Sheet 3: CRITERIA FOR INSTITUTIONAL REVIEW BOARD (IRB) APPROVAL OF RESEARCH INVOLVING HUMAN SUBJECTS

1. ROLE OF THE NIH'S IRBS

All domestic and foreign institutions or sites where research involving human subjects is conducted or supported by the Department of Health and Human Services (DHHS) are required to perform this research in keeping with Federal regulations, Title 45, Part 46 of the Code of Federal Regulations, Protection of Human Subjects (45 CFR 46), or other ethical standards that provide equivalent protections, a determination made by the DHHS Office of Human Research Protections (OHRP). 45 CFR 46 requires prospective and continuing review and approval of human subjects research activities by a committee, usually called an Institutional Review Board (IRB). The Intramural Research Program of the NIH, in cooperation with the Institutes and Centers, has established 11 IRBs. The primary mandate of the IRBs is to protect the rights and welfare of humans who are the subjects of research. In fulfilling this mandate, the regulations require that the membership of the IRB be diverse in order to provide expertise in and sensitivity to a broad range of scientific and ethical considerations.

2. IRB REVIEW OF RESEARCH ACTIVITIES INVOLVING HUMAN SUBJECTS

Federal regulations allow an IRB to approve research only after it has determined that **all** of the following requirements are satisfied:

(a) Risks to subjects are minimized by using procedures that are consistent with sound research design, and that do not unnecessarily expose subjects to risk. Whenever appropriate, researchers should employ procedures that are being performed on subjects for diagnostic or treatment purposes.

(b) Risks to subjects are reasonable relative to **(1)** anticipated benefits, if any, to subjects, and **(2)** the importance of the knowledge that may reasonably be expected to result.

(c) The selection of subjects is equitable. In making this assessment the IRB must take into account the purposes of the research and the setting in which it will be conducted. The IRB must be particularly attentive to the special problems that may arise when research involves vulnerable populations, such as children, pregnant women, prisoners, mentally disabled persons, or economically or educationally disadvantaged persons. If any of the subjects is likely to be susceptible to undue influence or coercion, the IRB may require additional safeguards in the study to protect such subjects.

(d) Informed consent will be sought from each prospective subject, or the subject's legally authorized representative, generally by means of a written consent document. The IRB will carefully review these documents to assure that they contain the required elements of informed consent (see 45 CFR 46.116) and that they are understandable to a lay person.

(e) The research plan makes adequate provisions for ensuring the safety of subjects.

(f) There are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(g) These requirements are incorporated in the NIH IRB review standards (see Attachment) and http://ohsr.od.nih.gov/irb/protocol.html). For all initial protocol reviews, these standards must be addressed and recorded in the minutes.

Protecting the subjects of research is a shared responsibility involving institutional officials, research investigators, IRBs and research subjects. If you want to know more about IRBs or the NIH's system of human subjects research review and regulation, please contact the OHSR, Building 10, room 2C146 (301-402-3444).

Attachment

IRB PROTOCOL REVIEW STANDARDS

Minimal regulatory requirements for IRB review, discussion and documentation in the meeting minutes

Regulatory review requirement	**Suggested questions for IRB discussion**
1. The proposed research design is scientifically sound & will not unnecessarily expose subjects to risk.	(a) Is the hypothesis clear? Is it clearly stated? (b) Is the study design appropriate to prove the hypothesis? (c) Will the research contribute to generalizable knowledge and is it worth exposing subjects to risk?
2. Risks to subjects are **reasonable** in relation to anticipated benefits, if any, to subjects, **and** the importance of knowledge that may reasonably be expected to result.	(a) What does the IRB consider the level of risk to be? (See risk assessment guide on back of form.) (b) What does the PI consider the level of risk/discomfort/ inconvenience to be? (c) Is there prospect of direct benefit to subjects? (See benefit assessment guide on back of form.)
3. Subject selection is equitable.	(a) Who is to be enrolled? Men? Women? Ethnic minorities? Children (rationale for inclusion/exclusion addressed)? Seriously-ill persons? Healthy volunteers? (b) Are these subjects appropriate for the protocol?
4. Additional safeguards required for subjects likely to be vulnerable to coercion or undue influence.	(a) Are appropriate protections in place for vulnerable subjects, e.g., pregnant women, fetuses, socially- or economically-disadvantaged, decisionally-impaired?
5. Informed consent is obtained from research subjects or their legally authorized representative(s).	(a) Does the informed consent document include the eight required elements? (b) Is the consent document understandable to subjects? (c) Who will obtain informed consent (PI, nurse, other?) & in what setting? (d) If appropriate, is there a children's assent? (e) Is the IRB requested to waive or alter any informed consent requirement?
6. Risks to subjects are minimized.	(a) Does the research design minimize risks to subjects? (b) Would use of a data & safety monitoring board or other research oversight process enhance subject safety?
7. Subject privacy & confidentiality are maximized.	(a) Will personally-identifiable research data be protected to the extent possible from access or use? (b) Are any special privacy & confidentiality issues properly addressed, e.g., use of genetic information?
Additional considerations	
1. Ionizing radiation.	If ionizing radiation is used in this protocol is it medically indicated or for research use only?
2. Collaborative research.	Is this domestic/international collaborative research? If so, are FWAs or other assurances required for the sites involved? Is there a CRADA?
3. FDA-regulated research	Is an IND or IDE involved in this protocol?

Risk/Benefit Assessment

RISK

Regulatory definition of minimal risk: Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (45 CFR 46.102(h)(i)).

Check appropriate risk category:

1. _____The research involves no more than minimal risk to subjects.

2. _____The research involves more than minimal risk to subjects.

    ____The risk(s) represents a minor increase over minimal risk, **or**

    ____The risk(s) represents more than a minor increase over minimal risk.

BENEFIT

Definition: A research benefit is considered to be something of health-related, psychosocial, or other value to an individual research subject, or something that will contribute to the acquisition of generalizable knowledge. Money or other compensation for participation in research is not considered to be a benefit, but rather compensation for research-related inconveniences.

Check appropriate benefit category(ies):

1. _____no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition;

2. ____no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge to further society=s understanding of the disorder or condition under study); or

3. ____the research involves the prospect of direct benefit to individual subjects.