

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

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**Policy Number: 23**

**Title: Risk/Benefit Analysis**

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

**Policy:**

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

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

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

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

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

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

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**Procedure Number: 23.A**

**Title: Procedure for Risk/Benefit Determination**

**Procedure:**

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

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

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

**II. IRB Committee Responsibilities**

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

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

### III. IRB Analyst or Higher Responsibilities

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

#### References:

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

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

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

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

IRB Policies 36-40, "Vulnerable Populations"

ICH-GCP (E6)

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