

P&P: RR 401 Version No: 1.3 Effective Date: 6/1/2013	INITIAL REVIEW	Supercedes: CPHS Policies and Procedures 9/1/2007
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1. POLICY

All activities, regardless of funding source or whether the activity is funded, that involve the engagement of University of California Berkeley (UCB) employees or agents (including faculty, staff, and students) in the conduct of human subjects research must be reviewed and approved by the UCB IRB, or determined to qualify for exempt status per FO 302 – Exempt Research.

Non-exempt research must meet certain criteria and obtain IRB approval before study related procedures can be initiated. These criteria, specified below, are based on the Belmont Report principles of justice, beneficence and respect for persons and are codified in federal human research regulations. In addition, certain other criteria pertaining to Federal and State requirements as well as University of California Berkeley policies may apply and must also be met. (Note: University policy and/or California state law may require IRB review of some research activities that would otherwise not require review under federal regulations).

Specific Policies

1.1 Important Definitions

- 1.1.1 **Research**, as defined in federal regulations at 45 CFR 46.102(d), means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Systematic investigation means a study or examination involving a methodical procedure or plan.

Generalizable knowledge means conclusions, facts, or principles derived from particulars (individual subjects, medical records, etc.) that are applicable to or affect a whole category (members of a class, kind, or group, a field of knowledge, etc.) and are intended for dissemination in the public domain, typically through publication.

It is important to note that although some projects involving qualitative data collection or projects that are exploratory in nature may not have specific aims and hypotheses at the outset of the research, these are still *systematic investigations designed to contribute to generalizable knowledge* if the intent of the project is to archive results for future research, compare results to other assessments, or draw conclusions for dissemination in the public domain.

- 1.1.2 **Human Subject** as defined by federal regulations at 45 CFR 46.102(f), means a living individual about whom an investigator conducting **research** obtains
- (1) data through intervention or interaction with the individual, or
 - (2) identifiable private information

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

Interaction includes communication or interpersonal contact between investigator and subject.

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). In order to meet the above definition, private information must be individually identifiable (i.e., the identity of the subject is known or may readily be ascertained by the investigator or associated with the information) in order for the investigation to constitute research involving human subjects. In general, private information is considered to be to be individually identifiable when it can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems, or when characteristics of the information obtained are such that by their nature a reasonably knowledgeable person could ascertain the identities of individuals.

- 1.1.3 ***Coded Private Information or Biological Specimens*** means that identifying information (such as name, social security number, medical record number) is replaced with a code comprised of numbers, letters, or a combination thereof; and a key to decipher the code exists, enabling linkage of the individual's identity to specimens or data.

Coded private information or specimens are not considered to be individually identifiable and therefore their use would not fall within the definition of research involving human subjects, if the following conditions are both met:

- (1) the private information or specimens were *not collected* specifically for the *currently proposed project* through an interaction or intervention with living individuals; and
- (2) the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain as a result of one of the following circumstances:
 - (a) the key to decipher the code is destroyed before the research begins;
 - (b) the investigators and the holder of the key have entered into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased (Note: DHHS regulations for humans subjects research do not require the IRB to review and approve this agreement);
 - (c) there are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigator under any circumstances, until the individuals are deceased; or
 - (d) there are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.

1.2 Minimal Criteria for Approval of Human Subjects Research

In order for a research project to be approved under federal regulations set forth at 45 CFR 46.111, the IRB must find that:

A. Risks to subjects are minimized:

- By using procedures that 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.
- Points the IRB may consider include, but are not limited to, the following:
 1. Are research staff qualified?
 2. Are subject numbers adequate/inadequate?
 3. Are procedures that would answer the scientific question being done anyway and, if so, can the data from these procedures be used to reduce the likelihood and magnitude of harm?

B. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be expected to result.

- In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies that subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
- Points the IRB may consider include, but are not limited to, the following:
 1. Is the research likely to achieve its proposed aims?
 2. Is the importance of the aims clear?
 3. Are there direct potential benefits to the participants?

C. Selection of subjects is equitable.

- In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, people with physical or developmental disabilities, or economically or educationally disadvantaged persons.
- Points the IRB may consider include, but are not limited to, the following:
 1. Are the burdens of the research distributed fairly?
 2. Are the benefits of the research distributed fairly?
 3. Is a population unfairly targeted?
 4. Is a population unfairly excluded?

D. 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

appropriate local, state and federal regulations (see IC 701 – General Requirements & Documentation, IC 702 – Waivers of Informed Consent, and IC 703 – Assent).

- One of the following is true:
 1. Informed consent including the required elements of informed consent will be sought from each prospective participant or the participant's representative.
 2. The informed consent process will be waived or altered.
- E. Informed consent will be appropriately documented as required by local, state and federal regulations (see IC 701, IC 702, and IC 703).
 - One of the following is true:
 1. Informed consent will be documented.
 2. The requirement for written documentation will be waived.
 3. The informed consent process will be waived.
- F. Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
 - Points the IRB may consider include, but are not limited to, the following:
 1. Is the research greater than minimal risk?
 2. Is the research likely to result in safety reports to the sponsor or IRB?
 3. What data is reviewed? When? By whom?
- G. Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
 - **Privacy** refers to persons and their interest in controlling access to themselves.
 - **Confidentiality** refers to agreements with the participant about how their data are to be handled.
 - Points the IRB may consider include, but are not limited to, the following:
 1. What are the participants' expectations of privacy?
 2. Will data release cause risk of harm?
 3. Are there legal or ethical requirements?
 4. What measures will be in place, if any, to protect subject confidentiality?
- H. 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, or economically or educationally disadvantaged persons, additional safeguards have been included in the study and in the IRB review process, to protect the rights and welfare of these subjects.
 - Points the IRB may consider include, but are not limited to, the following:
 1. Who is vulnerable to coercion and undue influence?
 2. Is there a power differential?
 3. Are there excessive motivating factors?
 4. Are there decisional issues? Does the subject have the capacity to consent?

1.3 Other Criteria

1.3.1 If the research subjects include Pregnant Women, Fetuses and Neonates, Children, or Prisoners, the project can only be approved if the IRB finds that the applicable criteria for the additional protection of these vulnerable populations set forth at 45 CFR 46 subparts B, C and D are met (per SC 501 – Pregnant Women, SC502 – Prisoners, and SC503 – Children).

1.3.2 The IRB may require verification of information submitted by an Investigator. The need to verify any information will be determined by the IRB at a convened meeting or by the IRB Chair/Designee during an Expedited review. The purpose of the verification will be to provide necessary protection to subjects when deemed appropriate by the IRB.

Projects that need third party verification from sources other than the Investigator that no material changes have occurred since previous IRB review is determined, will have such assessment performed as necessary (See QA903 – Site Visits and Third Party Verification).

1.3.3 Research regulated by the Food and Drug Administration (FDA) involves testing of unapproved articles (drugs, devices, biologics, etc.) or previously approved articles being tested for a new unapproved use under a marketing application. The regulations require that the sponsor obtain an Investigational New Drug Exemption (IND) or an Investigational Device Exemption (IDE) from the FDA. Studies that fall under FDA jurisdiction must comply with the applicable regulations (21 CFR 50, 540, 56, 312 and 812).

Note: in order for the FDA to accept for consideration data generated by research with human subjects conducted outside of the United States (in a foreign country) not under an IND, the study must have been conducted in accordance with the Declaration of Helsinki or the laws and regulations of the host country, whichever provides the greater protection. Marketing approval of a new drug based solely on foreign clinical data is governed by 21 CFR 314.106.

1.3.4 Additional criteria pertaining to California state law and/or University policy may be required.

1.3.5 This policy does not affect any federal, state, local, or foreign laws or regulations which may otherwise be applicable and which provide additional protections for human subjects.

1.4 Modes of Review

The federal regulations permit two modes of IRB review. The default mode is by a quorum of IRB members at a convened meeting (full committee review). However, if certain criteria are met, an application for initial review, continuing review, or an amendment may be reviewed by the IRB Chair/Designee per RR 401 – Expedited Review. Regardless of the mode of review, the IRB may approve the research, disapprove the research, or specify modifications required to secure IRB approval of the research per RR 407 – Categories of Action.

1.5 Approval Period

Research under federal oversight will generally be reviewed at intervals of one year. Research that is not under federal oversight and presents minimal risk of harm to participants will generally be reviewed at intervals of 3 years. The IRB may shorten approval periods depending upon to the degree of risk to which subjects are exposed due to participation in the research, or new knowledge of concern (e.g. investigator noncompliance, unanticipated problem etc.). See RR 403 – Continuing Review.

1.6 Documentation

See FO 303 – IRB Meeting Administration.

1.7 Reliance on Other IRBs for Review and Approval of Research Conducted at the University of California-Berkeley.

Under authority granted by the Board of Regents of the University of California, the Institutional Official may enter into joint review arrangements on behalf of the Institution, to rely upon the review of another qualified IRB or to serve as the IRB of Record for another institution, or make similar arrangements to avoid duplication of effort as allowed and upon modification of the Institution’s Federal-Wide Assurance (FWA) per GA 105 – Signatory Authority.

2. SCOPE

These policies and procedures apply to all OPHS staff and IRB members and to research involving human subjects.

3. RESPONSIBILITY

The OPHS staff are responsible for facilitating the review process, pre-reviewing submission, and ensuring that IRB members have all the tools and resources they need to complete their research reviews. When the IRB approves research with conditions, it may designate a staff member to verify that the conditions for approval have been satisfied.

The IRB reviewers (primary reviewer and, if applicable, secondary reviewer) are responsible for conducting a thorough review and recommending actions per RR 407 – Categories of Action for consideration by the IRB.

The IRB Chair/Designee is responsible for providing IRB members with ongoing guidance and leadership.

The OPHS Director (and/or IRB Manager) is responsible for IRB members’ adequate submission review training and keeping members apprised of regulatory requirements.

4. PROCESS OVERVIEW

OPHS staff will initially determine whether an application meets the definition of research involving human subjects. For all research involving human subjects the OPHS staff will then determine (in consultation with the OPHS Director or IRB Chair/Designee, as necessary) if the application is eligible for exempt determination or expedited review per FO 302 – Review for a Determination of Exemption and RR 402 – Expedited Review. An application that does not qualify for exemption or review by expedited procedures will be reviewed by the full committee (convened IRB) as described below.

In general, the application will be added to the agenda for the next meeting of the appropriate committee. A staff member will conduct a preliminary review and prepare a written evaluation of the protocol identifying administrative and regulatory issues. Staff then forward the application and the evaluation to all IRB members per FO 303 – IRB Meeting Administration. If a research project requires special consideration or expertise, the OPHS Director, IRB Manager, or IRB Administrator arranges for a consultant’s participation and the necessary documentation is forwarded to the special consultant.

At the IRB meeting, the primary reviewer (and/or secondary reviewer) presents the study responding to the staff member’s evaluation and elaborating on any aspect of the study s/he deems appropriate to discuss. The convened IRB may approve the application, disapprove the application, require minor revisions (conditional approval), or defer consideration to another convened meeting (see RR 407 – Categories of Action). The investigator is notified of the review outcome in writing. If minor revisions or clarifications are required, the IRB will designate an individual with appropriate expertise to review the investigator’s response in order to verify that the conditions for approval have been satisfied. However, if the IRB determines that the concerns/revisions are substantive, the investigator’s responsive materials will be brought back to another convened meeting for consideration.

After the application is approved, all approved informed consent, parent permission, and assent documents (English and foreign language) will be made available to the investigator along with the protocol approval letter. Any foreign language translations of approved consent documents must be submitted, either with initial application materials, as responsive materials to a conditional approval by the IRB, or as an amendment after initial approval of the research and English consent documents.

5. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.102

45 CFR 46.109

21 CFR 56.109

45 CFR 46.111

21 CFR 56.111

45 CFR Subparts B, C & D

OHRP Guidance on Research Involving Coded Private Information or Biological Specimens (Aug 2004)

21 CFR 50, 540, 56, 312 and 812

The Belmont Report