June 29, 2007

To: All UCB Investigators

In the human research community, it is the Lead Investigators and those interacting directly with participants who have the ultimate responsibility to conduct ethical research. The Institutional Review Board (IRB) and its staff also play a vital role in this endeavor by knowing and applying human subject regulations and guidelines, assisting and educating investigators, and helping to protect the rights and welfare of participants in human research at all times. Having current, written procedures for carrying out these responsibilities is important to this process.

The following materials reflect the most recent Policies and Procedures (P&P) of the University of California at Berkeley’s IRB, the Committee for Protection of Human Subjects (CPHS), and staff of the Office for the Protection of Human Subjects (OPHS). These policies and procedures are followed in approving, recommending modifications, and in extremely rare cases, suspending or terminating research involving human subjects.

UC Berkeley operates within the regulations and guidelines set forth by federal authorities, primarily the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA), and other bodies such as the International Conference of Harmonisation, all based upon ethical principles elucidated in the Belmont Report. Many of the policies and procedures are derived from these regulations.

As with any road map, it is unlikely that one individual will need all the information gathered in these P&Ps, but they are intended to be easily navigated to find what is needed.

I am grateful to OPHS Director Dr. Rebecca Armstrong and her staff for their meticulous work in preparing these documents. If you have any questions or suggestions, please feel free to contact me.

Malcolm Potts, M.B., BChir, Ph.D.
Chair, Committee for the Protection of Human Subjects
Bixby Professor, School of Public Health
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1. POLICY

Written procedures must be in place to ensure the highest quality and integrity of the review and oversight of research involving human subjects and for the adequate documentation of such oversight. The following regulations and guidance of OHRP, FDA, and the International Conference on Harmonisation (ICH), supported by institutional policies and procedures, ensures that the rights, safety, and welfare of the human subjects of such research will be overseen and protected in a uniform manner, regardless of changes in personnel.

Policies, Guidelines, and Standard Operating Procedures (SOPs) provide the framework for the ethical and scientifically sound conduct of human research.

Specific Policies

1.1 Definitions

1.1.1 Policy. A document issued by the University of California Office of the President (UCOP); the University of California Berkeley (UCB), the Vice Chancellor for Research or the Assistant Vice Chancellor for Research Administration and Compliance; or, the Committee for Protection of Human Subjects (CPHS) that provides for interpretation of regulations and may stipulate required practices of the Office for the Protection of Human Subjects (OPHS) and its Human Research Protection Program (HRPP), the IRBs (CPHS I & II), and/or investigators as it pertains to human subjects research.

1.1.2 Guideline. A document issued by the IRB that identifies recommended practices or procedures for investigators. The local guidelines may be based on guidelines issued by the Office for Human Research Protections; and/or they may just reiterate them; or, they are local IRB interpretations of regulations or current Committee positions on topics.

1.1.3 SOP. A document issued by the OPHS/HRPP and/or the IRB that identifies the processes and procedures by which the IRB and associated OPHS staff conducts protocol reviews, conducts day-to-day operations, and handles particular matters.

1.2 Review, Revision, and Approval

1.2.1 Changes to regulations, federal guidelines, or research practice as well as the policies and procedures of the UCOP and/or UCB may require that policies, guidelines, and/or SOPs be created or revised.

1.2.2 Policies, guidelines, and SOPs will be reviewed by the appropriate institutional official(s) at intervals established by the OPHS Director.
1.2.3 Documentation of review and approval is required by signature of the responsible and authorized individuals.

A. Approval of new or revised policies is required by the Institutional Official (IO) or his or her designee, the IRB Chair or OPHS Director as appropriate.

B. Approval of new or revised guidelines is required by the IRB Chair with review and endorsement of IRB members.

C. Approval of new or revised SOPs is required by the OPHS Director and may be endorsed by the IO (or designee).

1.3 Dissemination and Training

1.3.1 When new or revised policies, guidelines, and SOPs are approved, they will be disseminated to the appropriate individuals and departments via a variety of channels, including the Research Advocate newsletter, email, website, university memoranda, and/or training seminars as appropriate.

1.3.2 Training will be provided to all members of the IRB (CPHS) and the OPHS staff on any new or revised policy, guideline, and/or procedure. Provision of training must be documented by the OPHS Director or IRB Administrator (or other designee).

1.3.3 Each new IRB member or staff employee must review all applicable policies, guidelines, and SOPs prior to undertaking any responsibilities at the IRB or OPHS respectively. Documentation of training must be done by the OPHS Director or IRB Administrator (or other designee).

1.4 Forms

Forms are used to 1) ensure that policies are integrated into the daily operations of research and review throughout UCB, and 2) enable OPHS staff to manage review, tracking, and notification functions consistently. Forms are either controlled or non-controlled.

1.4.1 Controlled forms are regulatory documents that become part of the permanent record of IRB review and determination. Therefore, they must be reviewed and approved as described in sections 1.1 and 1.2.

1.4.2 Non-controlled forms are management tools that are not subject to the standards of control cited in sections 1.1 and 1.2.

2. SCOPE

These policies and procedures apply to all UCB Investigators, all IRB members including Chairs, Vice Chairs, Acting Chairs, OPHS Director and staff, and the Vice Chancellor of Research as the Institutional Official or his or her designees.

Given the unique relationship of the Lawrence Berkeley National Laboratory (LBNL), with its own Institutional Official and a Federal Wide Assurance designating UC Berkeley’s IRBs as their IRBs of record; and, a Memorandum of Understanding between the institutions which includes among other stipulations, LBNL research staff serving on the UCB IRBs,
certain requirements as outlined in the UCB Policies and Procedures will not be applicable to LBNL investigators given the authority of the IO of LBNL.

3. RESPONSIBILITY

Vice Chancellor for Research is responsible for granting final approval (as appropriate) to new and revised VCR policies and procedures. He or she is responsible for endorsing CPHS and/or OPHS Policies, Guidelines and SOPs that is, officially acknowledging that the documents are consistent with the interests of the human subjects participating, the institution and institutional policy.

The IO of LBNL (or his/her designee) is responsible for implementing any requirements specific to LBNL investigators pursuant to LBNL’s FWA and institutional policies and procedures germane to LBNL researchers in their interaction with UCB in the conduct of human subjects research.

The OPHS Director is responsible for establishing and periodically reviewing VCR policies and procedures and recommending modifications of them (as appropriate). The OPHS Director, in consultation with the IRB Administrator and other OPHS staff, is responsible for establishing and periodically reviewing and modifying (as appropriate) SOPs.

Designated ad hoc working groups of IRB members and OPHS staff are responsible for guiding, developing and periodically reviewing and modifying (as appropriate) IRB policies and guidelines, and, in collaboration with the IRB Chair and OPHS Director, establishing SOPs.

4. PROCESS OVERVIEW

The OPHS Director and IRB Administrator monitor appropriate sources and contacts for policy updates, note policies that may need revisions, and determine priority. The OPHS Director maintains records of current UCOP, VCR and IRB policies in the OPHS and archives hard copies of previous policies. The IRB Administrator consults with the OPHS Director regarding changes to SOPs.

The IRB Administrator and OPHS staff members discuss changes and determine if additional procedures are required or if forms need revisions.

The IRB Administrator in collaboration with the OPHS Director ensures that IRB policies, SOPs, guidelines, and forms are drafted and/or revised as necessary to meet regulatory requirements and reflect changes in internal processes. The OPHS Director and/or IRB Administrator presents documents to the IRB Chair and ad hoc committee members for review and approval (as necessary) and tracks changes.

The IRB Chair and IRB collaborate in formulating current IRB policies, regulatory interpretations and positions. OPHS staff assist in drafting and formalizing such guidance.

The Institutional Official (or OPHS Director, as appropriate) has final approval authority for new and revised policies and procedures.
The IRB Administrator is responsible for ensuring current forms etc. are available to the research community. He or she replaces and destroys public copies of obsolete forms. Then, the OPHS Director and IRB Administrator collaborate in notifying the research community and distributing new policies, guidelines, SOPs, and forms as needed.

5. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.108, 56.109, 56.113
45 CFR 46.103, 46.108
UC Berkeley, Official Campus Policies and Procedures
http://campuspol.chance.berkeley.edu/
UC Berkeley – Lawrence Berkeley National Laboratory Memorandum of Understanding
1. POLICY

Training of IRB members, investigators and Human Research Protection Program staff in the Office for the Protection of Human Subjects (OPHS) is critical if the IRB is to fulfill its mandate to protect the rights, safety, and welfare of research subjects in a consistent manner throughout the University of California Berkeley research community.

IRB members, OPHS staff, and others charged with responsibility for reviewing, approving, and overseeing human subject research should receive detailed training in the regulations, guidelines, ethics, and policies applicable to human subjects research.

Specific Policies

1.1 Training

1.1.1 Management level OPHS staff and members of any IRB who are overseeing research on human subjects, as defined in 45 CFR 46.102(f) and/or 21 CFR 56.102(e), that is managed, funded, or taking place in an entity under the jurisdiction of the Regents of the University of California, Berkeley will receive initial and ongoing training regarding the responsible review and oversight of research and these policies and accompanying procedures.

1.1.2 The Director of the Office for the Protection of Human Subjects, with endorsement of the Institutional Official (IO) or his/her designee, establishes the educational and training requirements for IRB members and OPHS staff who review biomedical and social-behavioral research involving human subjects at this institution and who perform related administrative duties. Initial and ongoing training is provided and documented by this institution through the Director and / or IRB Administrator.

1.1.3 Members of the IRB will participate in initial and continuing training in areas germane to their responsibilities.

1.1.4 Chairs will receive additional training in areas germane to their additional responsibilities.

1.1.5 OPHS staff will receive initial and continuing training in the areas germane to their responsibilities, including all OPHS Standard Operating Procedures.

1.1.6 IRB members and OPHS staff will be encouraged to attend workshops and other educational opportunities focused on IRB functions. The University of California Berkeley will support such activities to the extent possible and as appropriate to the level of responsibilities of members and staff.

1.1.7 UCB investigators who are funded by the National Institutes of Health (NIH) are required to meet the NIH Human subjects education and training requirement by either completing the online training made available by NIH or
by completing the appropriate module sequence of another UCB recognized and accepted online training program.

1.1.8 UCB investigators or key personnel who are undergraduate or graduate students must complete and pass the Collaborative IRB Training Initiative (CITI) training program module sequence most germane to their area of study.

1.2 Documentation

Training and continuing education shall be documented and added to the records of the IRB as described in these policies and procedures. Copies of training documentation for OPHS staff will also be kept in OPHS employees’ personnel files.

OPHS will maintain records of CITI training completed since September 1, 2005. Investigators must maintain documentation of any other human subjects training obtained.

2. SCOPE

These policies and procedures apply to all University of California Berkeley IRB members, investigators, OPHS staff and as appropriate, others involved in the oversight of human subjects research.

3. RESPONSIBILITY

The OPHS Director is responsible for oversight (development, conduct, and support) of all relevant training programs for IRB members, staff and as appropriate, others involved in the oversight of human subjects research. He or she serves as the CITI Coordinator for UCB.

IRB Chair and / or Vice Chair(s) participate in the initial orientation and training of new IRB members.

The Director, in collaboration with the IRB Administrator is responsible for developing, implementing and documenting educational programs for IRB members and staff as designed.

The OPHS staff are responsible for receiving training reports (documentation) from investigators and maintaining a current database and files of education and training completed.

4. PROCESS OVERVIEW

New Voting IRB Members

Once appointed, an OPHS administrative staff member arranges an Orientation and Training Session at which the new IRB member receives a New Member Packet including: an IRB member roster, the Institutional Review Board Member Handbook by Amdur, and the UCB IRB Member Handbook. A member of the OPHS administrative support staff will also notify the new IRB member of the next meeting and send a packet of agenda materials to review.
The new IRB member will not be assigned specific protocols to be the lead reviewer on until s/he has completed the Orientation and Training and attended one CPHS meeting.

- New IRB members are required to attend an orientation session hosted by the IRB Chair prior to attending their first meeting. This training session is developed and implemented by the IRB Chair and Director of OPHS, with assistance from other OPHS staff. Topics discussed include the role and responsibilities of being an IRB member, as well as the expectations of the position, particularly in regard to conflicts of interest and confidentiality issues dealing with his or her service on the IRB. The new member will also receive practical training as to how to review and present IRB submissions to the full board. The new IRB member will attend a meeting of the IRB as an observer, in order to meet colleagues and observe the review process.

- A new IRB Chair will complete the Office of Human Research Protections (OHRP) Assurance Training Modules prior to assuming his/her responsibilities.

- All IRB Members are required to read the Belmont Report.

- New IRB members are asked to complete the Collaborative IRB Training Initiative (CITI) online training program module for IRB members or complete the online training module known as “Human Participant Protections Education for Research Teams” (http://cme.cancer.gov/clinicaltrials/learning/humanparticipant-protections.asp)

- IRB members are encouraged to attend human subjects related conferences, seminars and workshops on and off campus. Financial support for such activities may be available from the Vice Chancellor for Research or the Assistant Vice Chancellor for Research Administration and Compliance.

- Additional one-on-one training for IRB members is provided as needed by the Director or IRB Administrator.

- New IRB Vice Chairs receive additional training for their additional responsibilities pertaining to expedited reviews.

**Continuing Education of IRB Members**

- IRB members periodically receive updated information to supplement or supplant existing information in their UCB CPHS Member Handbook.

- IRB members are encouraged to attend human subjects related conferences, seminars and workshops on and off campus. Institutional support may be available to support expenses related to attending off campus educational events.

- The IRB member email listserv is used by the Director to disseminate online resources (or links to resources) on timely topics, new regulations and/or guidelines from agencies and task forces or commissions.

- Time permitting and as needed time will be set aside at IRB meetings to provide information and education on timely topics germane to current issues the IRB must consider. These topics are presented by various internal and external IRB experts including OPHS staff members.

- One-on-one training is provided as needed by the IRB Administrator.

- The Vice Chancellor for Research and/or the Assistant Vice Chancellor for Research Administration and Compliance may support the attendance of the IRB Chair or Vice
Chairs at IRB 101 sessions, related pre-conference workshops, ARENA/PRIM&R meetings or other National/Regional meetings.

**Ex-Officio IRB Members**

- All new members are provided and asked to read training and resource materials such as—but not limited to—the UCB CPHS Member Handbook and the *Institutional Review Board Member Handbook*.
- Ex-officio IRB members are encouraged to attend human subjects related conferences, seminars, and workshops on and off campus.

**OPHS Staff Members**

- IRB Administrator(s) and other OPHS Staff are required to complete at least one basic human subjects training course such as the online CITI program for OPHS Staff and may complete others such as the NIH program, Indiana University-Purdue University at Indianapolis (IUPUI), and/or UC-Irvine’s Human Subject Training.
- Fulltime OPHS staff are also required to complete HIPAA training and other training as required by the institution as a condition of employment.
- Graduate students employed part-time as OPHS staff must complete and pass a Social-Behavioral human subjects research online training program and / or a Biomedical sequence as germane to the type of work done in the office.
- Undergraduate students employed in the OPHS must complete the NIH online Human Subjects Research training module.
- Optional supplemental training is available through the Investigator 101 CD ROM training program; reading materials such as *Protecting Study Volunteers in Research; Institutional Review Board Member Handbook; Institutional Review Board: Management and Function;* and periodicals such as the *Human Research Report*.
- OPHS staff are encouraged to participate in video or satellite teleconferences; online learning activities; and, read the IRB Forum listserv discussions.
- IRB Administrators or Senior Administrative Analysts are expected to attend IRB 101 or 250, IRB Administrator 101 and/or 201. Attendance will be supported at one or more human subjects research related conferences (regional and/or national) annually or as needed for development and maintenance of expertise in human subjects protections.
- Other OPHS staff members will be expected to attend conferences and workshops as pertinent to their job responsibilities.
- OPHS staff will participate in educational training activities hosted by the Director for staff development and training.
- All OPHS staff members are expected to be familiar with the UCB CPHS Member Handbook and the UCB CPHS webpage http://cphs.berkeley.edu
- All OPHS staff are required to read the Belmont Report.

**Other Administrators Associated with Oversight of Human Subjects Research**

- The Institutional Official (IO) and Director of OPHS will complete the Office of Human Research Protections Assurance Training Modules.
• The OPHS Director will attend human subjects research related conferences (regional and/or national) annually or as needed to facilitate the management and growth of the UCB Human Research Protection Program (HRPP); and, for professional development and maintenance of expertise in human subjects protections.

The Director will also participate in many of the educational activities outlined for OPHS Staff members.

UC Berkeley Investigators
• Who are funded by NIH must meet the NIH Human Subjects Education and Training requirement prior to engaging in human subjects research.
• Undergraduate and graduate students serving as lead investigators or key personnel members of a research team must complete and pass the CITI online training module sequence most germane to the research project they are engaged with.

5. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.107
45 CFR 46.107
Belmont Report
OHRP IRB Guidebook
NIH NOTICE: OD-00-039 Required Education in the Protection of Human Research Participants
Institutional Review Board Member Handbook by Amdur
University of California, Berkeley CPHS Member Handbook
OPHS Office Manual
CITI - UC Berkeley Information Page
1. POLICY

The Office of the Protection of Human Subjects (OPHS) staff are vital components in the effective operation of the University of California Berkeley’s Human Research Protection Program (HRPP). They provide consistency, expertise, and support to the IRBs, as well as serve as a daily link between the IRB, the research community, and other administrative units. The highest level of professionalism and integrity on the part of OPHS staff is expected.

Specific Policies

1.1 Job Descriptions and Performance Evaluations

Members of the OPHS staff will have a written description of the responsibilities expected of their positions. The performance of staff will be reviewed according to current Office of the Vice Chancellor for Research and University of California Berkeley policy.

1.2 Staff Positions

Staffing levels and function allocation will be determined according to Office of the Vice Chancellor for Research and University of California, Assistant Vice Chancellor for Research Administration, Berkeley policy, management assessment of support requirements, and budget constraints.

1.3 Hiring and Terminating OPHS Staff

The Director of the Office for the Protection of Human Subjects is responsible for implementing the human resource policies of the University of California Berkeley for recruiting, hiring, developing and terminating staff.

1.4 Delegation of Authority or Responsibility

Delegation of specific functions, authorities, or responsibilities by the IRB Chair to an IRB administrative staff member will be documented in writing. See SOP GA 105 – Signatory Authority for more details.

1.5 Documentation

The policies of the University of California, Berkeley’s Human Resource Services and the Vice Chancellor for Research will determine the means of identifying, documenting, and retaining formal staff interactions (e.g., performance reviews, termination procedures).

2. SCOPE

These policies and procedures apply to all OPHS staff members.
3. RESPONSIBILITY

The Director of the Office for the Protection of Human Subjects is responsible for establishing personnel requirements and hiring and evaluating the ongoing performance of the IRB Administrator and other administrative staff.

The Director works in close cooperation and consultation with the IRB Chair(s); the Assistant Vice Chancellor for Research Administration and Compliance to meet the needs of the IRBs and the institution while effectively balancing the sometimes competing interests of each entity. However, in any given situation, the Director and administrative staff will give foremost attention to the protection of human subjects in research by supporting the IRB in fulfilling its duties.

4. PROCESS OVERVIEW

Institutional Official will define management policies and procedures to promote the long-term commitment of employees and ensure the efficient and effective administration and enforcement of IRB decisions.

The Assistant Vice Chancellor for Research Administration and Compliance will maintain the job description for the Director, Office for the Protection of Human Subjects.

The Director will maintain the job descriptions for the IRB Administrator. He or she is responsible for ensuring that the IRB Administrator is adequately oriented and trained.

The Director, with the input of the IRB Administrator, will establish the requirements for other OPHS administrative staff. The Director will complete personnel recruitment, hiring, and termination as per VCR/HR policy. The IRB Administrator will be responsible for ensuring that IRB staff are adequately oriented and trained.

The Director will evaluate the performance of the IRB Administrator and the OPHS administrative staff.

5. ATTACHMENTS

ATT 001  Job Description – Director, Office for the Protection of Human Subjects
ATT 002  Job Description – IRB Administrator (Senior Administrative Analyst)
ATT 003  Job Description – Senior Administrative Analyst
ATT 004  Job Description – IRB Coordinators (Administrative Analyst)
ATT 005  Job Description – Support Staff (Administrative Specialist)

Table of Contents
1. POLICY

In the environment of research, openness and honesty are indicators of integrity and responsibility, characteristics that promote quality research and can only strengthen the research process. Therefore, conflicts of interest should be eliminated when possible and effectively managed and disclosed when they cannot be eliminated.

Specific Policies

1.1 Definition of a COI for IRB Members

An IRB member is said to have a conflicting interest whenever that IRB member, or his or her domestic partner or first degree relative (e.g. child, sibling, parent):

- is an investigator or sub-investigator on the protocol under consideration;
- has entered into a financial arrangement with the sponsor or agent of the sponsor, whereby the outcome of the study could influence the value of the economic interest;
- acts as an officer or a director of the sponsor or an agent of the sponsor;
- has any equity interest in the sponsor exceeding $10,000 or 5% of the equity of the sponsor;
- has received any payments or other sorts from any sponsor that total in excess of $10,000; or
- has identified him or her self for any other reason as having a conflicting interest (e.g., having a close personal or professional association with the submitting Investigator).

Questions regarding Financial COI for Investigators and protocols are referred to the UCB Conflict of Interest Committee Coordinator per institutional policy.

The Institutional Official has the authority to determine when COI exists as defined by institutional policy and to impose and enforce disciplinary action in the event that COI is not disclosed.

1.2 Disclosure and Documentation of Financial Interest and COI

No regular or alternate member may participate in the initial or continuing review of any research project in which the member has a conflict of interest, except to provide information as requested.

It is the responsibility of each voting member or alternate member of the IRB to disclose any COI in a study submitted to the IRB and recuse himself or herself from the review of that protocol. Members with a COI may not be present during IRB voting.

The procedures for recusal of IRB members, including the IRB Chair, from deliberating and/or voting on all protocols for which there is a potential or actual conflict of interest are detailed in SOP FO 303 - IRB Meeting Administration.
1.3 **OPHS Employees**

OPHS staff whose job status or compensation is affected by research that is reviewed by the IRB must recuse themselves from any meeting during the time at which such a protocol is reviewed and voted on.

2. **SCOPE**

These policies and procedures apply to all IRB members and OPHS staff of UCB.

3. **RESPONSIBILITY**

The Vice Chancellor for Research is responsible for articulating and enforcing the conflict of interest policy at UCB.

The OPHS Director, serves as the liaison between UCB’s COI Committee Chair and/or COI Coordinator and the IRB.

IRB Administrator is responsible for monitoring the COI status and disclosures of IRB members.

IRB Chair is responsible for identifying COI disclosures at IRB meetings before each protocol review and discussion.

OPHS staff are responsible for documenting all COI disclosures in IRB meeting minutes.

IRB members and OPHS staff are required to be knowledgeable about conflict of interest issues and institutional policies pertaining to COI.

4. **PROCESS OVERVIEW**

IRB members will recuse themselves from voting where a COI exists or may appear to exist. They may be present for the discussion if the IRB determines that they may have information that is beneficial to the deliberations.

The OPHS staff documents COI disclosures in IRB meeting minutes.

The IRB Chair and Director ensure that IRB members with a COI do not participate in the IRB voting subject to their COI disclosures.

CPHS / OPHS communicate with the COI committee via administrative processes outlined in the OPHS Staff Handbook and all results of COI review pertaining to human subjects research by investigators is documented through correspondence from the COI to the CPHS Chairs and OPHS Director.

All Lead investigators on behalf of themselves and the research team – or in the case of student lead investigators, the faculty advisor as a principal investigator must sign and submit – a CPHS Checklist for COI with every initial and continuing review; and, with every amendment (modification) that involves a change in the funding of the project. Based on the
disclosure(s) on the Checklist, additional forms and documentation may be required by CPHS and/or the COI Committee for further review.

5. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.107
21 CFR 56.107
UC Berkeley COI Policies and Guidelines can be found at http://researchcoi.berkeley.edu/

6. ATTACHMENTS

ATT 007 CPHS Checklist for Financial Conflict of Interest
1. POLICY

The IRB Chair, IRB Vice Chair(s), and IRB Acting Chair(s) are authorized to sign any and all documents on behalf of the IRB in connection with the review and approval (or a determination of exempt) of research projects involving the use of humans as subjects, which have been reviewed and approved pursuant to University of California Berkeley and IRB policies and procedures. Individuals must sign their own name and no other, indicate their title under their signature, and date their signature.

The Institutional Official (or designee) and Director are authorized to sign documents confirming institutional review and approval.

Specific Policies

1.1 Definitions

1.1.1 Signature. A person’s name written in ink with his or her own hand.

1.1.2 Initials. The first letter of each word in a person’s name written in ink with his or her own hand.

1.1.3 Stamped signature. A person’s name that is reproduced in a rubber-stamp format to match the appearance of his or her signature. Stamped signatures may be used in lieu of signatures only if approved and documented by the Institutional Official.

1.1.4 Scanned Signature. A person’s name that is scanned and reproduced in a pdf format to match the appearance of his or her signature. Scanned signatures may be used in lieu of signatures only if approved and documented by the Institutional Official (or his or her designee).

1.1.5 Signature block. A person’s name (usually accompanied by his or her title and contact information) that is appended to the end of email messages and other electronic communication where signing or stamping a paper copy is not possible.

1.2 Authorization for Signatory Authority

Requests for authorization to sign documents not described in this policy may be made in writing to the OPHS Director.

1.3 Results of Reviews, Actions, and Decisions

The IRB Chair(s), IRB Vice Chair(s), IRB Acting Chair(s), or designated experienced IRB members are authorized and required to sign results of reviews and actions taken by the IRB that grant or may appear to grant Investigators with initial or continuing approval of research.

OPHS staff are authorized to add the scanned signature of the above IRB member who approved the research on the official approval letter notifying the investigator of the approval date and the date on which the protocol approval will expire.
The OPHS Director (or his or her designee) is authorized to signs the letters to investigators notifying them of a determination of exemption or a finding that the project the investigator proposed is found to be not human subjects research.

1.4 Routine Internal Correspondence
Designated OPHS staff members are authorized to sign any actions, letters, memos, or emails between and on behalf of the IRB and/or members of the faculty and staff of UC Berkeley or other investigators submitting to the UC Berkeley IRB that provide information concerning the review of research protocols AND do not imply or appear to imply approval of the protocols.

1.5 Correspondence with External Agencies
The OPHS Director and Institutional Official (or his or her designee) are authorized to sign any formal notification letters, memos, or emails sent to agencies of the federal government, funding agencies (whether private or public), or their agents.

The Assistant Vice Chancellor for Research Administration and Compliance, IRB Chair and members, and OPHS staff members may correspond informally with agencies of the federal government and funding agencies (whether private or public) to seek guidance, clarification, and other general information.

1.6 Decisions Made by Chair
Designated OPHS staff members are authorized to sign any letters, memos, or email sent representing the decision or opinions of the IRB Chair or his or her respective designees, as long as such correspondence does not imply review and approval of research projects.

1.7 Private Health Information
At UCB, the IRB has been designated as the Privacy Board under the Health Insurance and Portability Act (HIPAA) and therefore, the IRB Chair (or his/her designee) is authorized to sign IRB reviewed and approved documents for a Request for Waiver, Partial Waiver or Modification of Individual Authorization for Disclosure of Protected Health Information forms as required by the Privacy Rule.

2. SCOPE

These policies and procedures apply to all persons associated with the review of human subjects research at UC Berkeley.

3. RESPONSIBILITY

Institutional Official is responsible for establishing the overall procedure for delegating signatory authority. The IO is responsible for committing UC Berkeley to serve as the IRB of record for other institutions or investigators and authorizing such commitments.

The OPHS Director is responsible for implementing and controlling signatory authority delegations.
IRB Chair, IRB members, and OPHS staff are responsible for adhering to institutional signatory authority policies.

4. PROCESS OVERVIEW

The Institutional Official will establish signature authority delegation based on the nature of documents being signed and may designate signature authority in his or her absence.

The OPHS Director routinely signs all documents related to the review and determination of exemption for research projects and correspondence with external agencies (e.g. updating IRB registration and FWA documentation).

The IRB Chair, in consultation with the OPHS Director and IRB Administrator, decides what (if any) signatory authority the IRB Administrator or other OPHS staff members will be designated to undertake on his or her behalf.

5. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.103
45 CFR 46.115
45 CFR 160, 162 and 164 (HIPAA)
1. POLICY

Each IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. Each IRB should also be able to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.

Therefore, each IRB must consist of at least five regular, voting members. Qualified persons from multiple professions shall be considered for membership. The institution will make every effort to have as diverse as possible membership appointed to the IRBs, within the scope of available expertise needed to conduct its functions.

Specific Policies

1.1 Membership Selection Criteria

The members of each IRB shall be sufficiently qualified through experience and/or expertise, for reviewing research proposals in terms of regulations, applicable law and standards of professional conduct and practice, and institutional commitments and fields of research. Therefore, the IRB shall include persons knowledgeable in these areas.

Selection for membership shall include consideration of ethnic group, sex, cultural backgrounds, clinical experience, healthcare experience and sensitivity to such issues as community attitudes to assess the research submitted for review. There shall be at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. There shall be one member who has no affiliation with this institution, either self or family member. For review of FDA-regulated research, there shall be at least one member who is a physician.

1.2 Composition of the Board

Regular members: The backgrounds of the regular members shall be varied in order to promote appropriate reviews of the types of research activities commonly reviewed by each IRB. Regular members must include:

A. Nonaffiliated member(s): The nonaffiliated member(s), who can be either scientific or nonscientific reviewers willing and able to discuss research issues. Consideration will be given to recruiting individuals from which the University of California Berkeley routinely draws its research subjects and their knowledge and expertise should be fully utilized by the IRB.

B. Scientific members: The IRBs include physicians and M.S. and/or Ph.D. level physical, biological, or social-behavioral scientists. Such members satisfy the requirement for at least one scientist. When an IRB encounters studies involving science beyond the expertise of the members, the IRB will use a consultant to assist in the review, as provided by 45 CFR 47.107(f) and 21 CFR 56.107(f). However, when FDA regulated products are reviewed, the convened meeting must include a
physician member, therefore, at least one (1) member of the reviewing IRB must be a physician.

C. Nonscientific member: The intent of the requirement for diversity of disciplines is to include members whose main concerns are not in scientific areas. Therefore, nonscientific members are individuals whose education, work, or interests are not solely in medical or scientific areas.

D. Representatives of special groups of subjects: When certain types of research are reviewed, members or consultants who are knowledgeable about the concerns of certain groups may be required. For example, if an IRB reviews research involving prisoners, an individual who can represent this group (e.g., an ex-prisoner or an individual with specialized knowledge about this group) must be included in the IRB discussion.

E. Chairs: The individual IRB Chair(s) must be employed by the University of California Berkeley as members of the faculty and be fully capable of providing leadership to the IRB and the matters brought before it with fairness and impartiality.

F. IRB Alternates: All Alternates for IRB members must complete the same training as new IRB members prior to serving as an alternate and through their expertise, training and/or affiliation are designated to serve as an Alternate for one or more regular, voting IRB members.

2. SCOPE

These policies and procedures apply to the membership of all IRBs.

3. RESPONSIBILITY

Institutional Official is responsible for ensuring the IRB has adequate resources to identify and recruit qualified potential members.

The IO (or his/her designee) is responsible for collaborating with the IRB Chair(s), OPHS Director and IRB Administrator to identify and recruit potential IRB members.

The UC Berkeley Faculty Senate annually provides the IO (or his/her designee) with a list of suggested names to consider as potential IRB members.

The IO is responsible for appointing all IRB members (regular members and alternates).

The OPHS Director is responsible for ensuring compensation as needed for consultants and nonaffiliated members.

The IRB Chair, OPHS Director and IRB Administrator are responsible for training new IRB members.

The OPHS Director is responsible for designating Alternates to serve for IRB members.
4. PROCESS OVERVIEW

The IO (or his/her designee) acting through the OPHS Director and IRB Administrator ensure the overall diversity of the IRB membership (e.g., sex, race, ethnicity, community affiliation and professional experience) through establishing non-discriminatory selection methods.

The IO (or his/her designee) in collaboration with the Director and the IRB Chair select new members and replace members who resign or otherwise leave IRB service.

The IO appoints members to the IRB annually on or about July 1 except for vacancies that must be filled as needed.

The OPHS Director is responsible for ensuring that the IRB Registration documentation for IRB membership is kept current with the Office for Human Research Protections.

The OPHS Director maintains a roster of all regular and alternate members, a file on all members (to include their curriculum vita and other evidence of professional ability), and a roster of available consultants who are eligible and qualified to review protocols and attend meetings as invited consultants.

5. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.107
21 CFR 56.107
1. POLICY

The management of the membership of the IRBs and oversight of member appointments, IRB related activities, communications, and other administrative details are the responsibility of the Human Research Protection Program (HRPP), Office for the Protection of Human Subjects (OPHS) in cooperation with the Associate Vice Chancellor for Research (AVCR), Assistant Vice Chancellor for Research Administration and Compliance (AVCR-RAC). However, all appointments to the IRB are made by the Vice Chancellor for Research as the Institutional Official.

Specific Policies

1.1 Terms

1.1.1 The IRB Chair(s) will serve in this capacity for a one year renewable term. Reappointment for additional terms may occur by mutual agreement of the Institutional Official (IO), Director of OPHS and IRB Chair.

1.1.2 The IRB Vice Chair(s) will serve in this capacity for a term of one year. Reappointment for additional terms may occur by mutual agreement of the IRB Chair, Director, and IRB Vice Chair.

1.1.3 The IRB Acting Chair(s) will serve in this capacity on an as needed basis indefinitely as appointed by the IO.

1.1.4 IRB Members will serve on the IRB for a term of one year. Reappointment for additional terms may occur, by mutual agreement of the IO (or his or her designee), IRB Chair, AVCR-RAC, Director, IRB Administrator and IRB Member.

1.2 Appointments

Members of the IRBs are appointed by the Institutional Official upon recommendation of the IRB Chair(s), AVCR, AVCR-RAC, OPHS Director, Faculty Senate Committee on Research and IRB Administrator. Members will be solicited from UC Berkeley and surrounding communities.

1.3 Resignations and Removals

1.3.1 In the event that a member resigns before the conclusion of his or her term, the vacancy will be filled as quickly as possible.

1.3.2 The IO may remove an IRB Chair or IRB member from serving if it is in the best interest of the institution’s obligation to protect human subjects.

1.4 Compensation

Participation by UCB faculty or staff as IRB members is considered a component of their job responsibilities as established by their supervisors. Regular or alternate members who are not affiliated with the university and participate in full convened
meetings may receive modest reimbursement as consultants and miscellaneous expenses (e.g., parking).

Individuals serving as IRB Chair or Vice Chair may receive compensation as determined by the IO in accordance with the responsibilities and time commitment of the position.

1.5 Liability

Regular and alternate members have liability coverage as part of their IRB membership in their capacity as agents of UC Berkeley.

2. SCOPE

These policies and procedures apply to the IRB regular and alternate membership.

3. RESPONSIBILITY

IRB Chair is responsible for management of the activities of the IRB members relevant to meeting conduct and review of research.

IRB Members (including the IRB Chairs) are responsible for providing a current CV to the OPHS Director or designated OPHS staff at the time of their initial appointment, and annually thereafter.

4. PROCESS OVERVIEW

The IRB Chair and OPHS Director in consultation with the IO (or his/her designee), Faculty Senate Committee On Research, AVCR, and the AVCR-RAC, identifies members of UC Berkeley’s faculty and staff and members of the local community to serve on the IRB.

The IO (or his/her designee), IRB Chair and / or Director will discuss the responsibilities and time commitment of IRB membership with the interested parties. If the person is interested, his or her name is submitted to the Institutional Official recommending appointment of the individual to a particular IRB. If the Institutional Official (or his/her designee) concurs with the recommendation, the IO sends an appointment letter to the interested party, with copies to his or her department head and the OPHS Director.

5. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.107
21 CFR 56.107
1. POLICY

The primary responsibility of IRB members is the protection of the rights, safety, and welfare of the individual human beings who are serving as the subjects of research. In order to fulfill their duties, IRB members are expected to be versed in regulations governing human subjects protection, research ethics, and the policies of University of California Berkeley germane to human subjects protection.

Specific Policies

1.1 Duty to the University of California at Berkeley

The IRB is appointed as an Institutional Committee. As such, the IRB members serve the institution as a whole, rather than a particular school or department. Therefore, members must not allow their own interests or those of their department to supercede their duty to protect the rights, safety, and welfare of research subjects.

1.2 Term of Duty

1.2.1 Voting IRB members and IRB alternate members are expected to commit to a one-year term and, during that time, to fulfill certain duties. These duties will be described by the IRB Chair or OPHS Director prior to appointment. Each IRB member is expected to understand fully the duties of IRB membership prior to accepting appointment as an IRB member, IRB alternate member or IRB Vice Chair or Acting Chair.

1.2.2 The IRB Chair(s) are expected to commit to at least an annual term and, during that time, to fulfill certain duties. These duties will be described by the Institutional Official (IO, or his or her designee) or Director of the Office for the Protection of Human Subjects prior to appointment. The prospective IRB Chair is expected to understand fully the duties prior to accepting his or her appointment as IRB Chair.

1.3 Specific Duties

1.3.1 Voting Members. In general, IRB members (or their designated alternates) are expected to read all full board applications and research protocols; and, to attend and participate in the review discussion and vote on each proposed research protocol at the convened full board meetings to which they are assigned. In addition, IRB members are expected to participate on special subcommittees as assigned by the IRB Chair. There are three types of voting members:

A. Nonaffiliated members. Nonaffiliated members are expected to provide input regarding their knowledge about the local community and be willing to
discuss issues and research from that perspective as well as to comment on the comprehensibility of the consent document.

B. Scientific members. Scientific members are expected to assess whether risks to subjects are reasonable in relation to anticipated benefits. These members should also be able to advise the IRB if additional expertise in a nonscientific or other scientific area is required to assess if the protocol adequately protects the rights, safety, and welfare of subjects.

C. Nonscientific members. Nonscientific members are expected to provide input on areas germane to their knowledge, expertise, and experience, professional and otherwise. Nonscientific members should advise the IRB if additional expertise in a nonscientific area is required to assess if the protocol adequately protects the rights, safety, and welfare of subjects, and/or to comment on the comprehensibility of the consent document.

1.3.2 Primary and Secondary Reviewers
In addition to the duties described in section 1.3.1, each regular member will be expected to act as a Primary Reviewer for assigned protocols at convened meetings. Secondary Reviewers may also be assigned. The Primary and Secondary Reviewers present their findings resulting from review of relevant materials, provide an assessment of the soundness and safety of the protocol, and recommend specific actions to the IRB. The reviewers may be required to review additional material requested by the IRB for the purpose of study approval.

1.3.3 Delegation of Responsibilities
The Vice Chairs are expected to participate on a regular basis in assisting the Chair with his or her IRB duties. An Acting Chair as appointed by the IO may also be called upon to participate on an as needed basis to assist the Chair with his or her IRB duties. The Chair may appoint a voting IRB member to assist or act on his or her behalf in particular IRB matters on a case-by-case basis. The Chair also may delegate any of his or her responsibilities as appropriate to other qualified (experienced) individual(s). Such delegation documentation must be in writing and maintained by the Director.

2. SCOPE
These policies and procedures apply to all IRB members.

3. RESPONSIBILITY
The IO and AVCR-RAC are responsible for providing resources to support continuing education of OPHS Administrative staff members, IRB Chairs, and IRB members.

The IO (or his or her designee) and OPHS Director are responsible for clearly articulating all IRB members’ duties to potential and current IRB members, periodically reviewing members’ duties to ensure that members are carrying out their expected functions, and evaluating whether there is adequate staff support to ensure members are able to function as documented.
IRB Administrator is responsible for maintaining up-to-date descriptions of member responsibilities, answering questions from IRB members as needed, and making recommendations to the Director regarding changes to descriptions, staffing, meeting scheduling, and other factors that affect members’ ability to perform their roles.

4. APPLICABLE REGULATIONS AND GUIDELINES

OHRP IRB Guidebook

CPHS Member Handbook (current edition)
1. **POLICY**

Research activities in which the only involvement of human subjects/participants will be in one or more specific categories that are listed in section 1.1 of this policy may be exempt from the full requirements of 45 CFR 46, the “Common Rule.” However, individual investigators are not authorized to make this determination. The OPHS staff must make and document the determination of exemption based on regulatory and institutional criteria. All procedures for all subjects in a project must qualify for exemption in order for the project to be deemed exempt.

**Specific Policies**

**1.1 Exempt Research Activities**

The exemption categories listed below do not apply to research involving prisoners, nor subjects vulnerable to coercion, or persons considered to be legally incompetent, and certain types of research with children as noted below. Additionally, categories A thru E do not apply to research regulated by the Food and Drug Administration (FDA).

A. **Educational Practices:** 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.

B. **Educational Tests (Cognitive, Diagnostic, Aptitude, Achievement), Survey Procedures, Interview Procedures, or Observation of Public Behavior:** Research involving these procedures is exempt, if:
   
   i. the information obtained is recorded in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects; or
   
   ii. any disclosure of the subject’s responses outside of the research could not reasonably place the subject at risk of criminal or civil liability or be damaging to the subject’s financial standing, employability, or reputation.

This exemption does not apply to children except for research involving observation of public behavior when the investigator does not interact with the children.

C. **Educational Tests, Survey Procedures, Interview Procedures, or Observation of Public Behavior:** Research NOT exempt under Category B: Research involving these procedures is exempt, only if:
   
   i. subjects are elected or appointed public officials or candidates for public office; or
   
   ii. federal statute(s) require(s) without exception that confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
D. Existing Data: Research involving collection or study of existing data, documents, records, or specimens, if:
   i. these sources are publicly available; or
   ii. the information is recorded by the researcher in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

Research involving access to UC Berkeley medical records does not qualify for exemption from IRB review.

E. Research and Demonstration Projects Conducted by or Subject to the Approval of Department or Agency Heads: This research is exempt if it is designed to study, evaluate, or otherwise examine:
   i. public benefit or service programs; or
   ii. procedures for obtaining benefits or services under those programs; or
   iii. possible changes in methods or alternatives to those programs or procedures; or
   iv. possible changes in methods or levels of payment for benefits or services under those programs.

F. Taste and Food Quality Evaluation and Consumer Acceptance Studies: This research is exempt, if:
   i. wholesome foods without additives are consumed; or
   ii. a food is consumed that contains a food ingredient at or below the level and for a use found to be safe by the Food and Drug Administration (FDA) or approved by the Environmental Protection Agency (EPA) or the Food Safety and Inspection Service (FSIS) of the US Department of Agriculture (USDA); or
   iii. a food is consumed that contains an agricultural chemical or environmental contaminant at or below the level found to be safe by the FDA or approved by the EPA or the FSIS of the USDA.

1.2 Submission Requirements for Exempt Review

1.2.1 Investigators submitting a Request for Exempt Status must provide:
   - Research Exemption Request
   - Study Protocol (as appropriate)
   - Questionnaires and assessment instruments
   - Consent materials
   - Other supporting documentation as required by the IRB

1.3 Action Taken If Proposed Research Does Not Meet Criteria for Exemption

If the IRB Chair or OPHS staff determine that the proposed research does not meet the criteria for exempt status, the investigator will be contacted and asked to submit the appropriate application and documentation for either expedited or full committee review.
2. **SCOPE**

These policies and procedures apply to investigator claims for Exemption from 45 CFR 46 requirements.

3. **RESPONSIBILITY**

OPHS staff are responsible for reviewing and making a determination regarding research applications that claim exemption from 45 CFR 46.

The OPHS Director, CPHS Chair or Designee is responsible for providing consultation in the review of claims of exemption and has final authority in determining a finding of exempt status or to revoke determinations granted by OPHS staff.

4. **PROCESS OVERVIEW**

The investigator submits to the IRB a research exemption request and any additional required information/documentation (e.g., copy of survey instrument).

An IRB administrative staff member reviews the request to determine if the investigator has submitted all of the necessary paperwork and supporting documents for exempt review and ensures that all required elements are complete and in proper format. The staff member, in consultation with the OPHS Director, CPHS Chair of Designee as appropriate, evaluates the exemption request for (1) level of risk; (2) category of activity; and (3) other relevant considerations.

If the research qualifies as exempt (based on the standards outlined in Section 1.1), the staff sends a copy of the letter of exempt status to the investigator.

If the research does not qualify for exemption, an IRB administrative staff member contacts the investigator to request a full application for expedited or full committee review.

Investigators are not permitted to make the determination of exempt status on their own. Exemption can only be granted by the OPHS staff, the IRB, IRB Chair or Designee.

5. **APPLICABLE REGULATIONS AND GUIDELINES**

45 CFR 46.101
21 CFR 56. 104
21 CFR 56. 105

6. **ATTACHMENTS**

ATT 008    CPHS Application Cover Sheet
ATT 007    CPHS Checklist for Financial Conflict of Interest
ATT 009    Request for Determination of Exempt Status
1. POLICY

Except when an expedited review procedure is used, the IRB will review proposed research at convened meetings at which a quorum of members is present. The IRB may be one or more committees. Quorum permitting, each Committee will meet once a month, or at some other frequency determined by the OPHS Director and/or IRB Chair. The Chair may call an unscheduled meeting as necessary.

Specific Policies

1.1 Quorum

1.1.1 A quorum is defined as greater than 50% of the membership of IRB and must include at least one member whose primary concerns are in nonscientific areas.

1.1.2 When research regulated by the Food and Drug Administration (FDA) is reviewed, there shall be one member present who is a physician.

1.1.3 In order to meet the quorum requirements outlined above, a member’s alternate may attend in the member’s place.

1.1.4 A member participating via telephone connection can be used to establish a quorum.

1.1.5 A special consultant(s) cannot be used to establish a quorum.

1.1.6 Should the quorum fail during a meeting (e.g. due to recusal of those with conflicts, loss of a non-scientist, early departures), discussions may proceed; however, votes may not be taken.

1.2 Primary and Secondary Reviewers

Prior to the meeting, the OPHS Director and/or the IRB Administrator will designate a primary reviewer for each research protocol included on the agenda. A secondary reviewer may also be assigned. The primary and secondary reviewers’ duties as well as those of voting members at large are described in SOP OR 203 – Duties of IRB Members. All members are strongly encouraged to be physically present for convened meeting discussion and voting.

1.3 Use of Special Consultants

When the IRB reviews research that involves a vulnerable category of subjects (e.g., children, prisoners, or handicapped or mentally disabled persons), one or more individuals who are knowledgeable about and/or experienced in working with these subjects will participate in the review. If IRB members lack this expertise, special consultants will be used in the review of these protocols. These individuals may not vote with the IRB.
The IRB may also invite individuals with competence in special areas (other than vulnerable populations) to assist in the review of issues that require expertise beyond or in addition to that available on the IRB.

1.4 **Meeting Materials Sent Prior to IRB Meetings**

A meeting agenda, application materials and other documentation required for review will be prepared by the OPHS Staff. These will generally be distributed to IRB members five (5) business days in advance of the meeting to allow time for adequate review; however, exceptions may be made under extenuating circumstances. A copy of the agenda and attached materials will be maintained on file in the Office for the Protection of Human Subjects by the IRB Administrator with the meeting minutes.

Members must declare any potential conflict of interest (COI) they may have with research that is about to be reviewed at the outset of each meeting. Members who declare a COI on any matter will recuse themselves from participating in the discussion (except as requested by the IRB) and voting on that agenda item. The IRB minutes will reflect such recusals as they occur during meetings.

1.5 **Telephone Use**

1.5.1 Convened meeting using speaker phone:

Should a member be unable to physically attend a convened meeting, but available by telephone, the meeting may be convened using a speakerphone. In this manner, the member who is not physically present will be able to discuss the protocol with the rest of the members via speakerphone. Members participating by speakerphone may vote; provided that they have had an opportunity to receive and review the meeting materials in advance of the meeting.

1.5.2 Meetings Conducted Via Telephone Conference Calls:

On rare occasion, meetings may be convened via a telephone conference call. A quorum (as defined above) must participate for the conference call meeting to be convened. To allow for appropriate discussion to take place, all members must be connected simultaneously for a conference call to take place. “Telephone polling” (where members are contacted individually) will not be accepted as a conference call.

Members who are neither present at the convened meeting, nor participating in the conference call may not vote on an issue discussed during a convened meeting (no voting by proxy).

1.6 **Discussion and Vote**

1.6.1 At the meeting, the primary reviewer introduces the research and provides the first comments resulting from his or her in-depth review. After the primary reviewer has provided his or her comments, the IRB Chair will ask the secondary reviewer (if one is assigned) for his or her comments, and then any special consultants will be asked to provide their comments.
The discussion of each new research proposal, continuing review progress report, amendment, adverse/unanticipated event, protocol deviation or non-compliance on the agenda is led by the Chair and any designated reviewer(s). Discussion by all members present at the convened meeting is conducted on the necessary ethical and regulatory questions, controverted issues, determinations of scientific/scholarly validity, risk, benefit, and additional safeguards for vulnerable populations.

1.6.2 At the end of the discussion of an application, the Chair looks for a motion on an action, as well as a second. Hearing these, the Chair calls for a vote on the motion and the members may vote by voice as well as by raising their hands. The Chair asks for votes for the motion, then against, and finally for abstentions. A simple majority carries the vote. Following Roberts Rules of Order, the Chair of the meeting may not vote, unless it is for the purposes of breaking a tie. The Chair will strive to build consensus as much as possible and may take a straw vote before a binding vote in order to assess whether additional discussion is needed. A deeply divided vote may indicate that further discussion or deferral is appropriate. OPHS Staff will count the final vote and the vote is recorded in the minutes.

1.6.3 Members with a COI will recuse themselves from the deliberation and vote for protocols or matters with which they have a conflict. In addition, recused members will leave the meeting room during the review, unless requested by the IRB to answer specific questions.

1.7 Minutes

1.7.1 Recording: OPHS Staff will take minutes of each meeting. Minutes will be written in sufficient detail to show the following:

- Meeting attendance; including status of each attendee (regular member, consultant, etc.), and conflicts of interest, if any;
- Actions taken by the IRB on each agenda item requiring full IRB action, including, the basis for requiring changes in or disapproving the research;
- Summary of the discussion of controverted issues and resolution;
- Determination of the level of risk and the duration of approval;
- Voting results, including number for, against, members abstaining (listed by name), and members who recused themselves and reason for recusal, and any.
- Consideration of the requisite criteria for approval as well as any additional criteria for the protection of vulnerable populations.

1.7.2 Approval: Draft minutes will be distributed to members prior to the next IRB meeting for review and approval, or the next possible meeting.

- Corrections requested by the IRB will be made by the staff and the minutes will be printed in final form and made available to members at the following meeting.
• The OPHS Director and/or IRB Administrator will maintain copies of the minutes, as well as the agenda and pertinent materials on file (see SOP FO 305 – Documentation and Document Management).

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

The OPHS Director and/or IRB Administrator is responsible for IRB meeting procedural conduct and acts as a technical consultant when necessary.

The IRB Chair (or designee) is responsible for IRB meeting review, conduct, and leadership.

OPHS Staff are responsible for IRB meeting documentation.

4. PROCESS OVERVIEW

The OPHS Staff provide documentation required for review to all IRB members approximately five business days in advance of the meeting to allow time for adequate review. Staff draft the agenda for the IRB meetings in consultation with the OPHS Director and/or IRB Administrator regarding applications, issues, and announcements to be included as agenda items.

Once the OPHS Director and/or IRB Administrator have, in consultation with the Chair, finalized the agenda, staff provide a copy of the final agenda, monthly reports (e.g., Continuing Reviews, Amendments Approved via Expedited Review, Protocols Deemed Exempt, Expedited Review Report), the previous meeting’s minutes and materials for review to all members approximately five business days prior to the meeting. In some instances, questions and comments made by the primary reviewer and secondary reviewer, if applicable, will be compiled and sent via email to investigators to enable them to address issues in advance of the meeting. In such cases, a copy of investigators’ responses to the committee’s comments will be sent to the primary reviewer and secondary reviewer prior to the meeting, time permitting.

All relevant files (new applications, modification requests, continuing reviews, non-compliance notices) and all reports referenced in the agenda will be available upon request to the members at the meeting.

The IRB Chair presides over the meeting, using the agenda as a guide. IRB Members with conflicts of interest do not participate in the vote on protocols with which they have a conflict. However, they may be present for the discussion if the IRB determines that they may have information that is beneficial to the deliberation. Lead investigators of protocols under discussion may be invited to attend the meeting for the purpose of providing further clarification or answering any remaining questions the IRB may pose. However, investigators must not be present during deliberation and voting on any protocol.

IRB members are asked to return any completed checklists and worksheets to OPHS staff at the conclusion of the meeting to be filed in CPHS records. The OPHS staff record detailed minutes of the meeting, including summary of discussion, motions, and voting results. Staff
also record the names of members who abstain from voting or leave the meeting due a conflicting interest. All documentation from the meeting is handled according to UC Berkeley record retention policies.

5. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.103
45 CFR 46.108
21 CFR 56.108
45 CFR 46.109
21 CFR 56.109
FDA Information Sheets, 1998
1. POLICY

All activities, regardless of funding source, or whether the activity is funded, involving the engagement of University of California Berkeley (UCB) faculty, staff or 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 SOP 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. (NB: 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 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.

Research involving coded private information or biological specimens, under specific conditions, is not considered to involve “human subjects” (OHRP Guidance Aug 2004). Nevertheless, all investigators conducting research with coded private information or specimens are required to submit a description of the research to OPHS so that a formal determination can be made.

Coded private information or specimens are not considered to be individually identifiable and therefore 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 (NB: 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 will 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 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 burdens distributed fairly?
2. Are the benefits 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 SOPS 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 SOPS 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 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 SOP 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 SOP 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 base 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 Approval Period

Studies are reviewed at intervals appropriate to the degree of risk to which subjects are exposed due to participation in the research, or accumulation of new knowledge, but not less than once per year.

1.5 Modes of Review

The federal regulations permit two modes of 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 SOP RR 401 – Expedited Review.

1.6 Documentation

See SOP 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 SOP 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 and ensuring that IRB reviewers have all the tools and resources they need to complete their research reviews.

The IRB reviewers (primary reviewer and, if applicable, secondary reviewer) are responsible for conducting a thorough review and making appropriate approval recommendations 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 Administrator) 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 is eligible for exempt, expedited or full committee review in consultation with the IRB Chair/Designee as necessary. If an application for IRB approval of research involving human subjects does not qualify for
exempt status or review by expedited procedures, the application will be reviewed by the full committee/convened IRB.

A staff member will conduct a preliminary administrative review, prepare a Staff Summary and add the application to the agenda for the next meeting of the appropriate committee. Staff will compile the necessary documentation (e.g., Staff Summary, Application and all supporting documents) and forward it to all IRB members per SOP FO 303 – IRB Meeting Administration. If a research project requires special consideration or expertise, the OPHS Director or IRB Administrator arranges for the consultant’s participation and the necessary documentation is forwarded to the special consultant.

Prior to the IRB meeting, IRB members review the application packet including the research protocol (1) to ensure its adherence to federal, state, local, and university guidelines; (2) to determine whether any special considerations may be applicable; and (3) to ascertain if any evidence exists that third party verification is needed.

At the IRB meeting, the primary reviewer (and/or secondary reviewer) presents the study responding to the staff member’s summary comments (preliminary review) 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 SOP RR 407 – Categories of Action). The investigator is notified of the review outcome in writing. If minor revisions or clarifications are required (conditional approval), the IRB Chair/Designee or a subcommittee of IRB members may be given responsibility for review of the investigator’s response in an expedited manner. However, if the IRB determines that the concerns/revisions are substantive, the responsive materials will be brought back to another convened meeting for consideration.

Once the research has been approved, a staff member sends the investigator a copy of the approval letter and the approval-stamped English informed consent documents (if any).

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
6. ATTACHMENTS

ATT 010 University of California System Memorandum of Understanding and associated forms
ATT 011 OHRP Approval of Federalwide Assurance
ATT 012 Institutional Review Board Registration (CPHS I & II)
ATT 008 CPHS Application Cover Sheet
ATT 007 CPHS Checklist for Financial Conflict of Interest
ATT 013 CPHS Protocol Narrative Form
ATT 014 Full Board Staff Summary Template - New Application
ATT 015 IRB Protocol Review Standards Checklist
1. POLICY

An expedited review procedure consists of a review of research involving human subjects by an OPHS staff member and the IRB Chair, or by one or more experienced reviewers designated by the Chairperson from among the members of the committees.

In order to be eligible for expedited review, all aspects of the research must include activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures included in one or more of the specific categories listed in the regulations at Federal Register Volume 63, No 216.

Specific Policies

1.1 Important Definitions

1.1.1 Minimal risk is defined by 45 CFR 46.102 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.

1.1.2 Children are defined by 45 CFR 46.402 as persons who have not yet attained the legal age for consent to treatment or procedures involved in the research, under the applicable law of jurisdiction in which the research is conducted (be it local, national, foreign or domestic).

1.2 Applicability

1.2.1 The activities listed in the regulations at Federal Register Volume 63, No 216 should not be deemed to be of minimal risk simply because they are included on the list. Inclusion on this list means only that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

1.2.2 The categories in this list apply regardless of the age of subjects, except as noted.

1.2.3 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, the expedited review procedure may not be used where identification of the participants and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to their financial standing, employability, insurability, reputation, or be stigmatizing.

1.2.4 The expedited review procedure may not be used for classified research involving human subjects. Furthermore, UC Berkeley policy prohibits investigators from conducting research involving human subjects that is considered classified by the US government.

1.2.5 The expedited procedure may not be used for research involving prisoners, unless the prisoner representative of the IRB is one of the designated reviewers.
1.2.6 The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of whether the research is reviewed by the convened IRB (the full committee) or by expedited procedures.

1.3 Expedited Review Categories (this information is quoted directly from the regulations at Federal Register Volume 63, No 216.)

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

(a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

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

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

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

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

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

Examples: (a) hair and nail clippings in a nondisfiguring 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 scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

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

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

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

(7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

(8) Continuing review of research previously approved by the convened IRB as follows:
   (a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
   (b) where no subjects have been enrolled and no additional risks have been identified; or
   (c) where the remaining research activities are limited to data analysis.

(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.

1.4 Authority of the IRB Chair and Designee

The IRB Chair may exercise all of the authorities of the IRB, except that he or she may not disapprove the research application. A research proposal may be disapproved only after review by the convened IRB. The Designee may exercise authority as permitted and specified by the Chair.
1.5 Notification of the IRB

The OPHS staff provide IRB members with a monthly list of all new applications, continuation applications, and amendments approved under expedited review. The list is provided to members by the next convened meeting. If that is not possible, it is provided no later than the convened meeting of the following month.

1.6 Documentation

When research is reviewed by expedited procedures, IRB records, must include documentation of the research, the permissible category or categories of expedited review that apply (for example, surveys per F(7)) and that the research is minimal risk.

1.7 Additional Items That May be Reviewed by the Chair or IRB Member Designee

1.7.1 Response to conditional approval by the full committee:

Minor revisions to consent materials and other documentation, or clarifications submitted by the investigator in response to a request by the convened IRB as condition(s) of final approval may be reviewed by the IRB Chair/Designee, or a subcommittee of IRB members designated by the convened IRB.

1.7.2 Minor changes:

- An IRB Chair/Designee may use the expedited review procedure to review minor changes in research protocols that were previously approved via expedited and/or full committee review during the period for which approval is authorized. Any protocol revision that presents more than a minimal risk of harm to the subjects must be reviewed by the full committee at a convened meeting.

- Serious adverse event and safety reports: These reports will be handled in accordance with SOP RR 408 – Serious and Unexpected Adverse Events

2. SCOPE

These policies and procedures apply to all non-exempt human subjects’ research.

3. RESPONSIBILITY

OPHS staff are responsible for facilitating the review of expedited applications and pre-reviewing submissions that qualify for expedited review as well as providing a list of protocols reviewed under expedited procedures to IRB members at convened meetings. Staff will consult with the IRB Chair/Designee and/or OPHS Director as necessary in order to determine if an application may be reviewed by expedited procedures.

The IRB Chair/Designee is responsible for the review and approval of all applications eligible for expedited review.

Other IRB members may be consulted and/or conduct reviews as needed or requested by the IRB Chair based on their specific expertise. An ad hoc consultant may also be asked to review the research, if the Chair/Designee, OPHS Director, or a senior staff member feels that the research activities involve issues that necessitate the additional consultation of someone with relevant expertise outside the realm of the IRB members. However, it is important to note that an ad hoc consultant does not have authority to grant approval.
4. REVIEW PROCESS OVERVIEW

Expedited Review of New Study, Amendment, Renewal & Response to Conditions

OPHS staff coordinate the review process and perform a preliminary check of applications that appear to qualify for expedited review. If additional documentation or information is necessary, the responsible staff member initiates correspondence (usually by email) to the investigator. When the investigator responds, the staff member verifies that all items have been addressed and the application is complete. The application and response are then routed to the IRB Chair/Designee at which point he or she will review the research. If any concerns are identified, the Chair/Designee will return the application along with his or her comments to the staff member who will communicate these comments to the investigator. If there are no concerns, or once the concerns have been addressed, the IRB Chair/Designee will grant approval.

Following approval, the staff member sends the investigator a copy of the approval letter and the approval-stamped English Informed Consent documents (if any).

If there are any issues that cannot be resolved or if the Chair/Designee determines that the application does not meet the criteria for review by expedited procedures, the application must go to the full committee, the convened IRB, for review; the IRB Chair/Designee cannot disapprove a study via the expedited review process.

5. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.109
21 CFR 56.109
45 CFR 46.102
45 CFR 46.110
21 CFR 56.110

Federal Register Volume 63, No 216
45 CFR 46.111
21 CFR 56.111

45 CFR Subparts B, C & D
FDA Information Sheets, 1998
The Belmont Report

6. ATTACHMENTS

ATT 008 CPHS Application Cover Sheet
ATT 007 CPHS Checklist for Financial Conflict of Interest
ATT 013 CPHS Protocol Narrative Form
ATT 016 Staff Review Sheet - New Expedited Application
ATT 015 IRB Protocol Review Standards Checklist
1. POLICY

IRB approval does not indicate unlimited approval. Periodic review of research is necessary to determine whether the research should be continued, modified/adjusted, or terminated. The IRB conducts continuing review of research taking place within its jurisdiction at intervals appropriate to the degree of risk, but not less than once per year.

Specific Policies

1.1 Interval of Review for Purposes of Renewal

The IRB must conduct continuing review of protocols for purposes of renewal of the IRB approval period not less than once per year. “Not less than once per year” (45 CFR 46.109e) means that the research must be reviewed and approved on or before the one-year anniversary of the previous IRB review date, even though the research activity may not have begun until some time after the IRB gave its approval. If the IRB performs continuing review of the research within 30 days before the expiration of the current approval, the anniversary date may be retained as the date by which the next continuing review must occur. For each study, the IRB will decide the frequency of continuing review necessary to ensure the continued protection of the rights and welfare of the research subjects.

1.2 Extensions of Approval Period

There is no provision for grace periods extending approval for the conduct of the research beyond the expiration date of IRB approval. When continuing review and approval does not occur on or before the expiration date specified, approval automatically expires and the investigator must suspend research activities, including participant recruitment or enrollment, until the research has been reviewed and approved by the IRB.

However, if the investigator is in communication with the IRB and in the opinion of the IRB or Chair subjects participating in such a study would suffer a hardship should participation be discontinued, participation may continue beyond the expiration date for a reasonable amount of time. Nevertheless, new subjects cannot be enrolled in a study for which approval has expired. Additionally, prospective research data cannot be collected, and interactions or interventions may not take place until a continuing review report or other progress report is reviewed and approved.

1.3 Criteria for Renewal

Continuing review must be substantive and meaningful. When considering whether or not to renew a study, the IRB revisits the same criteria used to grant initial approval (see SOP RR 401 – Initial Review). Therefore, in order to renew approval of the research, the IRB, or the reviewers of protocols reviewed under an expedited procedure, must minimally determine that:
• risks to subjects are minimized;
• risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of knowledge expected to result;
• the selection of subjects is equitable;
• informed consent is appropriately sought from the subject or his or her legally authorized representative, in accordance with and to the extent required by state local and federal regulations;
• informed consent is properly documented as required by state, local and federal regulations;
• where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects;
• where appropriate, adequate provisions have been made to protect the privacy of subjects and to maintain the confidentiality of data; and
• when some or all subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

1.4 Continuing Review Process

1.4.1 Continuing review application – The investigator must submit to the IRB a complete continuing review application that includes:
• A copy of the updated protocol, if amended;
• A copy of the current informed consent document and any newly proposed or modified consent document;
• The number of subjects entered to date and since the last review;
• A summary of adverse events and any unanticipated problems involving risks to subjects or others and any withdrawal of subjects from the research or complaints about the research since the last IRB review;
• A summary of any interim findings since the last review;
• Any recent scientific literature or other relevant information that has come to light and might affect the risk/benefit ratio for subjects or their willingness to participate in the research.
• Any relevant multi-center trial reports; and
• New financial conflict of interest disclosure(s).

1.4.2 Consent document – The IRB shall review the consent document and ensure that the information is still accurate and complete. Any significant new findings that may relate to the subject’s willingness to continue participation must be provided to the subject in accordance with regulations set forth at 45 CFR 46.116(b)(5). Review of currently approved or newly proposed consent documents must occur during the continuing review of the research by the IRB, but informed consent materials should be reviewed whenever new information becomes available that would require modification of the consent document.
1.4.3 Current approved protocol – A copy of the protocol including any previously approved modifications will be sent to at least one member of the IRB (the primary reviewer) of the continuing review. Upon request, any member of the IRB will also have complete access to the protocol file and relevant minutes prior to or during the convened meeting.

1.4.4 Amendments – Any changes to a research protocol should be submitted to the IRB for review as generated during the course of the study. They may also be submitted at the time of continuing review. A separate description of the change(s) and all appropriate/relevant documentation must accompany the continuing review application.

1.4.5 Continuing review of clinical trials monitored by a Data and Safety Monitoring Board (DSMB) – When a clinical trial is subject to oversight by a DSMB whose responsibilities include review of adverse events, interim findings, and relevant literature (e.g., DSMBs operating in accordance with the National Cancer Institute Policy for Data and Safety Monitoring of Clinical Trials), the IRB conducting continuing review may rely on a current statement from the DSMB indicating that it has reviewed study-wide adverse events, interim findings, and any recent literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB. However, the IRB must still receive and review reports of local, on-site unanticipated problems involving risks to subjects or others and any other information needed to ensure that its continuing review is substantive and meaningful.

1.4.6 Mode of review – A protocol that was originally reviewed using the expedited review procedure may receive its continuing review on an expedited basis unless the protocol has changed or will change such that expedited review would no longer be appropriate. Conversely, an expedited review procedure may be used for the continuing review of research previously approved by the convened IRB in limited circumstances as described by expedited review categories (8) and (9) (see SOP RR 402 – Expedited Review).

1.4.7 Expedited review of continuing research – When an expedited review procedure is used, the IRB Chair or designated IRB member conducts the review on behalf of the full IRB using the same criteria for renewal as stated in section 1.3 of this policy. If the reviewer feels that there has been a change such that expedited review may no longer be appropriate, he or she may refer the study to the convened IRB for review. It should be noted that the Chair cannot disapprove an application through expedited review procedures.

1.5 Significant New Findings

The IRB may review reports generated from a DSMB, adverse event reports, current literature, and other sources to ascertain the status of the study and assess whether or not the risk/benefit ratio is still acceptable. The IRB will also determine whether or not new information needs to be conveyed to subjects, if a segment of the population may be bearing an undue burden of research risk, or a segment of the population is being denied access to promising therapy.
1.6 Study Completion

Continuing IRB review is required if any of the following activities are ongoing: (i) research-related interactions or interventions with human subjects; (ii) obtaining of identifiable private information; and, (iii) analysis of identifiable private information. Once all of the afore mentioned activities as described in the IRB-approved research plan are finished, then the research study is considered complete and the investigator is no longer required to obtain continuing review and approval for that study by the IRB. The investigator should at this time submit a Study Closure Form (per SOP RR 406 – Study Completions) to notify the IRB of the study’s completion.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

The study investigator is responsible for fulfilling requirements associated with the renewal process in sufficient time for the IRB to carry out continuing review of the research before current approval expires.

The OPHS Director (and/or IRB Administrator) is responsible for establishing the processes for conducting ongoing reviews of research.

The IRB Chair/Designee is responsible for preliminary assessments of adverse events, significant new findings and the need for third party verification.

4. PROCESS OVERVIEW

Continuing Review – Courtesy Reminder

The expiration date of the approval period is clearly listed on the approval letter for each protocol. It is the investigator's responsibility to keep track of the expiration and initiate the renewal process in sufficient time for the IRB to conduct the review before current approval expires. However, the OPHS staff will, as a courtesy, send the investigator reminders at 8 and 6 weeks in advance of the expiration of IRB approval.

If a continuing review application is not received and the approval period expires, an OPHS staff member will send a notice of study closure to the investigator (per SOP RR 409 – Suspension or Termination of a Protocol) informing the investigator to stop all research activities including recruitment and enrollment of research subjects.

Continuing Review - Expedited

When a continuing review application/renewal request that qualifies for expedited review is submitted, OPHS staff facilitate the review process and perform a preliminary review of the submission. If additional documentation or information is necessary, the responsible staff member initiates correspondence (usually by email) to the investigator.
When the investigator responds, the staff member verifies that all items have been addressed and the application is complete. The application and response are then routed to the IRB Chair/Designee at which point he or she will review the research. If any concerns are identified, the Chair/Designee will return the application along with his or her comments to the staff member who will communicate these comments to the investigator. If there are no concerns, or when the concerns have been addressed, the IRB Chair/Designee will grant approval by signing the summary sheet prepared by the staff member.

Once the continuation of the research has been approved, the staff member sends the investigator a copy of the approval letter and the English approval-stamped consent documents (if any).

If there are any issues that cannot be resolved or if the Chair/Designee determines that the application does not meet the criteria for review by expedited procedures, the application must go to the full committee, the convened IRB, for review; the IRB Chair/Designee cannot disapprove a study via the expedited review process.

**Continuing Review – Full Committee**

When a Continuing Review Report/Renewal Request that requires review by the convened IRB is submitted, it is added to the agenda of the next meeting of the appropriate committee. OPHS staff compile the necessary documentation (e.g., continuing review form, consent documents) per SOP FO 303 – IRB Meeting Administration.

Prior to the IRB meeting, the primary and secondary reviewers (and special consultants, as needed) review the renewal request (1) to ensure its adherence to federal, state, local, and university guidelines and summarize findings; (2) to determine whether any special considerations may be applicable; and (3) to ascertain if any evidence exists that third party verification of submitted information is needed.

At the IRB meeting, the primary reviewer (and/or secondary reviewer) presents the study responding to staff comments and elaborating on any aspect of the study s/he deems appropriate to discuss. Other members may ask questions and engage in discussion regarding the protocol. The IRB may approve the renewal request, require revisions, or disapprove continuation of the research (see SOP RR 407 – Categories of Action). The investigator is notified of the review outcome in writing. If minor revisions or clarifications are required, the IRB Chair/Designee or a subcommittee of IRB members may be given responsibility for review of the investigator’s response in an expedited manner. However, if the IRB determines that the concerns/revisions are substantive, the responsive materials will be sent to another convened meeting for consideration.

Once the continuation of the research has been approved, a staff member sends the investigator a copy of the approval letter and the English approval-stamped consent documents (if any).

If the IRB does not re-approve the research, a staff member will send the investigator a letter (per RR 409 – Suspension or Termination of a Protocol) identifying the reason for the suspension or termination.
5. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.109
21 CFR 56.109
45 CFR 46.111
21 CFR 56.111
45 CFR 46.110
21 CFR 56.110

Federal Register Volume 63, No 216
45 CFR 46 Subparts B, C & D
OHRP Guidance on Continuing Review (Jan 2007)
The Belmont Report

6. ATTACHMENTS

ATT 008  CPHS Application Cover Sheet
ATT 007  CPHS Checklist for Financial Conflict of Interest
ATT 017  CPHS Study Renewal/Continuation Form
ATT 018  Full Board Staff Summary Template – Continuation
ATT 019  Staff Review Sheet – Expedited Continuation
1. POLICY

In general, all changes/modifications to approved research must be submitted for IRB review and approval before they can be implemented. The only exception to the requirement for prior IRB review and approval is in an instance when the changes are “necessary to eliminate apparent immediate hazards to the subject” (45 CFR 46.103b4, 21 CFR 56.108a). In such cases, the actions taken should be reported to the IRB within 7 calendar days per SOP RR408 – Unanticipated Problems and Adverse Event Reporting, and approval should be sought for permanent changes to prevent the hazards in the future.

Specific Policies

1.1 Definition and Examples

Amendment means any modification made to an approved protocol. Amendments may include, but are not limited to, procedural changes, adding or removing key personnel, requesting additional subjects beyond the original approved number, new funding sources, new or revised advertisements, changes to the informed consent documents, changes to surveys or questionnaires, and/or addition of a research site.

1.2 Submission Requirements for Amendment Requests

Investigators must submit requests for changes to the IRB in writing. These requests must include the following:

A. A description of and justification for the changes.
B. A revised consent document (if changes have been made).
C. Any revised instruments or other documentation affected by the amendment (e.g., recruitment materials, protocol etc).
D. A new disclosure of financial conflict of interest (if applicable)
E. Any other relevant documentation required by the IRB

1.3 Determination of Review Level

The OPHS staff will determine the level of review required in consultation with IRB Chair/Designee and/or OPHS Director when appropriate.

- If the research was previously deemed to present minimal risk to the participants and the amendment poses no change in level of risk, the amendment will be considered through expedited review.
- If the research was previously deemed to present minimal risk and the amendment appears to present an increase in risk, the amendment will be considered by the convened IRB (full committee).
• If the research was previously deemed to present greater than minimal risk to the participant and the amendment appears to pose no change in level of risk, the amendment will be considered by the convened IRB.

• If the research was previously deemed to present greater than minimal risk and the amendment presents an increased risk, the amendment will be considered by the convened IRB.

• All minor changes in previously approved research may be reviewed by expedited procedures.

1.4 Minimal Criteria for Approval of Amendment

When considering whether to approve an amendment to a study protocol, the IRB revisits the same criteria used to grant initial approval (see SOP RR 401 – Initial Review). Therefore, the IRB or Chair/Designee must minimally determine that:

• risks to subjects are minimized;

• risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of knowledge expected to result;

• the selection of subjects is equitable;

• informed consent is appropriately sought from the subject or his or her legally authorized representative, in accordance with and to the extent required by state local and federal regulations;

• informed consent is properly documented as required by state, local and federal regulations;

• where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects;

• where appropriate adequate provisions have been made to protect the privacy of subjects and to maintain the confidentiality of data; and

• when some or all subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

OPHS staff, in consultation with the IRB Chair/Designee when appropriate, are responsible for the initial assessment of level of risk associated with the proposed amendment. However, the final determination of level of risk must be made by the convened IRB or, if the application is reviewed by expedited procedures, by the Chair/Designee.

The IRB Chair/Designee is responsible for performing expedited review of amendment requests that involve no more than minimal risk.
OPHS staff are responsible for facilitating the review process and conducting a preliminary review for all amendment requests.

4. PROCESS OVERVIEW

Amendment Review - Expedited

When an amendment request that qualifies for expedited review is submitted, an OPHS staff member will coordinate the review process and perform a preliminary review of the submission. If additional documentation or information is necessary, he or she initiates correspondence to the investigator. When the investigator responds, a staff member verifies that all items have been addressed and the application is complete. The application and response are then routed to the IRB Chair/Designee at which point he or she will review the research. If any concerns are identified, the Chair/Designee will return the application along with his or her comments to the staff member who will communicate these comments to the investigator. If there are no concerns, or when the concerns have been addressed, the IRB Chair/Designee will grant approval.

Once the amendment to the research has been approved, the staff member sends the investigator a copy of the approval letter and the approval-stamped English consent documents (if any).

If there are any issues or concerns that cannot be resolved during the expedited review process, the application must go to the full committee for review. The IRB Chair?Designee cannot disapprove an amendment to the research by expedited procedures.

Amendment Review – Full Committee

When an amendment request that requires review by the convened IRB is submitted, it is added to the agenda of the next meeting of the appropriate committee and an OPHS staff member compiles the necessary documentation (e.g. Staff Summary, Application and supporting documents).

Prior to the IRB meeting, the primary and secondary reviewers (and special consultants, as needed) review the renewal request (1) to ensure its adherence to federal, state, local, and university guidelines and summarize findings; (2) to determine whether any special considerations may be applicable; and (3) to ascertain if any evidence exists that third party verification of submitted information is needed.

At the IRB meeting, the primary and secondary reviewers provide a summary review and recommendation. Other members may ask questions and engage in discussion regarding the protocol. The IRB may approve the amendment request, disapprove the application, require minor revisions (conditional approval), or defer consideration to another convened meeting (see SOP RR 407 – Categories of Action). The investigator is notified of the review outcome in writing. If minor revisions or clarifications are required, the IRB Chair/Designee or a subcommittee of IRB members may be given responsibility for review of the investigator’s response in an expedited manner. However, if the concerns/revisions are substantive, the investigator will be required to submit responsive materials for full committee review.
Once the amendment to the research has been approved, a staff member sends the investigator a copy of the approval letter and the English approval-stamped consent documents (if any).

5. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.103
21 CFR 56.103
45 CFR 46.109
21 CFR 56.109
45 CFR 46.110
21 CFR 56.110
45 CFR 46.111
21 CFR 56.111
45 CFR 46 Subparts B, C & D
The Belmont Report

6. ATTACHMENTS

ATT 008  CPHS Application Cover Sheet
ATT 007  CPHS Checklist for Financial Conflict of Interest
ATT 020  CPHS Study Amendment Form
ATT 021  Full Board Staff Summary Template – Amendment
ATT 022  Staff Review Sheet – Expedited Amendment
1. POLICY

Federal regulations authorize the IRB to establish procedures for the concurrent monitoring of research activities involving human subjects. Periodic review of research activities is necessary to determine whether the research should be continued, modified/adjusted, or terminated.

IRB approval for the conduct of a study may be withdrawn if the risks to the subjects are determined to be unreasonably high (e.g., there is evidence that more than an expected number of adverse events have occurred, unexpected serious adverse events have occurred, or the investigator is not conducting the investigation in compliance with IRB or institutional guidelines). Such findings may result in more frequent review of the study to determine if approval should be withdrawn or enrollment stopped until corrective measures can be taken or the study terminated. Methods of monitoring ongoing research include, but are not be limited to, the following activities:

- Review for Purposes of Verification
- Review of Unanticipated Problems and Serious Adverse Events
- Revisions of Research Protocols
- Review of Significant New Findings
- Reports from Outside Sources
- Review of Reports of Noncompliance
- Review of Protocols at the time of Award of External Funds

Specific Policies

1.1 Site Visits and Third Party Verification

The IRB has the authority to observe, or have a third party observe, the informed consent process of research it has approved, and/ or verify that the study is being conducted as required by the IRB and within the institutional policies and procedures and site-specific procedures, as appropriate. See SOP QA 903 – Review for Purposes of Verification for details.

1.2 Review of Unanticipated Problems and Adverse Events

Subject safety is of the greatest importance for both the individual subject and the goals of the study. The investigator must promptly report unanticipated problems and adverse events to the IRB per SOP RR 408 – Unanticipated Problems and Adverse Event Reporting.
1.3 Amendment (Revision) Review

Changes in approved research, during the period for which approval has already been given, may not be initiated without prior IRB review and approval (full committee or expedited review, as appropriate), except where necessary to eliminate apparent immediate hazards to human subjects per SOP RR 404 – Amendment (Revision) Review.

1.4 Review of Significant New Findings

During the course of a study, the IRB may review reports generated from a Data and Safety Monitoring Board (DSMB), adverse event reports, current literature, and other sources to ascertain the status of the study and assess whether or not the risk/benefit ratio is still acceptable. The IRB will also determine whether or not new information needs to be conveyed to subjects, if a segment of the population may be bearing an undue burden of research risk, or a segment of the population is being denied access to promising therapy.

1.5 Reports From Outside Sources

It is the responsibility of the OPHS staff and IRB members to act on information or reports received from any internal (within the University) or external source that indicates a study being conducted at any facility under the jurisdiction of the IRB could adversely affect the rights, safety, or welfare of research subjects.

1.6 Review of Reports of Noncompliance

All reports of inappropriate involvement of human subjects in research must be investigated by the IRB Chair and OPHS Director and may be referred to the IRB for investigation. The results of the investigation will be reported to the IRB, the IO, and the appropriate University official(s). Regulatory authorities and Sponsors may also be notified. Such reports of noncompliance may come from any source including IRB members, investigators, subjects, institutional personnel, the media, anonymous sources, or the public. See RR 410 – Noncompliance for additional detail.

1.7 Review of Protocols at the time of Award of External Funds

The IRB is responsible for ensuring that the human subject research activities as described in Department of Health and Human Services (DHHS) awards are compatible with what has been reviewed and approved by the IRB per SOP RR 411 – Grant Protocol Review.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

The OPHS Director, in consultation with the IRB Chair, is responsible for establishing the processes for conducting ongoing reviews of research.
IRB Chair/Designee is responsible for preliminary assessments of adverse events, significant new findings and the need for third party verification. The IRB Chair may constitute a subcommittee of the IRB to review adverse events.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 812.64
21 CFR 56.108, 56.109, 56.113
45 CFR 46.103, 46.109, 46.115
FDA Information Sheets, 1998
1. POLICY

As a result of its review, the IRB may decide to approve or disapprove the proposed research activity, or to specify modifications required to secure IRB approval of the research activity. When reviewed by the convened IRB, these actions will be taken by a vote from a majority of voting members. The member must be present physically or via an approved channel of mediated communication per FO 303 – Meeting Administration for details, excepting those members recused in accordance with the IRB’s conflict of interest policies. When reviewing research in an expedited manner, the IRB Chair (or Designee) can take any of the following actions except to disapprove a study.

Specific Policies

1.1 Actions

The IRB may take one of the following actions as a result of its review of research submitted for initial review or for continuing review. The investigator will be notified of such actions in writing.

A. Approval: The IRB has identified no revisions or questions about the research and the application is approved as submitted. The study has been found to meet the requisite criteria for approval and the research may be carried out as described.

B. Conditional Approval: The IRB has identified items of concern including specific minor revisions or clarifications and requires a written response from the investigator. The members may ask the investigator to clarify a point, provide additional information or make revisions to application materials such as the protocol or consent form. The study has been approved by the IRB in principle such that the investigator’s response may be reviewed and approved in an expedited manner by the IRB Chair/Designee or by a subcommittee of members appointed by the IRB. No research activities may take place until the response has been reviewed and the research has been approved.

C. Deferral: The overall goal of the research may be worthwhile, however, the IRB has identified substantive clarifications and/or modifications that are needed in order to meet one or more criteria for approval of research (see SOP RR 401 – Initial Review and SOP RR 402 – Continuing Review). The members have explicitly asked for the study to return for additional review pending a response from the investigator. The investigator must respond to these concerns in writing for the study to be reconsidered at another convened meeting.

D. Disapproval: The IRB disapproves the study in principle and the research may not take place. This is decided when the research raises significant scientific or ethical concerns and fails to meet one or more of the requisite approval criteria. This action must be taken at a convened meeting.
1.2 Risk Level

For each new application the IRB will determine whether the research presents minimal risk or greater than minimal risk of harm to subjects. For amendments and continuing research, the IRB will determine whether the risk level has increased, decreased or remains unchanged.

1.3 Approval Period and Additional Monitoring

The IRB will determine the interval for continuing review. The norm is to grant approval for 365 days. The approval period begins on the date approval is granted by the convened IRB, IRB Chair/Designee or subcommittee and ends on the anniversary of the date of review by the IRB or, in the case of expedited approvals, the date of review by the IRB Chair/Designee. However, the IRB may approve the research for a shorter period and will consider, at least, the following criteria to assess whether a period of less than one year is appropriate: (i) degree of risk to the subjects; (ii) history of non-compliance with this study, the investigator or collaborators; and (iii) fluctuating standard of care or other conditions bearing on the study design and assessment of risks and benefits of the research.

The IRB will also determine whether additional monitoring of the research is necessary per SOP RR 405 – Monitoring Ongoing Research. Methods of monitoring ongoing research may include, but are not be limited to, site visits, third party verification, observation of the research and/or consent process as well as data and safety monitoring.

1.4 Investigator Appeal of IRB Action

1.4.1 Internal Appeal. Investigators may appeal an IRB decision regarding the revisions required by the IRB to the protocol and/or informed consent form and/or other components of the IRB Application; or, the disapproval of a study. Appeals must be submitted in writing within 30 days of IRB notification of actions and should provide new information that would aid in evaluating the request for re-consideration. In addition, the investigator may appear before the IRB to supply information or answer questions. The appeal will be reviewed at a regularly scheduled convened meeting usually within 30 days of receipt.

1.4.2 External Appeal. If the investigator has exhausted internal appeal, he or she may appeal to the Vice Chancellor for Research who may then convene an ad hoc committee to provide a non-binding recommendation(s) to the IRB to resolve the issue. If the recommendation(s) are not accepted by the IRB, the appeal is denied, IRB’s the decision is final. IRB decisions to not approve specific aspects or an entire research protocol cannot be overturned by any other agent of the University.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.
3. RESPONSIBILITY

The OPHS Director is responsible for ensuring that all IRB decisions and actions are based on institutional requirements.

The IRB Administrator is responsible for keeping IRB Reviewers apprised of regulatory requirements.

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

4. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.109
21 CFR 56.109
45 CFR 46.111
21 CFR 56.111
45 CFR 46.113
21 CFR 56.113
1. POLICY

This policy defines the obligation to report any unanticipated problem involving risks to subjects or others and serious adverse events.

All adverse events that are serious, unanticipated, and possibly associated with the study must be reported to the IRB. Based upon these reports, the IRB may reconsider its approval of the study, require modifications to the study, revise (shorten) the continuing review timetable, and/or require that currently enrolled subjects be given additional information regarding the event or risk.

Although the IRB only requires reporting of unanticipated problems that are serious adverse events, unanticipated, and possibly associated, the Investigator is responsible for tracking all unanticipated problems and/or adverse events in a research study, including new physical and psychological symptoms. Trends and frequencies of adverse events that do not require immediate reporting should be reported to the IRB at the time of continuing review.

Specific Policies

1.1 Definitions

1.1.1 Adverse event: Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research. Adverse events may also be psychological in nature.

1.1.2 External adverse event: From the perspective of one particular institution engaged in a multicenter clinical trial, external adverse events are those adverse events experienced by subjects enrolled by investigators at other institutions engaged in the clinical trial.

1.1.3 Internal adverse event: From the perspective of one particular institution engaged in a multicenter clinical trial, internal adverse events are those adverse events experienced by subjects enrolled by the investigator(s) at that institution. In the context of a single-center clinical trial, all adverse events would be considered internal adverse events.

1.1.4 Serious Adverse Event: Any adverse event temporally associated with the subject’s participation in research that meets any of the following criteria:

(1) results in death;
(2) is life-threatening (places the subject at immediate risk of death from the event as it occurred);
(3) requires inpatient hospitalization or prolongation of existing hospitalization;
(4) results in a persistent or significant disability/incapacity;
(5) results in a congenital anomaly/birth defect; or
(6) 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 
(examples of such events include allergic bronchospasm requiring 
intensive treatment in the emergency room or at home, blood dyscrasias or 
convulsions that do not result in inpatient hospitalization, or the 
development of drug dependency or drug abuse).

1.1.4 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:
(1) the known or foreseeable risk of adverse events associated with the 
procedures involved in the research that are described in (a) the protocol– 
related documents, 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
(2) 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.

1.1.5 Unanticipated problem involving risks to subjects or others.
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 a subject’s participation 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) related to 
the research than was previously known or recognized.

1.1.6 Possibly related to the research
There is a reasonable possibility that the adverse event, incident, experience or 
outcome may have been caused by the procedures involved in the research.

1.2 Reporting Requirements
1.2.1 The Lead Investigator must report to the IRB all unanticipated problems 
involving risks to subjects or others and serious adverse events that are possibly 
related to the research. [NOTE: When in doubt, if there is any possibility that 
the event is related to the study intervention or procedures, the event should be 
reported.]
1.2.2 Deaths MUST be reported to the IRB if they occur within 30 days of study intervention.

1.2.3 Timeline requirements:

   A. If the unanticipated problem involving risk to subjects or others or a serious adverse event occurred at a UCB research site, it must be reported to the IRB within seven (7) calendar days of recognition/notification of the event. The Lead Investigator (LI) is responsible for ensuring that this reporting is done. The written report must be received by OPHS within ten (10) working days.

   B. If the serious adverse event or unanticipated problem occurred at an external site as part of a multi-site research project, it must be reported to the IRB within thirty (30) calendar days of recognition/notification of the event.

   C. Any other unanticipated problem should be reported to the IRB within two (2) weeks of the investigator becoming aware of the problem.

1.2.4 The reporting requirements of other organizations (e.g. Sponsor, FDA) also must be completed and are not satisfied or precluded by submitting an unanticipated problem or serious adverse event report to the IRB. Likewise, submitting adverse event reports to other organizations (e.g., Sponsor, FDA) does not satisfy the reporting requirement to the IRB. The Director of OPHS is responsible for reporting to OHRP as required and reporting to the appropriate Institutional Official.

1.2.5 The LI is responsible for assessing and documenting unanticipated problems and serious adverse events and reporting to the IRB, as required by this policy, regardless of who observed or became aware of the event.

   A. In the absence of the lead investigator, a co-investigator can fulfill these requirements to meet the reporting timeline.

   B. In the absence of either the lead investigator or a co-investigator project coordinator, a student member of the research team or other research personnel must contact the OPHS for direction.

   C. In instances where a student (graduate or undergraduate) suspects an unanticipated problem or serious adverse event, it is expected that the faculty advisor will be immediately made aware of any suspicious event that occurs during the study. After consultation, a determination should be made as to reporting to the IRB.

1.2.6 The investigator should use his or her own judgment when determining if an event is considered reportable. When in doubt, the investigator should contact the OPHS for guidance.

1.2.7 If an IRB-approved protocol includes more stringent reporting requirements, or if a Data and Safety Monitoring Board (DSMB) requires reporting events to the IRB, the more stringent requirements must be adhered to.
1.2.8 Any unanticipated problems or adverse events that do not meet the above reporting requirements may be reported at the time of continuing review and/or via independent Data and Safety Monitoring Board reports, if applicable.

1.2.9 For purposes of confidentiality, subject names must not be identified in the event report.

1.2.10 The requirements apply to studies that are open with the IRB. However, if any serious adverse events; or unanticipated problems involving risk to subjects or others; or other unexpected non-serious events occur after the approval period and it appears that a relationship may exist between the event and the research, the Investigator is strongly encouraged to report the event to the IRB.

1.3 Special Considerations

In addition to drug and intervention associated adverse events, investigators should be aware that there are other types of unanticipated problems events which might be associated with subjects' participation in research studies. These include:

1.3.1 **Serious negative social, legal, or economic consequences resulting from participation in a study.** Situations sometimes occur, especially in field-based studies, where a subject's confidentiality may inadvertently be compromised that may result in serious negative social, legal or economic ramifications for the subject (e.g., serious loss of social status, loss of a job, interpersonal conflicts).

1.3.2 **Serious psychological and/or emotional distress resulting from participation in a study.** Sometimes during the course of participating in a study, subjects may hear or experience something that causes them serious psychological or emotional distress. While, in many cases, these reactions are transitory, occasionally reactions may, in the judgment of the investigator, suggest the need for professional counseling or intervention (e.g., suicidal ideation).

1.4 IRB Actions

1.4.1 Initial review of Adverse Event Reports will be conducted by the IRB Chair (or his or her designee, e.g. OPHS Director). The IRB Chair is authorized to take the following actions in response to any Unanticipated Problem or Serious Adverse Event Report:

A. Perform an administrative review of the report that includes assessing whether the incident is an unanticipated problem and/or a serious adverse event.

B. Schedule the unanticipated problem involving risks to subjects or others and/or the serious adverse event report for review of the full IRB at the next available regularly scheduled meeting.

C. If warranted, convene an emergency meeting of the full IRB to review the report.
D. If warranted, temporarily suspend research if the rights, safety, and welfare of subjects is jeopardized until such time that the full IRB can convene to review the report.

1.4.2 In order to protect the ongoing safety of research subjects due to the nature or frequency of reported events, the following actions may be taken by the IRB:

A. Place the suspect specific study procedures on hold and/or delay further subject involvement in study pending further review and evaluation.

B. Require modifications to the research protocol and/or informed consent document.

C. Shorten the continuing review timetable (i.e., require more frequent continuing reviews)

D. Require the re-consenting of currently enrolled subjects.

E. Suspend the entire study (research protocol)

F. Terminate approval of the research protocol

G. Report the serious adverse event to the Institutional Official

1.4.3 If the event results in an amendment of the informed consent document or the research protocol, an Amendment of Protocol form must also be submitted to the IRB. See SOP RR 403 – Continuing Review and SOP RR 404 – Amendment Requests.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

IRB Chair is responsible for ensuring the appropriateness of all IRB decisions and actions.

OPHS Director is responsible for ensuring that all IRB decisions and actions are based on institutional and regulatory requirements.

IRB Chair and/or his or her designee (e.g. Director or senior OPHS staff) will receive all reports of Unanticipated Problems involving risks to subjects or Serious Adverse Events.

OPHS Director is responsible for reporting Unanticipated Problems involving risks to subjects or Serious Adverse Events to the IRB Chair, IRB and/or the IO as needed.

4. PROCESS OVERVIEW

Unanticipated problems that are serious adverse events, unanticipated, and possibly associated should be reported to the Director of the Office for Protection of Human Subjects as soon as possible and certainly within seven calendar days of the Lead Investigator learning of the incident. Initial reports may be received via fax, mail/delivery, phone, email, or during
a site visit. However, Investigators are required to submit an official CPHS (IRB) Unanticipated Problem or Serious Adverse Event Report form.

The Director or IRB Administrator ensures that incoming reports have been recorded and forwarded to the IRB Chair (or his/her designee) for review.

The IRB Chair reviews the Reports. He or she evaluates the incoming report and he or she determines what actions, if any, may be needed to protect the rights, safety, and welfare of research subjects due to the nature or frequency of reported unanticipated problem or serious adverse events. If additional review is necessary, the IRB Chair can schedule the adverse event report for review at the next regularly-scheduled full IRB meeting or convene an emergency meeting of the full IRB.

OPHS administrative staff members assist the IRB Chair in communicating the results of the review, discussion and outcome to the Investigator and other appropriate parties.

An OPHS staff member will provide a summary of all reports handled at an expedited level of review at the next convened meeting of the full IRB.

The Director is responsible for reporting to outside agencies the occurrence of serious adverse events or unanticipated problems as per the reporting requirements and guidelines of these pertinent agencies.

5. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.108(b)
45 CFR 46.111(a)(1), 46.113, 46.103(b)(5)
21 CFR 812.46

OHRP – Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events (January 15, 2007)

6. ATTACHMENTS

ATT 023 CPHS Report of Adverse Event or Unanticipated Problem
1. **POLICY**

The IRB shall have authority to suspend or terminate approved human subjects research that is not being conducted in accordance with the IRB’s requirements or that has been associated with unexpected serious harm to subjects. In addition, the IRB has the authority to suspend or terminate any human subjects research activity that has not been reviewed and approved or determined exempt by the IRB (see RR410 – Noncompliance). Any suspension or termination of approval shall include a statement of the reasons for the IRB’s action and shall be reported in writing promptly to the investigator, the Institutional Official (IO), the Director of OPHS, and if the research is federally funded, to the Office for Human Research Protections and the sponsor. Although only the procedures for the IRB suspending or terminating a protocol are discussed in this document, the IO also has the authority to suspend or terminate research protocols for institutional reasons.

**Specific Policies**

1.2 **Reasons for Suspension/Termination**

The IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with federal and state regulations, University of California Office of the President or UC Berkeley policy, or IRB requirements, or research that has been associated with unexpected serious harm to subjects (45 CFR 46.113). A research project may be suspended or terminated for a variety of reasons, including but not limited to:

A. Serious adverse event(s) and unanticipated problem(s)
B. Detrimental change in the risk-benefit ratio of the study
C. Conduct of research activities without prior IRB approval
D. Failure to obtain appropriate consent
E. Failure of investigators to complete required training
F. Other noncompliance issues

1.3 Authorities

1.3.1 The IRB is authorized to suspend or terminate research protocols.

1.3.2 The IRB Chair (or his/her designee - e.g. Vice Chair) is authorized to suspend research protocols in emergency situations (i.e., when the rights, safety, or welfare of subjects are in immediate jeopardy).

1.4 Suspension and Termination Process and Notification

1.4.1 When potential cause for further investigation is demonstrated, an inquiry into the specific circumstances giving rise to concern with a specific protocol will be conducted. The initial inquiry and investigation procedures are described in RR 410 – Noncompliance or as described in RR 408 – Unanticipated Problems and Adverse Event Reporting depending on the nature of the initiating incident. If a protocol is determined to be in noncompliance or a detrimental change in the risk/benefit occurs, further action will be taken by the IRB.

1.4.2 In most cases, the IRB will review the circumstances of the case and make a determination of suspension or need for termination. Other IRB members may be consulted as needed in the decision making process leading up to bringing the issue to the full committee.

1.4.3 In emergency situations, the IRB Chair in consultation with the IRB Vice Chairs, Director or IRB Administrator will make a determination of the need to suspend or terminate a study immediately.

1.4.4 The IRB Chair (or his or her designee) will draft a letter that includes the following:
   A. a description of the event
   B. the determination of the IRB (i.e., suspension, termination)
   C. justification for the determination
   D. requirements of the investigator (e.g., cease all data collection)

The letter will be forwarded to the Investigator, Investigator’s Faculty Advisor (if applicable), Investigator’s Department Head, IO, OPHS Director, any Sponsor(s), and applicable federal agencies (e.g., FDA, OHRP). A copy of the form is filed with the protocol’s IRB file.

1.4.5 The Lead Investigator is responsible for notifying (in a timely manner) all co-investigators, key personnel, and other research staff associated with the protocol as well as any subcontract grantees if the protocol has been suspended or terminated.
1.5 Participant Involvement in Suspended or Terminated Protocols

1.5.1 When a protocol is suspended or terminated, the Investigator must stop all activity on the protocol, including subject recruitment and enrollment, procedures, and analysis and/or publication of existing data.

1.5.2 When the suspension or termination of a research protocol involves the withdrawal of current participants from the research, the Investigator will be required to:

A. inform enrolled participants that the study has been suspended or terminated; and,
B. develop procedures for withdrawal that protect the rights, safety, and welfare of participants, and describe those procedures to participants.

1.5.3 In certain circumstances, project activities may continue if stopping study procedures/treatment would adversely affect the welfare of a subject. When the suspension or termination of a research protocol does not involve the withdrawal of current participants from the research, the Investigator will be required to:

A. notify the IRB office immediately of the need to continue any procedures/treatment;
B. inform enrolled participants that the study has been suspended or terminated; and,
C. report any serious adverse events or unanticipated problems involving risks to participants to the IRB.

1.6 Reinstatement of Suspended or Terminated Protocols

1.6.1 Suspended Studies. To reinstate a project that has been suspended, the investigator must resolve satisfactorily any pending issues as required by the IRB. After one year of suspension or the expiration date of the study (whichever comes first), if adequate progress has not been made on the pending issues then the IRB will administratively close the study protocol.

To reinstate a project that has been suspended the investigator must contact the OPHS in writing within 30 days of the suspension. The investigator must address the following in a letter:

A. Reason for requesting the study be reinstated.
B. Short summary of the purpose of the study and intended objectives/outcomes. This may be incorporated into the protocol narrative noting any changes, revisions or clarifications.
C. Description of how the study has changed, if any, since initial approval using the appropriate Amendment form and procedure for identifying changes in the protocol narrative.
D. Summary of status of the study, including:
   (1) how many subjects were enrolled;
(2) at what point in the treatment/procedures were the subjects at the time of suspension;

(3) any adverse events or amendments since last continuing review, including a description of each;

(4) any additional relevant information.

E. Documented plan to ensure that reason for suspension will not happen again and that the study will be in compliance with all applicable laws and regulations

F. Anticipated enrollment, if the study is reactivated

G. In the case that IRB-approval of a protocol is reinstated, the IRB may require that subjects who were previously enrolled be re-consented.

1.6.2 Terminated Studies. Terminated studies may be reinstated or reactivated with appropriate modifications to address the reason(s) the study was terminated. Investigators will need to submit a completely new application if they wish to resume a modification version of the terminated study.

2. SCOPE

These policies and procedures apply to all human subjects research conducted by investigators affiliated with UC Berkeley, regardless of whether the protocol was ever submitted, reviewed, or approved by the IRB or determined to be exempt.

3. RESPONSIBILITY

IRB Chair is responsible for authorizing protocol suspensions and bringing terminations to the IRB. He or she is also responsible for making suspension or termination determinations in emergency situations.

OPHS Director and/or any OPHS staff member is responsible for receiving reports of noncompliance, unanticipated problems involving risks to subjects and/or serious adverse events, or other information relative to Section 1.2 above and reporting it to the OPHS Director and IRB Chair.

IRB Chair and OPHS Director are responsible for ensuring that protocol suspensions and terminations are reported to appropriate individuals and organizations in a timely manner (e.g. initial verbal reports (as needed) followed by written notification).

OPHS Director or his/her designee is responsible for overseeing the process by which protocols that have not been updated with proper continuing review paperwork are identified and administratively closed.

4. PROCESS OVERVIEW

Suspensions or Terminations for Cause
When the IRB receives reports of circumstances which may affect the rights, safety, or welfare of human research participants, or reports of research not being conducted in accordance with federal or state regulations, University policy, or IRB stipulations, the IRB will make a determination as to whether the protocol should be suspended or terminated. Under normal circumstances and when the severity of the event in terms of risks to subjects is low (e.g., failure of the LI to complete required training), the determination will be made at the next regularly-scheduled IRB meeting. The IRB Chair may convene an ad hoc committee to meet prior to the next convened IRB meeting to review the case and make a determination of suspension or termination (or no action) if he or she feels it is warranted. In addition, the incident may be referred to the full IRB for discussion and resolution. If the severity of the event is deemed to be high (e.g., noncompliance that puts the rights, safety, or welfare of participants at immediate and/or increased risk), the IRB Chair will review the case and can make an interim determination of suspension. In this later case, the full IRB will review the circumstances of the case and make a determination to continue the suspension, terminate the protocol, or reinstate active approval.

If a study is suspended or terminated, the IRB Chair (or his or her designee) will notify the Investigator in writing of the suspension or termination. The Investigator must cease all project activities effective from the date of the first notice of the suspension or termination.

Administrative Study Closure

On a regular basis, an IRB administrative staff member will identify protocols that have expired and for which no continuing review paperwork or study completion (closure) forms were filed by the Investigator. He or she will notify the Lead Investigator that no renewal was received, all human subjects research must have ceased effective the day of expiration, and that the protocol (study) will be administratively closed if there is no response within a stated period of time. After the first holding time, the protocol is then held for an additional 30 days after which a Study Closure Letter is sent to the Investigator. A copy of the letter will be filed with the protocol. The pertinent file(s) will then be transferred to the record retention area for final long term storage.

5. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.113, 45 CFR 46.109(e)  
21 CFR 56.113

6. ATTACHMENTS

ATT 024 Study Closure Form

Table of Contents
1. POLICY

The IRB grants approval to protocols once it has deemed that proper safeguards have been put in place and that the safety, rights, and welfare of participants are being protected. Therefore, deviations from the approved protocol may alter the risk-benefit ratio for participants, may violate the rules of beneficence, justice, and respect for persons as set forth in the Belmont Report, and may jeopardize in some way the safety, rights, and welfare of participants. As such, noncompliance with IRB and/or institutional requirements as well as deviations that result in noncompliance with the approved protocol merit prompt investigation, review, and/or intervention by the IRB.

If there is evidence that the Investigator is not conducting the research in compliance with IRB and/or UCOP and/or institutional policy, IRB approval for the conduct of a study may be withdrawn. Such circumstances may result in more frequent review of the study to determine if approval should be withdrawn or enrollment stopped until corrective measures can be taken or the study terminated. Furthermore, it is important that staff, subjects, and all other interested parties have a means of communicating information about the conduct of a research project directly to the appropriate institutional officials.

Specific Policies

1.1 Definitions

1.1.1 Noncompliance. Noncompliance results from a deviation from the IRB approved protocol or the protocol which the IRB has determined to be exempt. The conduct of human subjects research that would have qualified for an exempt determination had it been reviewed by the IRB in advance of initiating the research is also considered a noncompliance.

1.1.2 Violation. These are serious noncompliances with non-exempt protocols where there may be an effect on individual risk; study benefit or results may be altered; and/or when non-exempt human subjects research has occurred without appropriate IRB review and approval; and/or, when a noncompliance repeatedly has or might occur again.

1.2 Reports of Noncompliance

Reports of potential noncompliance may come from any source including, but not limited to, IRB members, Investigators, OPHS staff, subjects, institutional personnel, the media, anonymous sources, or the public. It is the duty of the IRB to be receptive to and act in good faith on allegations of noncompliance. As such, all reports must be brought to the attention of the IRB Chair and Director. In addition, all reports of potential noncompliance involving external funding must be brought to the attention of the Assistant Vice Chancellor-Research Administration and Compliance (AVR-RAC).
for investigation and resolution, in cooperation with the IRB Administrator and the Sponsored Projects Office.

The IRB Chair and Director will investigate and resolve noncompliance issues that are simple or straightforward deviations. Simple noncompliance issues are defined as situations that:

- do not increase the risk to subjects; and,
- appear to be unintentional errors or omissions on the part of the Investigator; and,
- do not involve external funding.

The occurrence and resolution of these incidents of noncompliance will be reported to the IRB during full board meetings.

Reports of potentially serious noncompliance, a violation or situations that do not fit the criteria of simple noncompliance issues must be immediately reported to the Director. The results of violations, serious and/or continuing noncompliance investigations will be reported to the Institutional Official (IO) and other appropriate University officials by the Director. Regulatory authorities or Sponsors may also be notified by the IO (or his or her designee).

1.3 IRB Actions in Response to Reports of Noncompliance

If a simple noncompliance is found to have occurred, the IRB Chair in consultation with the Director will determine the appropriate action. Action by the IRB Chair can include but is not limited to:

- Requiring remedial training (e.g. online educational program, attendance at workshop, one-on-one training)

- Requiring subjects to be re-consented.

- Permitting the use of data that was collected as a result of the noncompliance.

Should noncompliance continue or be repeated at a later date, appropriate action will be determined at a convened meeting. Action by the IRB may include but is not limited to:

- Ask the researcher to voluntarily halt the research until the Investigator is in compliance. If necessary, the IRB may officially suspend and/or terminate the research. If the research is suspended or terminated, OHRP will be notified if the research is funded by a government agency. Likewise, the FDA will be notified if the research involves an FDA regulated product or agent. The Agency Program Director of any federally funded project in noncompliance and suspended or terminated will also be notified.

- Requiring the Investigator to participate and complete further training.

- Disallowing use of the data.

- Limiting the investigator’s human subject research privileges.

- Not permitting publication or dissemination of the results of the research.

- Making recommendations to the IO for further sanctions, stipulations, or restrictions to Investigator’s privilege to conduct human subjects research.
• Sharing information of noncompliance with other institutional committees (e.g., COI, IBC, Research Integrity Officer) as deemed necessary.

When serious noncompliance is discovered or reported, the IRB and when appropriate the institution will act promptly to stop the research, ensure remedial action regarding any breach of regulatory or institutional human subject protection requirements, and address the question of the Investigator's fitness to conduct future human subject research. Serious or continuing noncompliance with federal policies on the protection of human subjects or the policies, procedures or determinations of the IRB must be reported promptly to the Director, IRB Chair and IO as well as the appropriate department or agency head for funded proposals, Sponsors if appropriate, and to OHRP and/or FDA as appropriate.

The IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB policies, is not in compliance with federal regulations, or deviates from the approved protocol. All federally funded protocols that are suspended and/or terminated will be reported to the OHRP and FDA as appropriate. The IRB will attempt to resolve apparent instances of noncompliance without interrupting the conduct of the study, especially if the rights, safety, and welfare of subjects may be jeopardized by the interruption.

The IRB also has the authority to suspend or terminate any activity, study or project of which it becomes aware which meets the definition of “human subjects research” even if the activity, study or project has not been brought before the IRB for review and approval or a determination of exemption.

2. SCOPE

These policies and procedures apply to all research submitted to the UC Berkeley IRB for review and approval and to all human subjects research conducted by UCB investigators even if the research was not brought before the IRB for review and approval; or a determination of exemption; or a finding of “not human subjects research”.

3. RESPONSIBILITY

OPHS Staff are the persons responsible for accepting all allegations of noncompliance or concerns about the conduct of human subjects research. The Director and IRB Chair make determination of the probable validity of the complaint is made. The IRB Chair determines if the potential noncompliance is of a simple or serious nature and, if serious, the IRB Chair convenes an ad hoc IRB subcommittee to conduct an investigation. The Director administratively supports and participates in investigations into serious noncompliance. The subcommittee reviews the allegation of noncompliance, conducts interviews as needed (hearings), reviews all pertinent data or findings of the investigation, deliberates, and may make recommendations to the full IRB as to a course of action.
4. PROCESS OVERVIEW

Reports of noncompliance may come in through any Research Administration and Compliance staff member via fax, mail/delivery, phone, internet, or during an office or site visit. If notified by phone, staff must document receipt of the phone call in the protocol file.

The OPHS Director is the person responsible for accepting all allegations of noncompliance or concerns about the conduct of human subjects research. In cooperation with the IRB Chair, he or she determines the probable validity of the complaint. If there is reasonable potential validity to the complaint, the IRB Chair determines if the potential noncompliance is of a simple or serious nature. If a simple noncompliance is found to have occurred, the IRB Chair in consultation with the Director will determine the appropriate action.

However, if the noncompliance is deemed to be reasonably valid and serious, the IRB Chair convenes an ad hoc subcommittee to conduct an investigation (which includes but is not limited to a review of the noncompliance report submitted by the investigator, supplemental data, interviewing the lead investigator and others as needed). The Director administratively supports and participates in investigations into serious noncompliance. The ad hoc IRB subcommittee reviews the allegation of noncompliance, conducts interviews or hearing as needed, and reviews all pertinent data or findings of the investigation. The results of this investigation are presented to the full IRB where the appropriate course of action is decided. The full IRB may ask for additional more investigation of the matter prior to making any decision. If the IRB determines that the noncompliance is serious and a violation has occurred the IRB Chair, in cooperation with the OPHS Director, reports this in writing to the IO.

The IRB will notify the Investigator in writing, detailing the alleged noncompliance, specifying corrective action, and stating the consequences. Copies of such correspondence shall also be sent to the Sponsor, the individual’s supervisor, OHRP and the Institutional Official as appropriate and required by this SOP.

IRB Administrator ensures that the determinations and requirements of the IRB are communicated to the Investigator as soon as possible. IRB Administrator ensures that all verbal communications are documented (either electronically or on paper) and retained in the study file.

If the IRB determines that the noncompliance is serious and a violation has occurred the IRB Chair, in cooperation with the OPHS Director, reports this in writing to the IO along with any recommendations from the IRB.

5. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.109, 56.113, 56.120
45 CFR 46.109, 46.113
UCB Faculty Handbook: Research Misconduct
http://rac.berkeley.edu/compliancebook/misconduct.html and,
http://research.chance.berkeley.edu/page.cfm?id=105
1. POLICY

The use of the term “vulnerable” in the context of human research protections does not refer to susceptibility of harm, but rather the inability or a threat to the ability of an individual to give voluntary informed consent. When some or all subjects are likely to be vulnerable to coercion or undue influence the IRB must ensure that additional safeguards have been included in the study to protect the rights and welfare of these subjects. Pregnant women as a population are considered vulnerable primarily because of the involvement of a third party with a unique and inextricable relationship to the mother (the fetus) that may be affected by the research and cannot give consent. Therefore, with one exception as noted below at 1.2.2, the IRB may only approve research involving pregnant women, fetuses and/or neonates which satisfies the applicable criteria below in addition to the requirements delineated in SPO RR 401 – Initial Review.

Specific Policies

1.1 Important Definitions

1.1.1 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.

1.1.2 Fetus means the product of conception from implantation until delivery.

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

1.1.4 Delivery means complete separation of the fetus from the woman by expulsion or extraction or any other means.

1.1.5 Neonate means a newborn.

1.1.6 Nonviable neonate means a neonate after delivery that, although living, is not viable.

1.1.7 Viable means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. The Secretary may from time to time, taking into account medical advances, publish in the FEDERAL REGISTER guidelines to assist in determining whether a neonate is viable for purposes of this subpart. If a neonate is viable then it may be included in research only to the extent permitted and in accordance with the requirements of SC501B – Vulnerable Populations: Children and RR401 – Initial Review.

1.1.8 Secretary means the Secretary of Health and Human Services (DHHS) and any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.

1.1.9 Children are persons who have not yet attained the legal age for consent to treatment or procedures involved in the research, under the applicable law of
jurisdiction in which the research is conducted (be it local, national, foreign or domestic).

1.2 Research involving Pregnant Women or Fetuses

1.2.1 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 non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses.

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.

C. Any risk is the least possible for achieving the objectives of the research;

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 IC701 – General Requirement and Documentation of Informed Consent.

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 accordance with the informed consent provisions of IC701 – General Requirement and Documentation of Informed Consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.

F. Each individual providing consent under paragraph D or E above is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.

G. For children who are pregnant, assent and permission are obtained in accord with the provisions of SC503 – Children as Vulnerable Population.

H. No inducements, monetary or otherwise, will be offered to terminate a pregnancy.

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.

J. Individuals engaged in the research will have no part in determining the viability of a neonate.

1.2.2 Exception: In the case of social/behavioral research the above-mentioned conditions are not applicable because the research does not involve the development of important biomedical knowledge and there is no to minimal risk to the fetus.
1.3 Research involving Neonates

1.3.1 Viable Neonates: a neonate that has been determined to be viable may be included in research only to the extent permitted by and in accordance with SC503 – Children as a Vulnerable Population, and RR401 – Initial Review.

1.3.2 Neonates of uncertain viability may not be involved in research until it has been ascertained whether or not a neonate is viable or the following conditions are met:

A. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.

B. Individuals engaged in the research will have no part in determining the viability of a neonate.

C. The IRB determines that either of the following conditions has been met:
   i. The research holds out the prospect of enhancing the probability of survival of the particular fetus to the point of viability, and any risk is the least possible for achieving the objectives of the research.
   ii. The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no risk to the fetus resulting from the research.

D. The legally effective informed consent of either parent of the fetus 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 accordance with IC701 – General Requirement and Documentation of Informed Consent, unless altered or waived in accordance with IC702 – Informed Consent Waivers.

E. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

1.3.3 Nonviable neonates: a nonviable neonate may not be involved in research unless all of the following conditions are met:

A. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.

B. Individuals engaged in the research will have no part in determining the viability of a neonate.

C. Vital functions of the neonate will not be artificially maintained.

D. The research will not terminate the heartbeat or respiration of the neonate.

E. There will be no added risk to the neonate resulting from the research.

F. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means.

G. The legally effective informed consent of both parents of the neonate is obtained in accordance with IC701; however, the waiver and alteration provisions of do not apply here. 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, 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 replace the consent of the parent.

H. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

1.4 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.

B. If information associated with this material is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent regulations apply.

1.5 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 will conduct or fund research that the IRB does not believe meets the requirements of 1.2 or 1.3 (above) 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 (e.g., science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the FEDERAL REGISTER, has determined either:
   i. That the research in fact satisfies the conditions of 1.2 (above), as applicable; or
   ii. The following:
      a. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates;
      b. The research will be conducted in accord with sound ethical principles; and
      c. Informed consent will be obtained in accord with the informed consent provisions of IC 701 and other applicable subparts of this part.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

The OPHS Director and/or IRB Administrator is responsible for maintaining up-to-date review tools for review of research pertaining to vulnerable groups based on new and evolving applicable regulations and guidelines. The Director and Administrator are also responsible for ensuring that the IRB members are apprised of new and evolving regulations and guidelines pertaining to vulnerable populations, for selecting primary reviewers with
appropriate expertise to conduct the reviews of such research, and for securing appropriate consulting expertise as needed for selected reviews.

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

IRB Members are responsible for conducting appropriate review of research planned for vulnerable populations, including an assessment of potential for coercion, in consultation with any appropriate experts and resources.

4. PROCESS OVERVIEW

When proposed research involves vulnerable populations, the IRB must take special precautions to ensure research participants’ rights, safety, and welfare. In all cases involving vulnerable populations, the OPHS Director and/or IRB Administrator must stay abreast of applicable regulations and guidelines. IRB Chair(s) and Members must be cognizant of the subjects’ needs when evaluating the protocol and are responsible for determining any additional protective stipulations to be applied to the research.

When proposed research involves pregnant women and fetuses, OPHS staff, IRB Chair(s), and IRB members will ensure that the protocol contains the appropriate consent and/or assent processes.

5. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46 Subpart B
45 CFR 46.111
21 CFR 56.111
The Belmont Report
OHRP IRB Guidebook
1. POLICY

The use of the term “vulnerable” in the context of human research protections does not refer to susceptibility of harm, but rather the inability or a threat to the ability of an individual to give voluntary informed consent. When some or all subjects are likely to be vulnerable to coercion or undue influence the IRB must ensure that additional safeguards have been included in the study to protect the rights and welfare of these subjects. Prisoners as a population are considered vulnerable because the constraints of incarceration may affect an individual’s ability to give voluntary, informed consent. Therefore, the IRB may only approve research involving prisoners which satisfies the applicable criteria below in addition to the requirements delineated in SOP RR 401 – Initial Review.

Specific Policies

1.1 Important Definitions

1.1.1 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.

1.1.2 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. It is important to note that this definition of minimal risk differs from the definition included in SOP RR 401 – Initial Review.

1.1.3 Secretary means the Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services (DHHS) to whom authority has been delegated.

1.2 Composition of the IRB

When the IRB reviews a protocol involving prisoners as subjects, the composition of the committee must satisfy the following requirements:

A. A majority of the committee (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the committee.

B. 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.
1.3 Inclusion of Prisoners

If prisoners will participate in the research, or subjects may reasonably be expected to become incarcerated at some time point during the course of the study, the IRB may approve research involving prisoners only if it finds that the following conditions are met:

A. The research under review represents one of the permissible categories of research described in section 1.4 below.

B. Any possible advantages accruing to the prisoner through participation in the research, when compared to the general living conditions, medical care, quality of food, amenities, and opportunity for earnings in prison, are not of such a magnitude that the prisoner’s ability to weigh the risks and benefits of the research in the limited-choice environment of the prison is impaired.

C. The risks involved in the research are commensurate with risks that would be accepted by non-prison volunteers.

D. Selection procedures within the prison are fair to all prisoners and immune from arbitrary intervention by prison authority or prisoners. Unless the investigator provides the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of eligible prisoners for the research project.

E. Any information given to subjects is presented in language that is appropriate for the subject population.

F. Adequate assurance exists that parole board(s) 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 clinical investigation will have no effect on his/her parole.

G. Where there is need for follow-up examination or care of subjects after the end of their participation in the research, adequate provision has been made for such examination or care, taking into account the varying lengths of prisoner sentences, and for informing subjects of this fact.

1.4 Categories of Permissible Research

Research involving prisoners is permissible only if the research involves one or more of four permissible categories, or if the research meets the criteria described in a DHHS Secretarial waiver that applies to certain epidemiological research (68 FR 36929, June 20, 2003):

A. The first two categories are (i) the study of the possible causes, effects, and processes of incarceration, and of criminal behavior, and (ii) the study of prisons as institutional structures or of prisoners as incarcerated persons. Research in these two categories is permissible only if the study presents no more than minimal risk, and no more than inconvenience to the subjects.

B. The third category (iii) is research on conditions particularly affecting prisoners as a class. Examples of such research include 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 addition, and sexual assaults. Research in this category may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and has published notice in the Federal Register of his or her intent to approve the research.

C. The fourth category (iv) is research on practices, either innovative or accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In this category, if the IRB-approved proposal is a study in which some prisoners will be assigned to a control group and these prisoners may not benefit from their participation in research, such research may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and has published notice in the Federal Register of his or her intent to approve the research. OHRP interprets control groups which may not benefit from research to include a control group receiving standard of care that the prisoners would otherwise receive, services as usual, or a placebo.

D. The DHHS Secretarial waiver for certain epidemiological research conducted or supported by DHHS functions as a fifth category of permissible research. The criteria for this category are that the research must have as its sole purpose (i) to describe the prevalence or incidence of a disease by identifying all cases, or (ii) to study potential risk factor associations for a disease. The IRB must still review the research under the requirements for prisoners described in this policy and certify to OHRP that an appropriately constituted IRB has reviewed the proposal and made all other required findings. Authorization from OHRP must be received prior to initiating any research involving prisoners.

1.4 **When Subjects Become Prisoners**

If a human subject involved in ongoing research becomes a prisoner during the course of the study, and the relevant research proposal was not reviewed and approved by the IRB in accordance with the requirements for research involving prisoners, the investigator must promptly notify the IRB. All research interactions and interventions with, and obtaining identifiable private information about, the now-incarcerated prisoner-subject must be suspended immediately, except as noted below. Upon receipt of the investigator's report that a previously enrolled research subject has become a prisoner, if the investigator wishes to have the prisoner subject continue to participate in the research, the following steps must be taken:

A. The IRB must at the earliest opportunity, after receiving the investigator’s notice, re-review the protocol in accordance with the requirements for research involving prisoners. The IRB should also review the consent document and process in consideration of constraints imposed by incarceration. Upon this review, the IRB can either (a) approve the involvement of the prisoner-subject in the research in accordance with this policy or (b) determine that this subject must be withdrawn from the research.

B. The IRB must send a certification to OHRP and wait for a letter of authorization in reply. Otherwise, the prisoner subject must stop participating in the research, except as noted below.

C. In special circumstances in which the investigator is in communication with the IRB and the IRB or Chair determines that it is in the best interests of the subject to remain
in the research study while incarcerated, the subject may continue to participate in the research until the IRB can re-review the study in accordance with the requirements for research involving prisoners. In these circumstances, some of the findings required by section 1.3 may not be applicable. For example, the finding required under 1.3D regarding the selection of subjects within the prison may not be applicable if the subject was recruited outside of an incarcerated context. The IRB should document findings of non-applicability accordingly.

1.5 Additional Considerations

1.5.1 Children: When a prisoner is a minor (e.g., an adolescent detained in a juvenile facility is a prisoner), SOP SC503 – Children as a Vulnerable Population also applies.

1.5.2 Prisoners in California: The State of California has provisions regarding research with prisoners that deviate from the federal regulations. Except for specific exceptions, biomedical research may not be conducted on any prisoner (PC §3502). “Biomedical research” means research relating to or involving biological, medical or physical science.

1.5.3 Additional Approvals: Additional approvals may be required depending on the rules of the prison system (e.g., California Department of Corrections). It is the investigator’s responsibility to identify and meet these requirements.

1.5.4 Non-DHHS Supported Research: If an investigator wishes to engage in non-HHS supported research, certification to the Secretary is not required. However, the IRB will apply the standards of this policy and the Federal Regulations when reviewing the research.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

The OPHS Director and/or IRB Administrator is responsible for maintaining up-to-date review tools for review of research pertaining to vulnerable groups based on new and evolving applicable regulations and guidelines. The Administrator is also responsible for ensuring the IRB members are apprised of new and evolving regulations and guidelines pertaining to vulnerable populations, for selecting primary reviewers with appropriate expertise to conduct the reviews of such research, and for securing appropriate consulting expertise as needed for selected reviews.

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

IRB Members are responsible for conducting appropriate review of research planned for vulnerable populations, including an assessment of potential for coercion, in consultation with any appropriate experts and resources.
4. PROCESS OVERVIEW

When proposed research involves vulnerable populations, the IRB must take special precautions to ensure research participants’ rights, safety, and welfare. In all cases involving vulnerable populations, the IRB Administrator must stay abreast of applicable regulations and guidelines. IRB Chair(s) and Members must be cognizant of the subjects’ needs when evaluating the protocol and are responsible for determining any additional protective stipulations to be applied to the research.

When proposed research involves prisoners, the OPHS Director and/or IRB Administrator will ensure that a prisoner representative is selected to be a primary reviewer for the protocol.

5. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46 Subpart C
45 CFR 46.111
21 CFR 56.111
OHRP Guidance on Involvement of Prisoners in Research (May 2003)
OHRP IRB Guidebook
OHRP FAQs
The Belmont Report
1. POLICY

The use of the term “vulnerable” in the context of human research protections does not refer to susceptibility of harm, but rather the inability or a threat to the ability of an individual to give voluntary informed consent. When some or all subjects are likely to be vulnerable to coercion or undue influence the IRB must ensure that additional safeguards have been included in the study to protect the rights and welfare of these subjects.

Special ethical and regulatory considerations apply when research involves children as subjects. The three main principles elucidated in The Belmont Report and codified in federal research regulations—respect for persons (autonomy), beneficence, and justice—must be balanced in appropriate ways. Children are inherently more vulnerable than adults, requiring a higher level of protection in research. At the same time, the IRB has the responsibility to assure equitable selection of children as research participants, so that they may receive a rightful share of the benefits of research. Since children are legally incapable of giving valid informed consent, provisions also must be made regarding assent by the child or minor and/or permission of the parent(s) or guardian (see SOP IC 103, “Assent and Parental/Guardian Permission”). The IRB will apply the requirements and guidance found in federal regulations 45 CFR 46, Subpart D, “Additional Protections for Children Involved as Subjects in Research,” to evaluate any research involving children as participants.

Specific Policies

1.1 Definitions

1.1.1 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 (be it local, national, foreign or domestic).

(Note: In California, the legal age for such consent is usually 18 years old, but some exceptions apply under state law. These or applicable laws of other states or countries where the research is being conducted will be considered).

1.1.2 Assent means a child’s affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

1.1.3 Permission means the agreement of parent(s) or guardian to the participation of their child or ward in research.

1.1.4 Parent means a child’s biological or adoptive parent.

1.1.5 Guardian means an individual who is authorized under applicable State or local law to consent on before of a child to general medical care.

1.2 Inclusion of Children in Research

1.2.1 Enrolling children in research, especially clinical research, may present difficult considerations for IRBs. Several factors make a case for such inclusion:
Children differ markedly from both animals and adults, and therefore, these models cannot substitute as alternatives to testing or gathering data from children.

Lack of appropriate research in children could increase their risk of harm from exposure to practices/treatments untested in this population, and optimal therapies could not be developed for diseases/conditions that specifically affect children.

However, research with children requires that the IRB give careful consideration to special issues related to risk/benefit ratio and consent.

1.3 Determination of risks vs. benefits

1.3.1. The IRB must consider 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 the authority to approve the study.

Federal regulations 45 CFR 46, Subpart D include four categories of permissible research with children. Risk is defined in terms of minimal and greater than minimal risk, and may only be approved by the IRB if it finds as follows:

1) 45 CFR 46.404 - Research not involving greater than minimal risk to the children/subjects, if:
   - the research presents no greater than minimal risk to the children; and
   - adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in 45 CFR 46.408.

2) 45 CFR 46.405 - Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child/subject involved in the research, if:
   - the risk is justified by the anticipated benefits to the subjects;
   - the relation of the anticipated benefit to the risk presented by the study is at least as favorable to the subjects as that provided by available alternative approaches; and
   - adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in 45 CFR 46.408.

3) 45 CFR 46.406 - Research involving greater than minimal risk and no prospect of direct benefit to the individual child subjects involved in the research, but likely to yield generalizable knowledge about the subject's disorder or condition, if:
   - the risk of the research represents a minor increase over minimal risk;
   - the intervention or procedure presents experiences to the subjects that are reasonably commensurate with those inherent in their actual, or expected medical, dental, psychological, social, or educational situations;
   - the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the disorder or condition; and
   - adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in 45 CFR 46.408.
4) **45 CFR 46.407** - Research that the IRB believes does not meet the conditions of 45 CFR 46.404, 46.405, or 46.406, but 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.

If the IRB believes that the research does not meet the requirements of 45 CFR 46.404, 46.405, or 46.406, but finds that it presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, it may refer the protocol to HHS for review. The research may proceed only if the Secretary, HHS, or his or her designee, after consulting with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following an opportunity for public review and comment, determines either: (1) that the research in fact satisfies the conditions of 45 CFR 46.404, 46.405, or 46.406, or (2) the following:

- the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
- the research will be conducted in accordance with sound ethical principles; and
- adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in 45 CFR 46.408.

1.3.2 In addition to the above determinations, where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under 45 CFR 46.404 or 46.405. Where research is covered by 46.406 and 46.407 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.

1.4 For any research involving children, the IRB shall determine requirements for obtaining assent from the children/subjects and/or permission from their parent(s)/guardian (see SOP IC 703, “Assent and Parental/Guardian Permission”).

2. **SCOPE**

These policies and procedures apply to all research submitted to the UC Berkeley IRB.

3. **RESPONSIBILITY**

The IRB Administrator is responsible for maintaining up-to-date review tools for review of research pertaining to vulnerable groups based on new and evolving applicable regulations and guidelines.

The IRB Chair is responsible for ensuring the IRB members are well versed in new and evolving regulations and guidelines pertaining to vulnerable populations, for selecting primary reviewers with appropriate expertise to conduct the reviews of such research, and for securing appropriate consulting expertise as needed for selected reviews.

The IRB reviewers are responsible for conducting appropriate review of research planned for vulnerable populations, including an assessment of potential for coercion, in consultation with any appropriate experts and resources.
4. PROCESS OVERVIEW

When proposed research involves vulnerable populations, the IRB must take special precautions to ensure research participants’ rights, safety, and welfare. In all cases involving vulnerable populations, the IRB Administrator must stay abreast of applicable regulations and guidelines. IRB Chair(s) and members must be cognizant of the subjects’ needs when evaluating the protocol and are responsible for determining any additional protective stipulations to be applied to the research.

When proposed research involves children, OPHS staff, IRB Chair(s), and IRB members will ensure that the protocol contains consent, permission, and/or assent documents as appropriate.

5. APPLICABLE REGULATIONS AND GUIDELINES

The Belmont Report
45 CFR 46: Subparts D
45 CFR 46.122
21 CFR 56.111
NIH Policy on Inclusion of Children in Research (March 1998)
OHRP IRB Guidebook

6. ATTACHMENTS

ATT 025  OPHS Staff Guidelines – Children as Subjects in Minimal Risk Research
ATT 026  OPHS Worksheet – Minimal Risk Research with Children
ATT 027  OPHS Worksheet – Permissible Research with Children
1. POLICY

The efficiency and effectiveness of the IRB is supported by contact with other entities and individuals within the University of California Berkeley. The Vice Chancellor for Research and/or the Assistant Vice Chancellor for Research Administration and Compliance may establish additional reporting relationships between the Office for the Protection of Human Subjects (OPHS), designated IRBs and other officials or committees as deemed appropriate. A designated IRB may require that proposed research be reviewed by other institutional committees or the relevant committees of collaborating institutions.

Specific Policies

1.1 Communication with specific individuals

1.1.1 Institutional Official (IO)

The IO of UC Berkeley receives an Annual Report from the Committee for the Protection of Human Subjects (CPHS) authored by the IRB Chair(s) and the Director of the OPHS.

The IO of Lawrence Berkeley National Lab (LBNL) receives an Annual Report from the Committee for the Protection of Human Subjects (CPHS) authored by the IRB Chair(s) and the Director of the OPHS.

The Director communicates with the IO on an as needed basis for regulatory documentation (e.g. Inter-Institutional Agreements). The IRB Chair and Director communicate with the IO (or his/her designee) as needed on other IRB business. The Assistant Vice Chancellor for Research Administration and Compliance communicates regularly with the IO about the IRB and OPHS business during standing meetings.

1.1.2 Investigators

OPHS staff communicate directly with investigators through one-on-one consultations (face to face, email, facsimile or by phone) in advising and in the pre-reviewing process. However, all revisions and clarifications communicated on behalf of the IRB are done so in writing.

Investigators may be invited to a convened IRB meeting if the IRB Chair feels that their presence may facilitate the review and discussion of their protocol. Occasionally with very complex protocols, an IRB member or sub-committee of IRB members may meet with an investigator to help him or her better understand the Committee’s concerns and work with the investigator to find acceptable solutions.
1.2 Communication with specific entities

1.2.1 Institutional Biosafety Committee (IBC)

The Biosafety Program provides compliance assistance, technical information, and training to assist UC Berkeley faculty and staff in meeting the requirements of local, State and Federal regulations and established policies for the possession, use or transport of biohazards and potentially biohazardous materials. The Committee for Laboratory & Environmental Biosafety (CLEB) functions as the Institutional Biosafety Committee. CLEB formulates and recommends campus policy on laboratory and environmental safety aspects of teaching and research programs involving biohazards and potentially biohazardous materials in accordance with applicable local, State and Federal regulations and established policies. OPHS administrative staff facilitate regulatory compliance by requesting information about Biological Use Authorization (BUA) from investigators; and, by providing periodic summary reports of human subject research protocols using or collecting biological materials from subjects to the Biosafety Officer.

1.2.2 Animal Care and Use Committee (ACUC)

For a research protocol that involves the use of human and animal subjects, an OPHS staff member will notify the Animal Care and Use Committee by forwarding a copy of the CPHS application to the ACUC office. The ACUC will make a determination about whether the use of animals in the study protocol is covered by an ACUC protocol and notify the IRB if appropriate. The IRB will take the ACUC determination into account when making a decision to approve or deny the application if animal subject use is integral to the human subjects research protocol.

1.2.3 Radiation Safety Committee (RSC)

All proposals to administer radioactive material to humans or ionizing radiation for research purposes from sources external to the body must be approved by the RSC, Radiation Human Use Committee, Radioactive Drug Research Committee, and the CPHS, as appropriate. Protocols submitted from the Lawrence Berkeley National Laboratory (LBNL) must have the appropriate radiation safety committees at LBNL review their protocols and submit documentation attesting to such approval with their CPHS Application.

Upon identification of an affirmative response to the use of radioactive or ionizing radiation the Director of OPHS (or his/her designee) and the Radiation Safety Officer will communicate as per their standard operating procedures for intra-office communication. The IRB will take the RSC determination into account when making a decision to require changes to the protocol and/or informed consent forms; and, approve or deny the application for the human subjects research.

1.2.4 Non-ionizing Radiation Safety (Laser) Committee

The University of California at Berkeley Laser Safety Program is intended to provide staff, researchers, students and visitors with a safe laser use environment. All Class 3a,
3b, and 4 lasers on the campus must be registered with the UC Berkeley Non-Ionizing Radiation Safety Program. The Office of Environment, Health & Safety administers this program for the UC Berkeley Non-Ionizing Radiation Safety Committee (NIRSC). The campus Laser Safety Officer (LSO) is responsible for implementation of the Non-Ionizing Radiation Safety program.

Upon identification of an affirmative response to the use of lasers in human subjects research the Director of OPHS (or his/her designee) and the Laser Safety Officer will communicate as per their SOP for intra-office communication. The IRB will take the NIRSC determination into account when making a decision to require changes to the protocol; and, approve or deny the application for the human subjects research.

1.2.5 Research Integrity Officer

If an issue comes to the attention of the IRB, the IRB Chair, or the Director of OPHS which may require the involvement of the Research Integrity Officer as per UCB policy; then, the Chair of the IRB is responsible for reporting and communicating in writing to the RIO the nature of the concerns. The RIO is responsible for investigating any issues or concerns and communicating the final outcome to the IRB Chair and Director should the findings have a potential impact on the investigator’s conduct of human subjects research.

1.2.6 Conflict of Interest (COI) Committee

The OPHS Director is responsible for coordinating communication between the COI Committee, COI Administrative Staff and the IRB for research protocols that indicate a potential financial conflict of interest as identified on the CPHS Checklist for Financial Conflict of Interest – Human Subject Studies. When a positive (yes) response is noted on the Checklist, OPHS staff prepare a packet consisting of the CPHS Application Coversheet (copy), COI Checklist (original) and the UCB Financial Conflict of Interest Form (original, if submitted), and a copy of the Protocol Narrative; and, this is forwarded to the COI Committee with a cover memo from the OPHS Director. The Director maintains a log of COI submissions and copies of the COI Checklist and the UCB Financial Conflict of Interest Form are kept in the protocol file.

CPHS does not approve an application nor make a determination of exemption until notified by the COI Committee that there is: 1) no substantive financial conflict of interest present; or, 2) the conflict is being managed and the COI Committee’s management plan may necessitate revision or modification of the consent form prior to final IRB approval of the protocol or a determination of exemption by the IRB.

1.2.7 Sponsored Projects Office

Sponsored Projects Office (SPO) is a partnership of staff responsible to Assistant Vice Chancellor for Research Administration and Compliance (AVC-RAC). The SPO staff are responsible for Contract and Grant proposal review, awards negotiation and management, and contras grant administration and compliance. SPO and OPHS work collaboratively
to ensure regulatory compliance as it pertains to the external funding of research. Individual research administrators communicate directly with OPHS to confirm IRB approvals before SPO releases funding. OPHS staff also carbon copy IRB approval and administrative closure letters to a designated SPO email address at the time of approval if the project is externally funded through SPO.

SPO and the IRB through OPHS coordinate on the review and comparison of Department of Health and Human Services (DHHS) funded human subjects research as per RR 411 – Grant Protocol Review.

1.2.8 Stem Cell Research Oversight (SCRO) Committee
The Assistant Vice Chancellor for Research Administration and Compliance and the Director of OPHS serve as voting members of the SCRO. The OPHS Director is responsible for coordinating communication between the SCRO and the IRB for research involving both committees.

1.2.9 Graduate Division
The OPHS Director is responsible for coordinating communication between the Dean of the Graduate School, the Graduate Division staff and the IRB involving policies regarding graduate student investigators. In addition, the Graduate Division is copied (Cc’ed) on all IRB determinations of exemption, findings of “not human subjects research” or approval letters involving graduate students as lead investigators or key personnel on a protocol.

1.2.10 Departmental or Unit Liaison
The OPHS Director (or designee) will serve as a liaison for departmental or unit pre-IRB submission review processes and facilitate communication between CPHS and/or OPHS and supporting components campus-wide.

1.2.11 Industry Alliances Office (IAO)
The OPHS Director is responsible for coordinating communication between the staff of the IAO and the IRB involving protocols with industry sponsorship. In addition, the IAO is copied (Cc’ed) on all IRB determinations of exemption, findings of “not human subjects research” or approval letters involving industry sponsorship of a protocol.

2. SCOPE
These policies and procedures apply to all human subjects research submitted to the IRB.
3. RESPONSIBILITY

The OPHS Director and/or IRB Administrator is responsible for overseeing all IRB and OPHS communications.

4. PROCESS OVERVIEW

Contact with the intra-institutional entity will be initiated by the OPHS Director or IRB Administrator (or his or her designee) with the appropriate entity, depending on the issue in question. Specific, detailed standard operating procedures are followed for each different unit.
1. POLICY

As set forth in the governing principles of The Belmont Report and codified in federal human research regulations, investigators who wish to involve human subjects in research are obliged to seek their voluntary and informed participation through an informed consent process. Securing and maintaining consent is an ongoing process that begins with recruitment and continues through the end of the participants’ involvement in the study.

Except as described in SOP IC 702 (“Waivers of Informed Consent”), no investigator may involve a human being as a research subject unless s/he has obtained legally effective informed consent of the subject or the subject's legally authorized representative. Consent must be sought only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.

As part of this process, the IRB requires documentation of informed consent by use of a written consent form approved by the IRB and signed and dated by the subject or the subject’s legally authorized representative, unless an alternative method for obtaining informed consent is approved by the IRB (as below). (Note: Obtaining assent and parental permission for research involving children/minors is discussed separately in SOP IC 703, “Assent and Parental/Guardian Permission”).

Specific Policies

1.1 The Consent Form May Be Either of the Following:

A. A written consent document that embodies the elements of informed consent described in 45 CFR 46.116(a) and 21 CFR 50.25. This form may be read to the subject or the subject's legally authorized representative, but in any event, the Investigator shall allow adequate opportunity for the form to be read to or by the subject or representative before it is signed. The subject or representative must also be given a copy of the form.

B. A "short form" written consent document stating that the required elements of informed consent have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be an impartial witness to the oral presentation (i.e., the witness cannot be the person obtaining the consent). The IRB must approve a written summary of what is to be said to the subject or representative. The subject or the representative signs only the short form itself. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining the consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative in addition to a copy of the short form.

1.2 Required Elements of Informed Consent

A. A statement that the study involves research, an explanation of the purposes of the research, the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures that are experimental.

B. A description of any reasonably foreseeable risks or discomforts to the subject.
C. A description of any benefits to the subject or to others that may reasonably be expected from the research.

D. A disclosure of appropriate alternative procedures or courses of treatment, if any, which might be advantageous to the subject.

E. A statement that describes the extent to which, if any, confidentiality of records identifying the subject will be maintained, and if applicable, notes the possibility that the FDA and/or other agencies or individuals may inspect the records.

F. For research involving more than minimal risk, an explanation as to whether any compensation is provided 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.

G. 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.

H. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

1.3 Additional Elements

When appropriate, one or more of the following elements of information shall also be provided to each subject:

A. 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.

B. Anticipated circumstances under which the subject's participation may be terminated by the Investigator without regard to the subject's consent.

C. Any additional costs to the subject that may result from participation in the research.

D. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

E. A statement that significant new findings developed during the course of the research, which may relate to the subject's willingness to continue participation, will be provided to the subject.

F. The approximate number of subjects involved in the study.

1.4 Other Requirements

A. Understandable language: The information presented in the consent documents must be in language likely to be understood by the subject population. Technical and scientific terms should be adequately explained using common or lay terminology. In general, forms should be written at no higher than an eighth-grade reading level when the target population is adults.

B. No exculpatory language: Informed consent documents may not contain any exculpatory language through which the subject is made to waive or appear to waive legal rights, or release or appear to release the Investigator, the Sponsor, or the University of California, Berkeley from liability for negligence.
C. FDA-regulated test articles: For all research involving test articles regulated by the FDA, informed consent documents must include a statement that the purpose of the study includes evaluation of both the safety and the effectiveness of the test article. The consent form must also include a statement that the FDA has access to the subject's medical records.

D. Person of consent form: The preferred style of the consent document is second-person (e.g., “You will be asked to…”). This style is intended to convey a dialogue between the researcher and the subject. First-person style is acceptable (though not required) for the consent section at the end of the documents (e.g., “I have read this form, have had my questions answered, and agree to participate in the study by signing below.”)

1.5 **Documentation of Informed Consent**

Each subject or his or her legally authorized representative must sign and date a copy of the current IRB-approved consent form prior to enrollment or any participation in any phase of the study, unless the requirement for consent or documentation thereof is waived by the IRB. This consent form with original signatures must be retained by the Investigator per the UC Records Retention Policy. The subject and/or his or her legally authorized representative must also be given a copy of the document.

The IRB may approve procedures for documentation of informed consent that involve (a) a written consent form signed by the subject or his/her legally authorized representative; (b) a short form written consent form and summary with oral presentation; or (c) in limited circumstances, waiver of signed written consent form. Each of these three options is described in detail below. It is the responsibility of the IRB to determine which of the procedures described below is appropriate for documenting informed consent in research protocols that it reviews.

1.5.1 Written consent form signed by subject or legally authorized representative. In most circumstances, the IRB will require that informed consent is documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. The Investigator should allow adequate opportunity for the form to be read to or by the subject or representative before it is signed. A copy of the document must be given to the participant and/or the person signing the form.

1.5.2 The written informed consent document should embody, in language understandable to the subject, all the elements necessary for legally effective informed consent (see sections 1.2 and 1.3 above).

1.5.3 Subjects who do not understand English should be presented with an informed consent document written in a language understandable to them. See section 1.7.

1.6 **Oral Presentation Using Short Form**

As an alternative to standard written informed consent documents, oral presentation of informed consent information may be used.

In such cases, the subject must be provided with both:

- A short form written consent document stating that the elements of informed consent have been presented orally to the subject or the subject’s legally authorized representative; and
- A written summary of the information that is presented orally.
1.6.1 A witness to the oral presentation is required. The witness must sign both the short form written consent document and a copy of the written summary.

1.6.2 The subject or the legally authorized representative must sign the short form written consent document.

1.6.3 The person obtaining consent (e.g., the Investigator) must sign a copy of the written summary of the information that is presented orally. The person obtaining consent may not also serve as the witness to the consent.

1.7 Translations for Subjects Who Do Not Speak English

1.7.1 Written Informed Consent: When non-English speaking participants are to be included in a research study, the following conditions must be met:

(i) The written informed consent document must be translated into a language understandable to the subject; and

(ii) The investigator must submit translations of the final, IRB-approved consent documents for the IRB files as soon as these translations are available. The investigator must affirm the accuracy of these translations and that only these translated versions of the forms will be used with subjects.

1.7.2 Oral Presentation with Short Form: Where informed consent is documented using this short form procedure (see section 1.6 above) with non-English speaking subjects, the following conditions must be met:

(i) the oral presentation and the short form written informed consent document should be in a language understandable to the subject;

(ii) the IRB-approved English language informed consent document may serve as the summary; and

(iii) the witness should be fluent in both English and the language of the subject.

At the time of consent, (i) the short form document should be signed by the subject or the subject’s legally authorized representative; (ii) the summary should be signed by the person obtaining consent as authorized under the protocol; and (iii) the short form document and the summary should be signed by the witness. When the person obtaining consent is assisted by a translator, the translator may serve as the witness.

The IRB must receive all translated versions of the short form document as a condition of approval. The investigator should also submit any translations of other final, IRB-approved consent documents (e.g., the summary) for the IRB files as soon as these translations are available. As appropriate, the investigator must affirm the accuracy of these translations and that only these translated versions of the forms will be used with subjects.

1.8 Consent Documentation with Subjects Who Are Illiterate or Unable to Talk or Write

1.8.1 The IRB may approve alternate procedures for documenting informed consent when the prospective subject speaks and understands English (or the language in which the consent process and forms are approved), but does not read and write it. Such individuals may indicate agreement to participate by “making their mark” on the consent document, when consistent with applicable state and/or local law.
1.8.2 The IRB may approve alternate procedures for documenting informed consent when the prospective subject understands and comprehends spoken English (or the language in which the consent process and forms are approved), but is physically unable to talk, write, or “make their mark.” Such individuals may be entered into a study if they are competent and able to indicate agreement or disagreement to study participation by other means. The consent form should document the method used for communication and the specific means by which the prospective subject communicated agreement to participate in the study. An impartial third party should witness the entire consent process and sign the consent document(s); a videotape recording of the consent process may also be recommended.

1.9 Waiver of Documentation

The IRB may waive the requirement for the Investigator to obtain a signed consent form for some or all subjects if the IRB finds either:

- That the only record linking the subject and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality, including knowledge of an individual’s participation in the study. (In this case, each subject will be asked whether he/she wants documentation linking him/her with the research, and the subject's wishes will govern); or
- 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.

1.9.1 In cases in which the documentation requirement is waived, the IRB may require the Investigator to provide subjects with a written statement regarding the research.

1.9.2 The IRB may waive documentation of parental or guardian permission in research involving children using the same criteria as above.

For situations in which the IRB may waive or alter some or all of the elements of the written informed consent, refer to SOP IC 702 (“Waivers of Informed Consent”).

2. SCOPE

These policies and procedures apply to all research submitted to the UC Berkeley IRB.

3. RESPONSIBILITY

The OPHS Staff are responsible for screening/pre-reviewing all informed consent documents and for communicating with Investigators to bring documents into compliance, before and/or after full Committee/IRB Chair review. The IRB members and/or IRB Chair or designee are responsible for final review and approval of consent documents.

4. PROCESS OVERVIEW

An OPHS administrative staff member will pre-review all applications to ensure that the consent form documents adhere to the Consent Form Guidelines. Staff will notify the Investigator of any omissions or necessary corrections before and/or after review, as
appropriate, by the full IRB (for applications requiring full Committee review) or IRB Chair or designee (for applications or responses requiring expedited review.)

The Consent Form document will be evaluated on the basis of both the CPHS Informed Consent Guidelines and the respective research protocol, including special attention to such issues as readability, appropriate language, and completeness of relevant information. The IRB members and/or IRB Chair or designee will subsequently confirm, reject, or add to this evaluation, and will give final approval as per the type of application.

After the application is approved, the English version of the Consent Form document(s) will be stamped with the IRB approval stamp and forwarded to the Investigator along with the protocol approval.

In addition to relevant information provided in the Informed Consent Guidelines posted on the CPHS website, the IRB staff are available to advise investigators on the informed consent process, in particular regarding special circumstances that may be involved (e.g., vulnerable subject populations, waiver of documentation of informed consent, etc.)

5. APPLICABLE REGULATIONS AND GUIDELINES
   45 CFR 46.116, 46.117
   21 CFR 50
   FDA Information Sheets, 1998

6. ATTACHMENTS
   ATT 028  CPHS Consent Form Guidelines (10/05)
   ATT 029  OPHS Worksheet – 45 CFR 46.117(c) Waiver of Documentation Requirement of Informed Consent
1. **POLICY**

The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waive the requirement to obtain informed consent, if the IRB finds that the research meets specific regulatory criteria.

**Specific Policies**

1.1 **IRB Waivers of One or More Requirements of Informed Consent**

1.1.a In accordance with 45 CFR 46.116 (c), the IRB may approve a consent procedure that does not include, or which alters, some or all of the elements of informed consent, or waive the requirement to obtain informed consent, provided the IRB finds and documents that:

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:
   i. public benefit or service programs;
   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; and

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

1.1.b In accordance with 45 CFR 46.116 (d), the IRB also may approve a consent procedure that does not include, or which alters, some or all of the elements of informed consent, or waive the requirement to obtain informed consent, provided the IRB finds and documents that:

A. the research involves no more than minimal risk to the subjects;
B. the waiver or alteration will not adversely affect the rights and welfare of the subjects;
C. the research could not practicably be carried out without the waiver or alteration; and
D. whenever appropriate, the subjects will be provided with additional pertinent information after participation.

1.1.c Waiver of Parental or Guardian Permission (see SOP IC 703, “Assent and Parental/Guardian Permission”)

*Note:* Waiver of some or all elements of informed consent under 45 CFR 46.116 will not apply to any research which falls under the jurisdiction of the FDA, as FDA regulations do not provide for waiver of consent except in specific emergency circumstances (see 1.2 below).
1.2 An Emergency Situation Prior to IRB Review and Approval

For research which falls under the jurisdiction of the FDA, obtaining informed consent shall be deemed feasible except in certain emergency situations described under guidelines 21 CFR 50.23 and 21 CFR 50.24. In emergency situations where informed consent cannot be obtained prior to interaction or intervention with a human subject, the Investigator must submit to the IRB, within five (5) working days of the emergency, documentation of the necessary exception.

In review of the documentation, the IRB will ensure that the Investigator and a physician not otherwise participating in the investigation have adequately certified the following in writing prior to interaction or intervention with the subject:

A. the human subject was confronted by a life-threatening situation necessitating the use of the test article;
B. informed consent could not be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject;
C. time was not sufficient to obtain consent from the subject's legal representative;
D. there was available no alternative method of approved or generally recognized therapy that provided an equal or greater likelihood of saving the life of the subject.

2. SCOPE

These policies and procedures apply to all research submitted to the UC Berkeley IRB.

3. RESPONSIBILITY

The IRB, IRB Chair, and/or IRB member designee is responsible for making a final determination of whether a waiver of informed consent is applicable and appropriate.

4. PROCESS OVERVIEW

The Investigator should include any request for waiver of informed consent or parental permission in the protocol along with justification for the waiver. An OPHS administrative staff member will evaluate this request as part of the pre-review of the application before appropriate routing, and the IRB members and/or IRB Chair or designee will subsequently evaluate the request, based on relevant regulations and guidance. A request for waiver of parental permission will not necessarily require Full Board review. The Chair and one other Committee member with appropriate expertise may review and approve such a request for waiver on an expedited basis if they deem this appropriate.

If a waiver of informed consent request is not approved, the Investigator will be notified and asked to provide further justification or resubmit a revised protocol that includes a written informed consent process.

5. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 50.23, 50.24
21 CFR 56.109(c), 56.109(d)
45 CFR 46.116
45 CFR 46.408

6. ATTACHMENTS

ATT 030  OPHS Worksheet – 45 CFR 46.116 Waiver of One or More Elements of Informed Consent
1. POLICY

Special ethical and regulatory considerations apply when research involves children as subjects. Children are inherently more vulnerable than adults, thus requiring a higher level of protection, and are also legally incapable of giving valid informed consent. The IRB will apply the requirements and guidance found in federal regulations 45 CFR 46, Subpart D, “Additional Protections for Children Involved as Subjects in Research” (see SOP SC 503, “Children as a Vulnerable Population”). This includes provisions for obtaining assent from the child or minor and permission from the parent(s) or guardian.

Specific Policies

1.1 Definitions

1.1.1 *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 (be it local, national, foreign or domestic).

(Note: In California, the legal age for such consent is usually 18 years old, but some exceptions apply under state law. These or applicable laws of other states or countries where the research is being conducted will be considered).

1.1.2 *Assent* means a child’s affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

1.1.3 *Permission* means the agreement of parent(s) or guardian to the participation of their child or ward in research.

1.1.4 *Parent* means a child’s biological or adoptive parent.

1.1.5 *Guardian* means an individual who is authorized under applicable State or local law to consent on before of a child to general medical care.

1.2 Assent

In instances where the subject is not legally capable of giving informed consent, the IRB must find that adequate provisions are made for obtaining the assent of the subject when in the judgment of the IRB, the subject should be capable of providing assent.

1.2.1 In determining whether subjects are capable of assenting, the IRB shall take into account the age, maturity, and psychological state of the subject involved. This judgment may be made for all subjects to be involved in research under a particular protocol, or for each subject, as the IRB deems appropriate.

1.2.2 When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

1.2.3 In most cases, seeking assent and documenting such assent in writing will be required if the subjects are at least seven years old. (Note: California State law requires obtaining assent from minors to participate in research, and for certain types of medical research specifies that consent [assent] be obtained from the subject if he/she is “seven years of age or older”).
1.2.4 Assent forms shall be written at the appropriate educational and maturity level of the youngest prospective subject in the age range. Depending on the age range of the minors involved, multiple assent forms may be required for different reading comprehension levels. For older children, one document may be developed to serve as a joint assent/permission form (see 1.3 below), with signatures to be obtained from both the child and the parent(s) or guardian on the same document.

1.2.5 The IRB has authority to require assent from children younger than seven if they are likely to comprehend and appreciate what it would mean to volunteer to participate in a given study.

1.3 Waiver of Assent

1.3.1 If the IRB determines that the capability of some or all of the subjects 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 subject and is available only in the context of the research, the assent of the subject is not a necessary condition for proceeding with the research.

1.3.2 Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived (see SOP IC 702, “Waivers of Informed Consent”).

1.4 Parental/Guardian Permission

1.4.1 The IRB shall determine that adequate provisions are made for soliciting the permission of each child’s parent(s) or guardian. Where parental permission is to be obtained, the IRB will require permission from one or both parents in accordance with specifications relating to the four categories of permissible research with children, as described in 45 CFR 46 (see SOP SC 504, “Children as a Vulnerable Population”).

1.4.2 Permission by parents or guardians shall be documented in accordance with 45 CFR 46.117 (see SOP IC 701, “General Requirements and Documentation for Informed Consent”).

1.5 Waiver of Parental/Guardian Permission

1.5.1 In accordance with 45 CFR 46.408, the IRB may waive the requirements for obtaining parental or guardian permission for research involving children if EITHER of the following sets of conditions is met:

A. The IRB makes and documents the required findings under either 45 CFR 46.116(c) or 46.116(d) (see SOP IC 702, “Waivers of Informed Consent,” 1.1.a or 1.1.b); OR

B. The IRB determines that a research protocol is designed to study conditions in children or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (e.g., neglected or abused children), and also finds that: (i) an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted; and (ii) the waiver is not inconsistent with federal, state, or local law.

The choice of an appropriate substitute mechanism will depend on the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.
1.5.2 A request for waiver of parental permission will not necessarily require Full Committee review. The Chair and one other Committee member with appropriate expertise may review and approve such a request for waiver on an expedited basis if they deem this appropriate.

1.6 Wards

1.6.1 Children who are wards of the state or any other agency, institution, or entity can be included in research approved under 45 CFR 46.406 or 46.407 only under certain conditions (see SOP SC 503, “Children as a Vulnerable Population”). If the research is approved, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individuals acting on behalf of the child as guardian or in loco parentis.

1.6.2 IRB decisions regarding assent/permission requirements will therefore take the above into consideration in addition to other relevant regulations and guidance.

Note: Waiver of informed consent (including assent and/or permission) under 45 CFR 46.116 and 46.408 will not apply to any research which falls under the jurisdiction of the FDA, as FDA regulations do not provide for waiver of consent except in specific emergency circumstances (see SOP IC 702, “Waivers of Informed Consent”).

2. SCOPE

These policies and procedures apply to all research submitted to the UC Berkeley IRB.

3. RESPONSIBILITY

The IRB Staff are responsible for screening/pre-reviewing all informed consent documents and for communicating with Investigators to bring documents into compliance, before and/or after full Committee/IRB Chair review. The IRB, IRB Chair, and/or IRB member designee is responsible for final determination of whether assent is indicated, and if so, whether and how assent must be documented. Likewise, the IRB, IRB Chair, and/or IRB member designee is responsible for final determination of whether parental/guardian permission is appropriate and that stipulations for obtaining or waiving permission are met.

4. PROCESS OVERVIEW

When children are to be included as participants, the Investigator should include discussion of special consent issues involved, and parental/guardian permission forms and child assent forms as appropriate (or request for waiver thereof), with the research application.

An OPHS staff member will pre-review the assent and/or permission documents to assess whether they are appropriate and adequate. Staff will notify the Investigator of any omissions or necessary corrections before and/or after review, as appropriate, by the full IRB (for applications requiring full Committee review) or IRB Chair or designee (for applications or responses requiring expedited review.)

The assent and/or permission documents will be evaluated on the basis of both the CPHS Informed Consent Guidelines and the respective research protocol, including special attention to such issues as readability, age-appropriate language, and completeness of relevant
information. The IRB members and/or IRB Chair or designee will subsequently confirm, reject, or add to this evaluation, and will give final approval as per the type of application. After the application is approved, the English version of the assent and/or permission document(s) will be stamped with the IRB approval stamp and forwarded to the Investigator along with the protocol approval.

In addition to relevant information provided in the Informed Consent Guidelines posted on the CPHS website, OPHS staff are available to advise investigators on the informed consent process, in particular regarding special circumstances that may be involved with vulnerable subject populations such as these.

5. APPLICABLE REGULATIONS AND GUIDELINES
   45 CFR 46 Subpart D

6. ATTACHMENTS
   ATT 031  OPHS Worksheet – 45 CFR 46.116 and 46.408 Waiver of Parental Permission
1. POLICY

The University of California, Berkeley IRB acknowledges that they have a responsibility and the authority to audit the operations of investigators and protocols to ensure the health, safety and well-being of subjects as well as to ensure regulatory compliance with federal and state law governing the conduct of human subjects research as well as university policies. UC Berkeley supports such monitoring and audits as part of its continuing effort to maintain high standards for human research protections.

Specific Policies

1.1 Site Visits and Third Party Verification

The IRB has the authority to observe, or have a third party observe, the informed consent process of research it has approved, and to verify that the study is being conducted as required by the IRB and within the Institutional policies and procedures and site-specific procedures, as appropriate. OPHS staff or IRB members may perform site visits or questionnaires or other means, either affiliated or not with the institution, to verify information in the protocol application, or in any interim or continuing review submissions.

The criteria for selecting Investigators to be reviewed for verification may include:

-Investigators who conduct studies that involve exceptionally high risk to subjects,
-Situations where subject involves complaints of third parties,
-Investigators with a history of noncompliance.

Sponsors may be asked to submit copies of monitoring reports, or may be requested to complete a questionnaire regarding the protocol and/or the investigative site.

Investigators may be asked to submit copies of signed informed consent forms or other documents to ensure their compliance with IRB requirements. The IRB may conduct interviews with screened and/or enrolled subjects as deemed necessary.

2. SCOPE

These policies and procedures apply to all IRBs and investigators affiliated with the University of California Berkeley.

3. RESPONSIBILITY

The Institutional Official is responsible for serving as the responsible institutional official in all regulatory agency matters regarding regulatory compliance, participating as needed in
regulatory agency audits, and providing support in responding to and correcting audit findings.

The Assistant Vice Chancellor for Research Administration (or designee) is responsible for all formal regulatory agency correspondence and interactions, establishing logistical support during regulatory agency audits, serving as key institution contact during such audits, and drafting responses to regulatory agency correspondence received following such audits.

IRB Chair, Members and OPHS Staff are responsible for participating in regulatory agency audits as determined by the OPHS Director, and in fully cooperating with government officials during their participation in such audits.

The IRB Chair and IRB (as needed) in consultation with the Director determine which investigators and/or protocols warrant additional monitoring, a site visit or third party verification. The OPHS Director is responsible for implementing monitoring as directed by the IRB and supervising any for cause or not for cause monitoring of investigator activities by OPHS staff.

The Assistant Vice Chancellor for Research Administration and Compliance in cooperation with the IRB Chair is responsible for assisting the OPHS Director in formal responses to regulatory agency audits and in implementing policy and procedure changes indicated by such audits.

4. PROCESS AND PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

An OPHS staff member contacts the Investigator and/or key site personnel to set a day and time to conduct a site visit. The days prior to the visit, he or she confirms the date and time with the Investigator and/or key personnel.

The site visitor brings a completed copy of the site’s most recent Study Summary Form—if available, the current protocol, informed consent document, and any adverse event reports submitted.

The site visitor confirms that the study is being conducted in compliance with the information provided on these documents by observation if possible, especially: the method of subject recruitment, and in particular, that there are safeguards in place for the recruitment of subjects vulnerable to coercion or undue influence, the process of obtaining informed consent, the consent form being used, the facilities available in an emergency.

If appropriate, he or she obtains information about (1) any adverse events that may have been reported; (2) any adverse events that may not have been reported; and (3) any unanticipated problems.

If project is inactive, suspended, or terminated, the site visitor will obtain information regarding this status. He or she will complete the Site Visit Report and submit it to the Director.

The Director routes the Site Visit Report to the IRB Chair for review. A discussion of the site visit may be scheduled on the agenda for next IRB meeting.

The IRB Chair will review the report and determine any necessary follow-up action.
5. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.115
45 CFR 46.115