor through the Vice Chancellor for Research.
43. **Emergency Research:** Research conducted in participants who are in a life-threatening or emergent situation, where available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
44. **Emergency Treatment IDE:** A mechanism through the FDA for providing eligible participants

with investigational devices for the treatment of an immediate serious or life-threatening illness for which there are no satisfactory alternatives.

45. **Emergency Treatment IND:** A mechanism through the FDA for providing eligible participants with investigational drugs, agents, or biologics for the treatment of an immediate serious or life-threatening illness for which there are no satisfactory alternatives.
46. **Emergency Use:** The use of an investigational drug, agent, biologic, or device with a human subject in an immediate serious life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval.
47. **Engaged in Human Subjects Research:** An individual is “engaged” when they will interact with living individuals and/or will have access to subject identifiable records or data for the purposes of study performance. For more specific information on the definition of engagement, including examples of engagement and non-engagement, review [OHRP’s Guidance document](#).
48. **Epidemiology and Infection Prevention Committee (EIP):** Research protocols involving the study of devices, biologic products or infectious agent in humans on the UCIMC campus or any UCI-affiliated clinical site (including clinical sites on campus or external affiliated sites) require review by the EIP. Securing EIP approval is the responsibility of the Lead Researcher.
49. **Exempt Review:** Studies determined by the IRB to meet the exempt criteria as defined by the Federal regulations.
50. **Expedited Review:** Studies determined by the IRB to meet the expedited criteria as defined by the Federal regulations.
51. **Expired Study:** When continuing review of the research does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically. The study expires on the date specified on the approval letter and the informed consent document. No research activities can occur after the expiration date.
52. **Export Control Review Process (XP CTRL):** At UCI, XP CTRL review is recommended as part of considering the feasibility of study conduct and prior to research initiated in countries subject to Office of Foreign Assets Control (OFAC) sanctions (e.g., Cuba, Iran, North Korea and Syria). Securing EXP CTRL review is the responsibility of the LR.
53. **External Adverse Events:** From the perspective of a UCI investigator engaged in a multi-center clinical trial, external adverse events are those adverse events experienced by subjects enrolled by investigators at other institutions engaged in the clinical trial (not under UCI IRB authority).
54. **FDA:** The DHHS Food and Drug Administration. The FDA oversees the safety of foods, drugs, devices, biologics and cosmetics for human use, and enforces DHHS regulations (21 CFR Parts 50 and 56) for the protection of human subjects and the general standards for the composition, operation, and responsibility of an Institutional Review Board (IRB) that reviews clinical investigations.
55. **Federalwide Assurance:** A contract or agreement that formalizes the institution's commitment to protect human subjects as approved by the Office for Human Research Protections (OHRP). The Federal Policy for the Protection of Human Subjects requires that each institution “engaged” in Federally-supported human subject research file an “Assurance” of protection for human subjects. The requirement to file an Assurance includes both “awardee” and collaborating “performance site” institutions. Per Federal Policy, awardees and their collaborating institutions become “engaged” in human subject research whenever their employees or agents (i) intervene or interact with living individuals for research purposes; or (ii) obtain, release, or access individually identifiable private information for research purposes.
56. **Fetus:** The product of conception from implantation until delivery.
57. **Finalize:** A term used to describe the point where consent is obtained from the subject. If a signed consent form is required the subject and researcher sign the form. If signed consent is not required the researcher obtains oral agreement to participate. A researcher that finalizes the consent process orients the subject to the study, answers any questions and signs the consent form, when applicable.

58. **Finder's Fee:** Compensation of any type (cash, office or medical supplies, educational stipends, gift certificates, priority in authorship listings, travel reimbursement, or anything else of value) to an individual made in exchange for referral or recruitment of a participant to a research study. Such payments, generally, are made to residents, physicians, nurses, or others in a position to identify potential participants that might qualify for enrollment into a study. The fee is paid only for participants who are actually enrolled into the study.
59. **Food and Drug Administration (FDA):** The FDA is the federal oversight agency responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.
60. **Good Clinical Practice (GCP) Training for National Institutes of Health (NIH) Research:** On September 16, 2016, the NIH issued a new policy that specifies NIH-funded investigators and staff should be trained in GCP. The NIH policy states that all NIH-funded investigators and staff "who are involved in the conduct, oversight, or management of clinical trials should be trained in Good Clinical Practice (GCP), consistent with principles of the International Conference on Harmonisation (ICH) E6 (R2)." UCI HRP offers several CITI courses that meet the NIH requirement.
61. **Guardian:** An individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care. In California, guardians are considered legally authorized representatives.
62. **HIPAA Authorization:** A customized document, usually as a part of the informed consent document, that gives UCI permission to use specified protected health information (PHI) for a specific purpose, or to disclose PHI to a third party specified by the individual other than for treatment, payment or healthcare operations.
63. **Health Insurance Portability and Accountability Act (HIPAA) Research Tutorial:** An internet-based tutorial developed by the University of California (UC) designed for researchers involved with accessing, creating or disclosing Protected (Personal) Health Information (PHI). All Lead Researchers and research personnel who access, create or disclose PHI are required to complete the tutorial.
64. **Human Fetal Tissue:** Tissue or cells obtained from a dead embryo or fetus after a spontaneous or induced abortion, or after a stillbirth.
65. **Human Research Tutorial:** An internet-based module on the protection of human participants in research. UCI offers two versions of the Basic Human Research Training course through the Collaborative Institutional Training Initiative (CITI): one for Biomedical Investigators and one for Social & Behavioral Investigators. Individuals choose the course that best matches their research activities. A CITI Refresher course is required every 5 years to ensure ongoing education about human research protections. There are also two versions of the refresher course.
All Lead Researchers and research personnel with direct intervention or interaction with participants or access to private, identifiable data are required to complete the tutorial.
66. **Human Stem Cell Research Oversight Committee (hSCRO):** A UCI Committee assures human stem cell activities are conducted in accord with local, state and federal regulations. hSCRO considers the ethical and social issues presented by human stem cell activities and reviews the scientific/scholarly merit of human stem cell activities. hSCRO review and approval is required prior to IRB review.
67. **Human Subject:** A living individual about whom a Investigator conducting research obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens; or an individual who is

or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient.

- a. **Intervention:** Includes both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subjects' environment that are performed for research purposes.
- b. **Interaction:** Includes communication or interpersonal contact between an Investigator or his/her research staff and the research participant or their private identifiable information.
- c. **Private Information:** Includes information about behavior that occurs in a setting in which an individual can reasonably expect that no observation or recording is taking place. It includes information, which has been provided for specific purposes by an individual, and the individual can reasonably expect will not be made public (e.g., a medical record). Private information must be individually identifiable in order to be considered information to constitute research involving human participants. This may include identifiable private information obtained from a primary participant about a third party.

- 68. **Human Research Protections (HRP):** The UCI Office of Research Administration (ORA) is an administrative unit of the Office of Research. Research Protections (RP) and Sponsored Projects are divisions of OR. Human Research Protections (HRP) is a unit within Research Protections (RP). For individuals engaged in human subject research, Human Research Protections (HRP). HRP facilitates and promotes the ethical involvement of human subjects in research by providing administrative support to the IRBs, and consultative services to Investigators and their research staff.
- 69. **Human Subject Research:** Any research or clinical investigation that involves human subjects.
- 70. **Humanitarian Device Exemption (HDE):** Exemptions granted by the FDA in which the manufacturer is not required to provide the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose prior to marketing. HDE allows for the device to be used in clinical treatment as well as clinical investigation.
- 71. **Humanitarian Use Device (HUD):** A device that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals per year in the United States.
- 72. **IRB:** Institutional Review Board established in accord with DHHS and FDA regulations.
- 73. **IRB Approval/Registration:** The determination of the IRB that the human subjects research has been reviewed and may be conducted by or for UCI within the constraints set forth by the IRB and by other institutional and Federal requirements.
- 74. **IRB Committee Member:** An individual serving as an IRB Committee Member including Chairs, the IRB, alternates or expert consultants regardless of voting privileges.
- 75. **IRB of Record:** An IRB is considered the IRB of record when it assumes IRB responsibilities for another institution and is designated to do so through an approved Assurance with OHRP. A Memorandum of Understanding is required, designating the relationship, for UCI to serve as the IRB of Record.
- 76. **IRB Reliance Agreement:** A formal, written document that provides a mechanism for an institution engaged in research to delegate IRB review to an IRB of another institution. Institutions may use different descriptive terms, (e.g., reliance agreement, cooperative agreement, IRB authorization agreement (IAA), or memorandum of understanding (MOU)). Agreements may cover single studies, categories of studies, or all human subjects research under an organization's Federalwide Assurance (FWA).
- 77. **Immediate Family Member:** Spouse, domestic partner, or child.
- 78. **Industry-Supported:** When a commercial entity contributes to the design or conduct of the study (as evidenced by a sponsor's protocol, sponsor's identification number and/or Investigator's brochure); coordinates the study as a multi-center trial; reimburses UCI or a UCI Investigator for costs associated with conducting the trial; or will have access to, or will publish or present the data gained from conducting the trial.
- 79. **Informal Resolution:** Oversight of minor or sporadic non-compliance incident by the IRB

Chair or Committee. Informal resolution is typically approved by the IRB Chair and is reported to IRB members at monthly convened meeting.

80. **Informed Consent**: An individual's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure.
81. **Institutional Biosafety Committee (IBC)**: A Committee required by Institutions receiving funding from the National Institutes of Health (NIH) for research involving recombinant DNA molecules. It is further charged with reviewing and approving research conducted with microorganisms pathogenic to humans, plants, or animals. The IBC also provides guidance on the proper acquisition, handling, transfer, and disposal of potentially hazardous or regulated biological materials.
82. **Institutional Official (IO)**: The individual who has the authority to sign the institution's Assurances, making a commitment on behalf of the institution that federal regulations and policies will be followed.
83. **Institutional Review Board (IRB)**: A specifically constituted review body established or designated by an entity to protect the rights and welfare of human subjects recruited to participate in biomedical or social science/behavioral research.
84. **Interaction**: Communication or interpersonal contact between investigator and subject.
85. **Internal Adverse Events**: From the perspective of a UCI investigator engaged in a multi-center clinical trial, *internal adverse events* are those adverse events experienced by subjects enrolled by the UCI investigator(s) (under UCI IRB authority). In the context of a single-site study, all adverse events would be considered *internal adverse events*.
86. **Intervention**: Both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
87. **Investigational Agent**: A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial. This includes products with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, products used for an unapproved indication, or products used to gain further information about an approved use.
88. **Investigational Device**: Any healthcare product that does not achieve its primary intended purposes by chemical action or by being metabolized. A medical device that is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. Investigational use also includes clinical evaluation of certain modifications or new intended uses of legally marketed devices.
89. **Investigational Device Exemption (IDE)**: A FDA approved IDE permits a device that otherwise would be required to comply with a performance standard or to have pre-market approval to be shipped lawfully for the purpose of conducting investigations of that device.
90. **Investigational Drugs/Investigational Biologics**: A new drug or biologic that is used in a clinical investigation. The term investigational biologic also includes a biological product that is used in vitro for diagnostic purposes. Investigational drugs or biologics may include:
- a. Products that are not generally recognized as being safe and effective for any use under the conditions prescribed, recommended, or suggested by the FDA; or
 - b. Products already approved by the FDA as safe and effective for specific indications that are being studied for new indications (or doses, strengths, or frequency).
91. **Investigational New Drug (IND)**: FDA permission that a new drug, agent, or biologic may be used in humans prior to FDA review of clinical data that demonstrates a particular product is safe and effective for a specific use. The FDA permission is evidenced by the assignment of an IND number by the FDA or the granting of an IND exemption.
92. **Investigational Drug Service (IDS)**: The IDS is a division of the UCIMC Pharmacy Department that must be consulted prior to study initiation regarding the proper storage, handling, and dispensing of investigational drugs, agents, and biologics to assure compliance with all IDS policies and procedures, as well as institutional, State, Federal (FDA) and Joint

- Commission on Accreditation of Hospital Organizations (JCAHO) requirements.
93. **Key Personnel:** Personnel considered of primary importance to the successful conduct of a research project. The term usually applies to the senior members of the project staff; however, sponsors may have differing definitions of Key Personnel. Key personnel are typically individuals who are involved in the design and conduct of the study, determining subject eligibility, performing data collection, interpreting and/or analyzing subject identifiable records or data; and authors on presentations or manuscripts related to the research.
94. **Laser Safety Committee (LSC):** UCI researchers proposing use of an investigational laser or the use of an FDA approved laser off label should consult with the Laser Safety Committee to determine if review would be appropriate. Securing LSC review or consult is the responsibility of the LR and is recommended before clinical research procedures are initiated.
95. **Lead Researcher:** The person with primary responsibility for meeting all ethical, scientific, and regulatory requirements for the conduct of a UCI research study, whether or not acting as the Principal Investigator (PI) for the award that funds the study.
96. **Legal Guardian:** An individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.
97. **Legally Authorized Representative (LAR):** A person authorized either by California statute or by court appointment to make legal decisions on behalf of another person. In human subjects research, an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.
98. **Limited Data Set:** Protected health information that excludes direct identifiers of the individual or of relatives, employers, or household members of the individual, with the exception of city, state, ZIP Code, elements of dates, and other numbers, characteristics, or codes not listed as direct identifiers.
99. **Local Research Context:** Knowledge of the institution and community environment in which human research will be conducted.
100. **Medical Experiment:** The severance or penetration or damaging of tissues of a human subject or the use of a drug or device, electromagnetic radiation, heat or cold, or a biological substance or organism, in or upon a human subject in the practice or research of medicine in a manner not reasonably related to maintaining or improving the health of the subject or otherwise directly benefiting the subject., the investigational use of a drug or device, withholding medical treatment from a human subject for any purpose other than maintenance or improvement of the health of the subject.
101. **Memorandum of Understanding (MOU):** A formal agreement between UC Irvine and another institution that identifies the UCI Institutional Review Board as the IRB of record for a specific protocol or a specific type of research or vice versa.
102. **Minimal Risk:** 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 lives of the general population* or during the performance of routine physical or psychological examinations or tests.
103. **Minimal Risk for Prisoners:** 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 examinations of healthy persons.
104. **Minimum Necessary Standard:** The least information reasonably necessary to accomplish the intended purpose of the use, disclosure, or request of PHI.
105. **Minor:** Person who has 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. In California, the legal age is 18 years old.
106. **Minor modification:** A proposed change in research related activities that does not significantly affect an assessment of the risks and benefits of the study and does not substantially change the specific aims or design of the study.
107. **Minor Non-compliance:** An action or omission taken by an Investigator that is administrative

in nature that does not compromise the rights and welfare of a participant. Example – reporting an unanticipated problem one day late or failure to date a consent form.

- 108. **Neonate**: A newborn.
- 109. **Non-Compliance**: Failure to comply with applicable laws, regulations, or institutional policies pertaining to the protection of human subjects, and/or with the requirements or determinations of an IRB.
- 110. **Non-Human Subjects Research**: Any activity determined by the IRB to not represent “Human Subjects Research.”
- 111. **Non-Significant Risk (NSR) Device Study**: A study of a device that does not meet the definition for a significant risk device and does not present a potential for serious risk to the health, safety, or welfare of participants.
- 112. **Nonviable**: An expelled or delivered fetus which, although it is living, cannot possibly survive to the point of sustaining life independently, even with the support of available medical therapy [45 CFR 46.203 (d) and (e)]. Although it may be presumed that an expelled or delivered fetus is nonviable at a gestational age less than 20 weeks and weight less than 500 grams [Federal Register 40 (August 8, 1975): 33552], a specific determination as to viability must be made by a physician in each instance.
- 113. **Not Less Than Once Per Year**: All approved research projects, with the exception of exempt research, must receive IRB continuing review at a minimum of once every 365 days, per Federal regulations. There are no exceptions or grace periods allowed.
- 114. **Office for Human Research Protections (OHRP)**: The office under the Department of Health and Human Services responsible for implementing DHHS regulations (45 CFR 46) governing biomedical and behavioral/social science research involving human subjects.
- 115. **Office of Research Oversight (ORO)**: The ORO in UCI Health Affairs conducts directed and random periodic compliance reviews of IRB-approved studies when the Lead Researcher is Health Affairs personnel (i.e., faculty, staff, or student) and/or the research is conducted at UCI Medical Center (UCIMC).
- 116. **Offsite Location**: Occurring outside of UCI owned, operated, or leased facilities (including international sites). For purposes of research oversight, private facilities located on UCI land are considered offsite locations.
- 117. **Offsite Locations Engaged in Research**: An offsite location is "engaged" in human subjects research when its employees or agents 1) intervene or interact with living individuals for research purposes, or 2) obtain individually identifiable private information for research purposes. Further, an offsite location is considered to be "engaged" in human subjects research when it receives Federal funds to support the research.
- 118. **On-going Monitoring**: Monitoring of the informed consent process or IRB-approved research to ensure compliance with federal regulations, state and local laws, and UCI IRB policies and procedures as well as adherence to the study protocol and reporting of study related activities.
- 119. **Parent**: A child's biological or adoptive parent. In California, parents are considered legally authorized representatives.
- 120. **Performance Site**: A site where human subjects research is performed.
- 121. **Performance Site(s) Engaged in Research**: A performance site becomes "engaged" in human subjects research when its employees or agents 1) intervene or interact with living individuals for research purposes, or 2) obtain individually identifiable private information for research purposes. Further, a performance site is considered to be "engaged" in human subjects research when it receives a direct Federal award to support the research.
- 122. **Performance Sites Not Engaged in Research**: A performance site is "not engaged" in human subjects research if its employees or agents do not 1) intervene or interact with living individuals for research purposes; or 2) obtain individually identifiable private information for research purposes. If a UCI Investigator or his/her staff, including site personnel contracted by UCI, performs all research related activities as well as screening, recruiting, or consenting at the performance site, the performance site would be considered "not engaged" in research, unless the non-UCI performance site releases identifiable private information to UCI

- Investigators without first obtaining participants' permission.
123. **Periodic Compliance Review**: Assessments at UCI conducted by other internal entities (e.g., UCI HealthSystems Compliance Office, Internal Audit Services) of IRB-approved studies or of departments involved in the conduct of human subjects research. These reviews evaluate proper execution and accurate documentation of an IRB-approved research project as well as adherence to federal regulations, state and local law, and IRB policies and procedures.
124. **Permission**: The agreement of parent(s) or guardian(s) to the participation of their child or ward in research.
125. **Placebo**: A chemically inert substance given in the guise of medicine for its psychologically suggestive effect; used in controlled clinical trials to determine whether improvement and side effects may reflect imagination or anticipation rather than actual potency of a drug.
126. **Placebo- controlled study**: A study where one arm of the study involves the use of a placebo for comparing with the treatment condition(s). Participants are usually randomly assigned to treatment conditions.
127. **Placebo washout period**: A period in a clinical investigation during which participants receive only a placebo prior to the initiation of the study.
128. **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.
129. **Preparatory to Research**: Any action taken in assessing the research question or hypothesis, such as accessing medical records, querying of databases for any type of individually identifiable health information, or any activity where PHI is accessed to prepare a research protocol.
130. **Principal Investigator**: The scientist or scholar responsible for the conduct of research or other activity, described in a proposal for an award. The Principal Investigator is responsible for all programmatic and administrative aspects of a project or program. The scientist or scholar with primary responsibility for the scientific, technical and administrative conduct of a funded research project.
131. **Prisoner**: 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. Probation and parole are treated the same and are usually NOT considered as incarceration. Ankle bracelets/in home restrictions are considered as incarceration. Mental and substance abuse facilities are considered incarceration if someone is mandated to attend in lieu of jail or prison; however, an individual in such a facility is NOT considered incarcerated if they voluntarily commit themselves.
132. **Privacy**: Control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others.
133. **Privacy Rule**: The Privacy Rule is a nickname for DHHS' regulation, "Standards for Privacy of Individually Identifiable Health Information," applicable to entities covered by the Health Insurance Portability and Accountability Act (HIPAA). The privacy provisions of HIPAA apply to health information created or maintained by health care providers who engage in certain electronic transactions, health plans, and health care clearinghouses. The DHHS Office for Civil Rights (OCR) is responsible for implementing and enforcing the Privacy Rule, effective April 14, 2003.
134. **Private Information**: information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (e.g., a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the

investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

135. **Protocol Review and Monitoring Committee (PRMC)**: A Committee required by Institutions receiving funding from the National Cancer Institute (NCI) for a comprehensive Cancer Center. The PRMC is charged with reviewing human research studies that involve patients with cancer, participants at risk for cancer, or research involving a specific cancer focus.
136. **Prospective**: Research utilizing human participants' specimens/data that will be collected after the research is approved by the IRB.
137. **Protected Health Information (PHI)**: Individually identifiable health information that is or has been collected or maintained by the covered entity in the course of providing healthcare that can be linked back to the individual participant.
138. **Protocol Deviation**: Accidental or unintentional changes to, or non-compliance with the research protocol that *does not* increase risk or decrease benefit or; does not have a significant effect on the subject's rights, safety or welfare; and/or on the integrity of the data. Deviations may result from the action of the participant, researcher, or research staff.
139. **Protocol Violation**: Accidental or unintentional changes to, or non-compliance with the IRB approved protocol without prior sponsor and IRB approval. Violations generally increase risk or decrease benefit, affect the subject's rights, safety, or welfare, and/or affect the integrity of the data.
140. **Quality Assurance Reviews**: Quality Assurance reviews are performed by the HRP Teams to verify that the electronic database is consistent with the IRB paper files and the paper files are collated in accordance with IRB policy and procedure.
141. **Radiation Safety Committee (RSC)**: The RSC, part of the Radiation Safety Division of Environmental Health and Services (EH&S), must approve all research protocols that involve radiation exposure (from x-rays or radio nuclides) to human subjects from routine diagnostic or therapeutic procedures used in a supporting role and which the subject would not otherwise receive as a part of their medical care.
142. **Radioactive Drug Research Committee (RDRC)**: A UC Irvine committee responsible for the review and approval of research protocols involving human research participants and radioactive drug exposure.
143. **Recruitment**: Seeking individuals to enroll or participate in a research project.
144. **Regulatory Committee Review**: A Regulatory Committee Review is initiated after a completed Administrative Review suggests that an incident of non-compliance appears to have occurred and when informal resolution was not achieved or when informal resolution is achieved but the Investigator has been determined to have engaged in a pattern of disregard for research regulations, policies or procedures. Regulatory Committee Reviews may be conducted by full committees or by subcommittees charged by the IRB Chairs. Whenever possible, the result of a Regulatory Committee Review will be informal resolution.
145. **Related**: An event is considered related if it is at least *possibly related to the research* (i.e., there is a reasonable possibility that the adverse event, experience or problem may have been caused by the procedures involved in the research).
146. **Relatedness**:
 - a. **Related** - An event that in the judgment of the researcher is definitely caused by the research activities or definitely affected the rights and welfare of the participants. A related event/problem has a strong temporal relationship and an alternative cause is unlikely.
 - b. **Probably related** - An event that in the judgment of the researcher is likely caused by the research activities or likely affected the rights and welfare of the participants. The event has a timely relationship to the research and follows a known pattern of response, but a potential alternative cause may be present.
 - c. **Possibly related** - An event that in the judgment of the researcher is possibly caused by the research activities or that possibly affected the rights and welfare of the participants. The event has a timely relationship to the research; however no known pattern of response exists, and an alternative cause seems more likely, or there is significant uncertainty about

the cause of the event.

- d. **Unrelated-** An event that in the judgment of the researcher is known and is in no way caused by any aspect of research activities or in no way affected the rights and welfare of the participants. If there is any uncertainty regarding causality of the event then the event must be assessed as possibly related to the research.

- 147. **Repository:** A storage site or mechanism by which identifiable human tissue, blood, genetic material or data are stored or archived for research by multiple Investigators or multiple research projects.
- 148. **Research:** Any systematic investigation (including research development, testing and evaluation) designed to develop or contribute to generalizable knowledge.
- 149. **Research Health Information (RHI):** Individually identifiable health information that is or has been collected solely for the purposes of research.
- 150. **Research Payments:** Cash and non-cash payments for reimbursement of time and expenses associated with participation in research activities.
- 151. **Research Personnel:** The Lead Researcher and all individuals responsible for the design or conduct of the study (including collaborators and colleagues at other institutions, engaged in human subjects research).
- 152. **Research Protections (RP):** Division of OR responsible for managing the University's programs for research compliance, specifically: human subjects research protections, animal care and use, and research involving human stem cells. This includes providing administrative support to UCI's IRB Committees, the Institutional Animal Care and Use Committee (IACUC), and the Human Stem Cell Research Oversight (hSCRO) Committee, and the Radioactive Drug Research Committee (RDRC).
- 153. **Research-Related Cost:** Those costs generated specifically as a result of the subject's participation in a research project and which would not otherwise have been generated in the course of the subject's routine and customary health care.
- 154. **Research (Scientific) Misconduct:** Fabrication, falsification, plagiarism or other practices that seriously deviate from those that are commonly accepted within the academic community for proposing, performing, or reviewing research, or reporting research results. Misconduct does not include honest error or honest differences in interpretations or judgments of data.
- 155. **Retrospective:** Research utilizing human participants' specimens/data that were previously collected (e.g., on the shelf) before the research was approved by the IRB.
- 156. **Right to Try:** In May 2018, the Federal Right to Try (RTT) Act was signed into law, creating a federal framework for patients to access investigational new drugs and biologics outside of clinical trials and outside of the U.S. Food and Drug Administration's (FDA) expanded access program. The federal law enables manufacturers and physicians to provide investigational drugs to eligible patients without risk of liability. It follows California's passage of the State's Right to Try Act, signed into law in 2016. Similar to the federal law, the California law enables manufacturers and physicians to provide investigational products to eligible patients without risk of liability under state law.
- 157. **Risk:** The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Federal regulations define only "minimal risk."
- 158. **Risk-Potential Benefit Profile:** An evaluation of the risks and potential benefits that have occurred during the course of the study.
- 159. **Sanction:** A punitive action designed to secure compliance with Federal regulations, UC and/or UCI IRB Policy, or the determinations or requirements of the UCI IRB by imposing a penalty. Sanctions are imposed in cases where cooperation from the Researcher does not occur or when it is determined that subjects or the Institution has been placed at risk.
- 160. **Safety Report (SR):** Alerts issued by the FDA or the study sponsor to inform all researchers using the same pharmacological compound about serious adverse events or reactions that have occurred in patients/participants.
- 161. **Scientific Review:** To approve human subjects research, the IRB must determine that

research subjects are treated ethically and equitably and that research design minimizes risks to subjects. Moreover, scientific review assures that the research has scientific validity, feasibility; statistical relevance and potential benefit to the participant and/or to society. The IRB will utilize the expertise of the biostatisticians in the Biostatistics, Epidemiology, & Research Design (BERD) unit of the Institute for Clinical and Translational Science (ICTS) to review the methodological and statistical information for specific types of research (e.g. UCI investigator authored, biomedical or clinical research, greater than minimal risk and no prior peer review, non-cancer related research or as required by the IRB), prior to IRB review.

162. **Serious:** An event is “serious” if it involves harm to one or more persons (who may or may not be participants), or required intervention to prevent one or more persons from experiencing harm.
163. **Serious Adverse Event (SAE):** Any adverse event temporally associated with the subject’s participation in research that meets any of the following criteria: results in death; is life-threatening (places the subject at immediate risk of death from the event as it occurs); requires inpatient hospitalization or prolongation of existing hospitalization; results in a persistent or significant disability/incapacity; results in a congenital anomaly/birth defect; or any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject’s health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.
164. **Serious Non-compliance:** Failure to comply with applicable laws, regulations, or institutional policies pertaining to the protection of human subjects and/or with the requirements or determinations of an IRB that has a significant adverse impact either on the rights or welfare of participants or on the integrity of the data.
165. **Short Form Consent:** A written informed consent document that summarizes the required elements of informed consent to be presented orally to the participant or his or her legally authorized representative.
166. **Significant Modification:** A proposed change in research related activities that significantly affects an assessment of the risks and benefits of the study or substantially changes the specific aims or design of the study.
167. **Significant Risk (SR) Device Study:** A study of a device that presents a potential for serious risk to the health, safety, or welfare of a participant and 1) is intended as an implant; 2) is used in supporting or sustaining human life; or otherwise prevents impairment of human health; 3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or 4) otherwise presents a potential for serious risk to the health, safety, or welfare of a participant.
168. **Sponsor-Imposed Suspension:** A determination from the sponsor of the study to place specific research activities on hold. This determination may be made for interim data analysis; inadequate drug availability; in response to a Data Safety Monitoring Board (DSMB) report/recommendation; or a pre-planned stopping point.
169. **Sponsor Investigator:** A *Sponsor-Investigator* is an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug or device is administered or dispensed. The term does not include any person other than an individual.
170. **Sponsored Projects (SP):** Division of OR responsible for reviewing, endorsing and submitting proposals to extramural sponsors for research, training and public service projects. Other institutional responsibilities include: negotiating and accepting awards on behalf of The Regents; drafting, negotiating and executing subcontracts; ensuring institutional compliance with applicable Federal and State regulations, sponsor policy and University policy; representing the campus and The Regents when interacting with sponsors; coordinating pre-award and post-award actions that require either institutional or sponsor prior approval; resolving problems related to sponsored projects; and reviewing UCI consultant agreements. Funding for human subjects research (e.g., grant, contract) will not be finalized without prior IRB review and approval.
171. **Sporadic Non-compliance:** A random action or omission taken by an Investigator that does

not compromise the rights and welfare of a participant yet indicates a lack of knowledge about Federal regulations, UCI Policy, UCI IRB Policy, or determinations or requirements of the UCI IRB.

172. **Standard of Care Costs**: Those costs generated in the course of the subject's routine and customary health care.
173. **State Death Data Records**: State of California issued death certificates and indices containing personal identifying information. The state of California requires IRB review of studies using California issued death records.
174. **Surrogate Decision-Maker**: In the case of an incompetent individual, or an individual who lacks decision-making capacity, the individual's surrogate decision-maker is designated in order of preference per California Health and Safety Code -Section 24178.
175. **Suspension**: An action initiated by the IRB to stop some or all research procedures pending future action by the IRB or by the Investigator or his/her research personnel.
176. **Termination**: An action initiated by the IRB to stop permanently some or all research procedures.
177. **Test Article**: Any drug (including a biological product), medical device, food additive, color additive, electronic product, or any other article intended for human use subject to regulation under the Federal Food, Drug, and Cosmetic Act.
178. **Third-party**: Any person or vendor (external to the University) who receives payment for providing research-related services and/or products.
179. **Treatment IDE**: A mechanism through the FDA for providing eligible participants with investigational devices for the treatment of a serious or life-threatening illness for which there are no satisfactory alternatives.
180. **Treatment Withholding Phase**: A period in a clinical investigation where the participants receive no active treatment.
181. **UCI-Affiliated Institutions**: Offsite locations that have formal agreements in place with UCI that allow the offsite location to conduct regulatory committee (i.e., IRB) review for research proposed solely to occur on their premises. Institutions that currently have agreements in place with UCI include Fairview Developmental Center, Kaiser Permanente Medical Care Program (Southern California component sites only), and Metropolitan State Hospital.
182. **UCI Facilities**: Facilities owned, operated, or leased by UCI including UCI campus, UCIMC, and any space rented to the University.
183. **UCI Personnel**: UCI students, staff, and faculty (including part-time, emeritus, and volunteer faculty), or any other agents of UCI.
184. **UCI Resources**: Funds, facilities, employee time, equipment, supplies, services, and non-public information.
185. **Unanticipated**: An event is "unanticipated" when it was unforeseeable at the time of its occurrence. Unanticipated and unexpected are not synonymous. A research protocol can monitor for an unexpected event, but cannot monitor for an unforeseen event. All unanticipated events are unexpected, but not vice versa.
186. **Unanticipated Problem Involving Risks to Participants or Others**: Any event, experience, or problem that is: (1) unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the IRB-approved documents, such as the protocol and informed consent document, and (b) the characteristics of the subject population being studied; (2) related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or problem may have been caused by the procedures involved in the research); and (3) suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.
187. **Unanticipated Adverse Device Effect**: Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any

other unanticipated serious problem to participants or others associated with a device that relates to the rights, safety, or welfare of participants.

188. **Unexpected:** An event is unexpected when its specificity and severity are not accurately reflected in the informed consent document
189. **Unexpected Adverse Event:** Any adverse event occurring in one or more subjects in a research protocol, the nature, severity, or frequency of which is not consistent with either:
- a. the known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; or
 - b. the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.
190. **University duties:** Responsibilities assigned by the University or tasks performed to meet expectations of one's employment, affiliation, appointment, or academic program.
191. **Viable (as it pertains to the neonate):** Being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. If a neonate is viable then it may be included in research only to the extent permitted and in accordance with the requirements for research involving children
192. **Violation:** Accidental or unintentional change to, or non-compliance with the IRB approved protocol without prior sponsor and IRB approval. Violations generally increase risk or decrease benefit, affects the participant's rights, safety, and welfare, or the integrity of the data. *This definition may not match the PI's or Sponsor's definition.* Examples: failure to obtain valid informed consent; failure to conduct research procedures related to primary aim of study; accidental distribution of incorrect study medication.
193. **Ward:** A child who is placed in the legal custody of the State or other agency, institution, or entity, consistent with applicable Federal, State, or local law.
194. **Witness:** Individual who signs and dates the consent form attesting that the requirements for informed consent have been satisfied; that consent is voluntary and freely given by the subject, guardian, or surrogate, without any element of force, fraud, deceit, duress, coercion, or undue influence. The witness should be an adult who is not a member of the study team.