

Policy Number: 19

Title: IRB Review Requirements

Date of Last Revision: July 5, 2007

IRB review of research must include consideration of each of the following criteria:

I. General Requirements

- A. A full Committee must review all submissions which do not qualify for expedited review or exemption from IRB review. Please refer to [OPRS/IRB Policy 5: IRB Review Process—Certification of Exemption from IRB Review](#) and [OPRS/IRB Policy 8: IRB Review Process—Expedited Review](#) for details.
- B. IRBs are required to adhere to all requirements for IRB review of research as outlined in 45 CFR 46, 21 CFR 50, 21 CFR 56 and state law.
- C. All requirements for informed consent, waiver or alteration of informed consent and waiver of signed informed consent apply to IRB review of research. Please refer to [OPRS/IRB Policy 29: Informed Consent Process and Documentation](#) for details.
- D. All requirements outlined in Health Insurance Portability & Accountability Act [HIPAA] apply to IRB review of research (see [OPRS/IRB Policy 49: HIPAA](#)).

II. Experimental Design and Scientific Validity

The IRBs review the experimental design, scientific rationale and statistical basis of a proposed study in order to conduct adequate analysis of its risks and benefits to the human subjects of the research. IRBs review the scientific design in order to ensure that subjects are not exposed to risks without scientific justification, and that the risks are reasonable in relation to the benefits. The scientific validity of a research may also be evaluated by assessing whether the research will yield useful data. This also helps ensure that subjects are not exposed to unreasonable risks.

III. Risk/Benefit Analysis

- A. IRBs must ensure that risks to subjects are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk. For example, risks may be minimized by ensuring that appropriate safeguards are in place, such as (a) adequate safety monitoring; (b) exclusion of populations at increased

risk; (c) coding of data; and, (d) adequately trained research personnel. IRBs must ensure that risks to subjects are minimized by using procedures already being performed on the subjects for diagnostic or treatment purposes [45 CFR 46.111 and 21 CFR 56.111].

- B. IRBs must also ensure that risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result [45 CFR 46.111 and 21 CFR 56.111].
- C. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). Before eliminating an activity from consideration, the IRB should be certain that the activity truly constitutes therapy and not research. The IRBs should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility [45 CFR 46.111 and 21 CFR 56.111].
- D. Research subjects may be exposed to physical, psychological, social, legal or economic risks as well as risks of an invasion of privacy or a breach of confidentiality. All such risks are considered by the IRB when assessing the risk/benefit ratio of proposed research.
- E. IRBs consider the estimated probability, severity, average duration and reversibility of any potential risks to the subjects when evaluating the risk/benefit ratio of the study.
- F. Research may benefit the subjects or society in terms of the knowledge expected to result. IRBs consider the anticipated benefits to subjects and the importance of knowledge expected to result when evaluating the risk/benefit ratio of a study.
- G. Financial or other forms of compensation are not considered a benefit, and are not considered when evaluating the risk/benefit ratio of the study.
- H. IRBs consider the subject population when evaluating the risks and benefits, as the degree of risk may vary depending on the subject population.
- I. IRBs must consider whether investigators have sufficiently identified, assessed, and responded to subjects' suicide risk. Please refer to [UCLA Guidelines on Research Protocols and Suicide Risk](#) for details.

IV. Subject Identification and Recruitment

- A. IRBs must ensure that the selection of subjects for each proposed study 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, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons [45 CFR 46.111 and 21 CFR 56.111].

- B. Justice is one of the principles of the Belmont Report. The principle of justice means that subjects are selected fairly and that the risks and benefits of research are distributed equitably. Investigators should take precautions not to systematically select subjects simply because of the subjects' easy availability, their compromised position, or because of social, racial, sexual, economic, or cultural biases institutionalized in society. IRBs require that investigators base inclusion criteria on those factors that most effectively and soundly address the research problem.
- C. IRBs require that any proposed exclusion of populations based on age, gender, reproductive status, ethnicity or other factors not related to the research problem be scientifically and ethically justified.
- D. IRBs require that enrollment of vulnerable populations be justified. Please refer to [OPRS/IRB Policies 20-26](#) regarding special subject populations for details.
- E. IRBs review and approve the identification and recruitment process for each subject population within a proposed study, and require that the identification and recruitment process is free of any coercion, undue influence and invasion of privacy.
- F. When appropriate, the IRBs suggest the use of recruitment tools and strategies which allow potential subjects to initiate contact with the research team to express interest. Please refer to [OPRS/IRB Policy 30: Recruitment Methods & Tools](#) for details.
- G. HIPAA regulations apply to the identification and recruitment process if they involve review of medical records. Investigators must obtain prospective HIPAA authorization or apply for a waiver of HIPAA authorization. Please refer to [OPRS/IRB Policy 49: HIPAA](#) for details.

V. Screening Activities

- A. Although screening activities do not necessarily result in data that are used to evaluate study outcomes, such procedures are reviewed by the IRB during consideration of proposed protocols in order to ensure appropriate consent is obtained, when required, and so that all potential risks to subjects may be evaluated. Please see Section VI of [OPRS/IRB Policy 30: Recruitment Methods & Tools](#) for additional details.

VI. Process and Documentation of Informed Consent

- A. According to federal regulations:

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 45 CFR §46.116 [45 CFR 46.111(a)(4)] and, in the case of FDA-regulated research, in accordance with and to the extent required by 21 CFR Part 50 [21 CFR 56.111(a)(4)].

Informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR §46.117 [45 CFR 46.111(a)(5)] and, in the case of FDA-regulated research, in accordance with and to the extent required by 21 CFR §50.27 [21 CFR 56.111(a)(5)].

See [OPRS/IRB Policy 3: Human Subjects Research Determinations](#) for details about whether research is FDA-regulated.

- B. IRBs review and approve the consent process for each subject population. The consent process must be free of coercion and undue influence.
- C. IRBs review and approve any waivers of informed consent. Please refer to [OPRS/IRB Policy 29: Informed Consent Process and Documentation](#) for details.
- D. IRBs consider qualifications of the individuals obtaining informed consent. Only those individuals who are continuously involved in the research and are qualified to answer any questions regarding the nature of a subject's participation and explain the alternatives to participation are approved to obtain informed consent.
- E. Informed consent is understood as an on-going process which starts with the initial presentation of a research activity to a prospective subject by the investigator and continues through the research activity until the subject ends his/her participation or the study closes. Thus, the IRBs may require an investigator to obtain ongoing verbal or signed informed consent at identified intervals for long-term studies.
- F. IRBs review and approve child [ages 7-12] and youth [ages 13-17] assent processes and child and youth assent forms, when applicable. Please refer to [OPRS/IRB Policy 21: Special Subject Populations: Children](#) and [OPRS/IRB Policy 29: Informed Consent Process and Documentation](#).
- G. IRBs must review and approve informed consent process and documentation for proxy informed consent, when applicable. IRBs also consider the need for an assent procedure. Please refer to [OPRS/IRB Policy 24: Special Subject Populations: Cognitively Impaired](#) for details.

VII. Data Safety Monitoring

- A. The IRBs must ensure that the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects [45 CFR 46.111 and 21 CFR 56.111].

1. The level of monitoring must be appropriate to the probability and severity of risks.
 2. The provisions for monitoring should be adequate to ensure that changes in the frequency or character of adverse events will be detected and reported to the IRB within a timeframe that ensures subject protection.
- B. IRBs consider the necessity for safety monitoring, including the need for and adequacy of a Data Safety Monitoring Board [DSMB], during their initial review of each protocol. If necessary, the IRBs may require the development of a Data Safety Monitoring Plan [DSMP] and the creation of a DSMB.
- C. A DSMP should include the following elements:
1. A detailed description of study stopping rules, including a scientific and ethical justification for the chosen rules.
 2. A description of an internal or external DSMB.
 3. Selection criteria for DSMB members, a list of the DSMB members and their expertise.
 - a. Scientific DSMB members should be knowledgeable in the area under investigation, possess current knowledge of the scientific and therapeutic developments in the specific area of the research, and be able to review the research within the context of the research field.
 - b. DSMB members should not have any conflicts of interest pertaining to the research.
 4. The frequency with which the Board will meet.
 5. The types of data that will be reviewed by the DSMB.
 6. DSMB's preliminary criteria and statistical methodology for decision-making regarding continuation, modification or termination of the research due to benefit or harm.
- D. Upon approval of the study, all DSMB safety reports must be submitted to the IRB in a timely fashion.
- E. IRBs require that the progress of clinical trials be adequately monitored in order to determine whether the information generated from the trial, or other related trials, should be provided to the subjects, affects recruitment of subjects, changes the ratio of risks and benefits, or leads to modification or discontinuation of the study.

VIII. Privacy and Confidentiality

- A. The IRBs must ensure that adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data are in place [45 CFR 46.111 and 21 CFR 56.111].
1. Privacy defined: Having control over the extent, timing and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others [OHRP Institutional Review Board Guidebook].
 2. Confidentiality defined: Treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others in ways that are inconsistent with the understanding of the original disclosure without permission [OHRP Institutional Review Board Guidebook].
- B. IRBs review the methods to be used to avoid an invasion of the subjects' privacy and to maintain confidentiality of the subjects' data.
- C. Confidentiality of data may be assured through following practices: 1) substituting codes for identifiers; 2) removing identifiable information from documents such as survey instruments; 3) limiting access to identified data; 4) training research staff in the importance and methods of maintaining confidentiality; 5) proper storage of research data. IRBs consider proposed methods of maintaining confidentiality when evaluating safeguards. More stringent methods of maintaining confidentiality may be necessary for studies in which sensitive data is collected, such as sexual behavior or criminal activities.
- D. If research data will be stored for purposes other than the aims and goals of the current study and/or will be made available to individuals not affiliated with the research, the investigators are required to submit standard operating procedures [SOPs] for storing and sharing of data. Please refer to requirements outlined in the UCLA guidance for [Standard Operating Procedures for Data Banks](#).
- E. If research samples will be stored for purposes other than the aims and goals of the current study and/or will be made available to individuals not affiliated with the research, the investigators are required to submit standard operating procedures [SOPs] for storing and sharing of samples. Please refer to requirements outlined in the UCLA guidance for [Standard Operating Procedures for Tissue Banks](#).
- F. IRB's may require some studies to obtain a Certificate of Confidentiality [COC]. COC's are issued by the National Institutes of Health (NIH) to protect identifiable research information from forced disclosure. A COC is usually employed in studies where investigators collect sensitive information, such as that which, "... if disclosed could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation." Please refer to the NIH Certificates of Confidentiality Kiosk for additional details.

1. COC's do not take the place of good data security or clear policies and procedures for data protection, which are essential to the protection of research participants' privacy. IRBs require that appropriate steps to safeguard research data and findings are in place.
 2. In the event that a COC is required, the IRB determines whether an investigator may begin recruitment and enrollment of subjects prior to receipt of COC. This determination is based on the nature of the information being collected and the duration of the study.
- G. As large amounts of sensitive personal information, including tax information, credit information, school records, and medical records, are keyed to Social Security Numbers (SSNs), when an investigator proposes to collect subjects' SSNs, the IRBs maximize subject privacy by evaluating the investigator's justification for the collection of social security numbers, procedures for securing the SSNs, and plan describing when and how the SSNs will be destroyed.

IX. Alternatives to Participation

- A. IRBs review the alternatives available outside of research context that are available for the subject populations, and which may be of benefit to the subjects. Subjects must be informed of all available alternatives to participation in research.
- B. When research participation is introduced as part of a class curriculum, students should not be penalized for deciding not to participate in research. In such instances, investigators may minimize undue influence for students to participate in research by offering an alternative assignment which entails similar effort and time commitment on the part of the student.
1. As research participation is not an activity that is evaluated with a grade, assignments offered to students as equitable alternatives to participation should not be graded; rather, the assignment should be evaluated as simply "complete" or "incomplete."

X. Financial Considerations

- A. IRBs ensure that financial obligations of the subjects are reasonable relative to participation in the study and do not unnecessarily pose additional financial burden on the subjects.
1. IRBs ensure that the investigators follow UC policy regarding subjects' and sponsors' financial obligations.
- B. IRBs ensure that the investigator has provided a compensation plan for participation in research, monetary or otherwise, which does not constitute undue influence.

- C. Please refer to [OPRS/IRB Policy 31: Payment for Participation in Research](#) and [OPRS/IRB Policy 32: Financial Obligations](#) for details.

XI. Special Subject Populations

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, IRBs require that additional safeguards are included in the study to protect the rights and welfare of these subjects. Please refer to [OPRS/IRB Policies 20-26](#) regarding special subject populations for details.

XIII. Drugs and Devices

IRBs follow the FDA regulations for use of drugs and devices in research. Please refer [OPRS/IRB Policy 34: FDA Requirements](#).

XIV. Conflicts of Interest

IRBs consider financial interests and potential conflicts of interest of investigators and IRB members as a part of their review. Please refer to [OPRS/IRB Policy 63: Investigator Financial Interests and Conflicts of Interest](#) and [OPRS/IRB Policy 67: IRB Member Conflict of Interest](#) for details.

XV. Research Staff Qualifications

IRBs review the qualifications of research team members to conduct the proposed procedures, and ensure that only those individuals with appropriate qualifications and licensure carry out the research procedures.

XVI. Deception

In research involving deception or incomplete disclosure, the IRBs evaluate the potential harm of debriefing on a case-by-case basis. In most research involving deception, particularly in research which may induce psychological stress, guilt or embarrassment, IRBs follow OHRP's suggestion that subjects be debriefed at the end of their participation. Debriefing should include an explanation of any deception involved and counseling for subjects in dealing with any distress experienced due to their participation in research. Approval of research involving deception requires approval of a waiver or alteration of the informed consent process. Please see [OPRS/IRB Policy 29: Informed Consent Process and Documentation](#) for additional details.

Regulations:

21 CFR 50
21 CFR 56
45 CFR 46
45 CFR 46.111
42 USC 241(d)

References:

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, The Belmont Report - Ethical Principles and Guidelines for the Protection of Human Subjects of Research, April 18, 1979. <http://hhs.gov/ohrp/humansubjects/guidance/belmont.htm>

U.S. Office for Human Research Protections' (OHRP, formerly OPRR) *Protecting Human Research Subjects Guidebook (1993)*, Chapter 3.

National Institutes of Health Certificates of Confidentiality Kiosk:

<http://grants1.nih.gov/grants/policy/coc/index.htm>

Dickert, Neal & Grady, Christine. *What's the Price of a Research Subject? Approaches to Payment for Research Participation*. *NEJM*, July 15, 1999; 341 (3):

<http://content.nejm.org/cgi/content/full/341/3/198>

Attachments:

- OPRS-4 UCLA OPRS Human Research News, "Informed Consent Procedures for Screening Potential Research Subjects and Interim Protocol Requirements for Research Banking Human Tissue or DNA," December 14, 2001.
http://oprs.ucla.edu/human/news/item?item_id=181264
- OPRS-9 UCLA OPRS Human Research News, "Research Protocols and Suicide Risk," May 26, 2006.
- OPRS-64 UCLA IRB/OPRS General Consent to Participate in Research Screening
- OPRS-77 UCLA IRB/OPRS Instructions for Obtaining a Certificate of Confidentiality
- OPRS-79 UCLA IRB/OPRS Guidance: Standard Operating Procedures for Data Banks
- OPRS-80 UCLA IRB/OPRS Guidance: Standard Operating Procedures for Tissue Banks