

IRB Reviewer Worksheet for Expedited Reviews

This reviewer worksheet is copied with modifications from Khan and Kornetsky's "Overview of Initial Protocol Review" printed in *IRB Management and Function* (2006). The reviewer worksheet serves the purpose of a reminder checklist of the mandated criteria IRB members must consider before approving a protocol. It is also a convenient and organized way to assist reviewers in discussing their critique of the protocol during a meeting. The worksheet is also the basis for further discussion and dialogue between the IRB and investigators.

Introduction, Specific Aims, Background, and Significance

Review of any research protocol must begin with the IRB member asking and answering these questions: "Why is this research important to conduct?" and "What will be learned from the proposed study?" IRB members should be provided with adequate data regarding earlier related studies and associated references. Applications must include a clear description of the objectives of the research, a statement of the study hypothesis (if any), and should adequately address how data will be obtained.

Worksheet Questions

1. Are the study aims/objectives clearly specified?
2. Are there adequate preliminary data to justify the research?
3. Are adequate references provided?
4. Is there appropriate justification for this research protocol?

Inclusion/Exclusion Criteria for Subjects

Appropriate inclusion and exclusion criteria for research participants are essential in order to justify human subjects research ethically. Selection of subjects must be equitable. Criteria for inclusion may consist of any combination of biomedical and behavioral characteristics. Poorly specified inclusion/exclusion criteria may result in inadvertent exclusion of eligible research subjects and an imbalance of or inappropriate enrollment of research subjects. IRBs are mandated to assure that special classes of subjects, especially vulnerable populations (i.e., women, minorities, and children), are included when appropriate. If for some reason inclusion criteria are not equitable, justification must be provided. Reviewer questions to consider include the following:

Worksheet Questions

1. Are inclusion and exclusion criteria clearly stated and reasonable?
2. Is the principle of distributive justice adequately incorporated into the inclusion and exclusion criteria for the research protocol? Is subject selection equitable?
3. Are minorities, women, children, or other vulnerable populations included in the study design? Is the inclusion or exclusion of special populations justified?

4. For subjects vulnerable to coercion or undue influence, are additional safeguards included to protect the rights and welfare of these subjects (e.g., prisoners, mentally ill, economically/educationally disadvantaged, employees)?

Recruitment of Subjects

IRB members must consider how, when, and by whom participants are to be identified and approached for recruitment. Reviewers must consider methods for recruiting subjects (traditional paper or Internet advertisements, databases, newsletters, recruitment by sending letters, from physician referrals, medical record reviews, etc.). It is important to consider what study staff member is best suited to approach potential research subjects, when and where subjects should be contacted, and the amount of time provided for potential subjects to consider participation. All recruitment materials and practices must be reviewed and approved by the IRB. The IRB must be assured that the recruitment process promotes voluntary participation and is not coercive in any way.

Worksheet Questions

1. Are the methods for recruiting potential subjects well defined?
2. Are the location and timing of the recruitment process acceptable?
3. Is the individual performing the recruitment appropriate for the process?
4. Are all recruitment materials submitted and appropriate?
5. Are there acceptable methods for screening subjects before recruitment (e.g., mailings, record reviews)?

Scientific Design

IRBs must feel confident that the scientific merit of a protocol justifies its risk/benefit ratio. IRBs are required to evaluate whether the study procedures are consistent with sound research design that minimizes risks to the subject.

Worksheet Questions

1. Is the scientific design adequate to answer the question(s)?
2. Are the aims/objectives likely to be achievable within a given time period?
3. Is the scientific design described and adequately justified?

Research Procedures

IRB reviewers must fully consider the procedures involved in research. Reviewers should ask this: "What procedures will the subject undergo for the purpose of this research? How is this different from what is done as part of standard clinical care? Reviewers must differentiate those procedures that are performed for research purposes from those that are performed for routine care or evaluation and determine whether the research is going to be conducted in a way that minimizes risks to subjects by employing procedures that are already being performed for diagnostic or treatment purposes. Reviewers are also responsible for understanding the actual studies, including the timing, the setting, and the qualifications of those conducting the

research. If there are flow charts or schemas, it is important that they be consistent with the text of the protocol and the informed consent document. Procedures for monitoring the subject during the research must also be evaluated. When questionnaires and behavioral or psychological assessments are included as part of the research evaluation, the reviewer should review these instruments. A description of what will happen to study data and to results should also be provided. The following questions are helpful in evaluating study procedures.

Worksheet Questions

1. Are the rationale and details of the research procedures accurately described and acceptable?
2. Is there a clear differentiation between research procedures and standard care and evaluation?
3. Are there adequate plans to inform subjects about specific research results that might affect the subject's health and/or decision to continue participation?
4. Is a debriefing following the procedures or tests needed? Has it been adequately provided for in the study?
5. Do appropriate procedures exist for insuring the safety of "at-risk" populations?
6. If necessary, do appropriate emergency procedures exist in the event of an accident or injury?

Statistical Analysis and Data Monitoring

Research protocols must contain well-conceived, well-formulated, and appropriate plans for interpretation of data and statistical analyses. The interpretation of data section should provide enough evidence to convince a reviewer that the proposed design has a reasonable chance of achieving the principal objectives of the research. IRB members should be given enough information to determine that the sample size and statistical power or precision associated with the sample size is adequate. In addition, forethought must be given to developing a sound method of data and statistical analysis, with adequate stratification factors and treatment allocation plans for the study design after study completion. IRB members must be adequately informed about plans for ongoing monitoring of the data.

Worksheet Questions

1. Is the rationale for the proposed number of subjects reasonable? Were formal sample size calculations performed and are they available for review?
2. Are the plans for data and statistical analysis defined and justified, including the use of stopping rules and endpoints?

Subject Privacy and Confidentiality

Reviewers must consider the extent to which research procedures could potentially invade privacy or breach confidentiality. These possibilities present a risk of harm to the subject. IRBs must consider the type and sensitivity of the information sought, how the information will be

recorded, precautions taken to protect confidentiality, and who has access to the research records. Precautions can and should be taken, depending on the nature of the research. This may include the possibility of applying for a Certificate of Confidentiality.

Worksheet Questions

1. Are there adequate provisions to protect the privacy and assure the confidentiality of the research subject?
2. Are there adequate plans and provisions to protect the confidentiality of data during and after research?
3. Is the use of identifiers or links to identifiers necessary, and how is this information protected? Are these measures adequate?

Potential Risks/Discomforts and Benefits

IRB members are charged with the responsibility of reviewing the potential risks, discomforts, hazards, or inconveniences of participating in a research protocol. This responsibility also includes evaluating the probability, magnitude, and duration of the risks involved. IRB members must identify the physical pain or discomfort as well as the psychological, emotional, or sociological harm, including invasion of privacy, loss of confidentiality, harassment, and lessening of an individual's dignity. Inconveniences such as loss of time or pay are also included in this category. Risk to a community or a group of individuals must also be considered. The initial reviewer must consider the potential risks as well as the precautions that will be taken to avoid or minimize potential risks.

Potential benefits can apply directly to the subject or to the advancement of scientific knowledge. IRBs must consider the magnitude and probability of direct benefit to a subject to be certain the research protocol does not overstate the benefits or potentially raise false expectations of benefit for the participants. It is important for the IRB to evaluate the risk/benefit ratio and to understand the rationale for believing the risk/benefit ratio is acceptable. The IRB must give special consideration to risks and benefits for research involving children, pregnant women, and other vulnerable populations such as the cognitively impaired and prisoners.

Worksheet Questions

1. Are the risks and benefits adequately identified, evaluated, and described?
2. Are the risks reasonable in relation to the benefits to be gained? Are the risks reasonable in relationship to importance of the knowledge to be gained?
3. Are the risks minimized to the greatest extent possible?
 - a. Does this study use procedures that are consistent with sound research design?
 - b. Does this study use procedures that do not unnecessarily expose subjects to risk.
 - c. When applicable, does the study use procedures already being performed on subjects for diagnostic/treatment purposes?

4. Example of more specific questions for vulnerable populations: If children are involved, within which category of risk/benefit does the protocol fall? Are all criteria within the category adequately addressed? (see Subpart D of 45 CR 46).

Subject Compensation and Costs

IRB members are charged with the responsibility of reviewing and approving compensation and/or reimbursement of costs to research subjects. Reimbursements may take the form of reimbursement for expenses associated with research participation such as travel expenses, lost wages, and parking costs. Compensation may be provided to participants for their time and effort. The IRB must be certain that the compensation or reimbursement offered is not so large as to be coercive. The compensation plan must be clearly described in the consent form.

Worksheet Questions

1. Is the amount or type of compensation or reimbursement reasonable and non-coercive?
2. Are there adequate provisions to avoid out-of-pocket expenses and costs by the research subject? If not, is there sufficient justification to allow subjects to pay for these expenses?

Informed Consent/Assent

The consent and assent sections of the reviewer worksheet are divided into four sections: 1) the consent document, which includes a list of required elements; 2) assent and witness requirement; 3) the consent/assent process; 4) any waivers or alterations of informed consent requirements.

1) The consent document. General federal requirements for informed consent are provided in 45 CFR 46 Section 116. The checklist provided below combines the informed consent requirements of the Department of Health and Human Services and SJSU. Each element listed must be included in the informed consent, unless it is not applicable.

1. Statement that the study involves research.
2. Purpose of research stated in plain language and reason why subject is asked to participate.
3. Study procedures or treatments, including duration.
4. Potential risks or discomforts to the subject.
5. Potential direct benefits to subjects or benefits to society.
6. Compensation or reimbursement. If applicable, additional costs associated with participating—who will pay for what.
7. How confidentiality will be protected; who has access to the data.
8. Statement that participation is voluntary and subject may withdraw and, if applicable, anticipated circumstances under which a subject's participation may be terminated.
9. Appropriate contact information.

2) Assent and witness requirement. Unlike the consent document, no federal regulations exist for assent documents. However, many institutions still require separate assent documentation, whereas others require a child's co-signature on a parental permission form. For protocols that involve children, each IRB must determine whether the obtainment of assent is required and, if so, an appropriate mechanism for obtaining and documenting assent. The IRB must also determine whether the permission of one or both parents should be obtained. Assent obtainment and documentation requirements need to be considered on a per-protocol basis. The following reviewer worksheet questions prompt the IRB members to make this special determination when required.

Worksheet Questions

1. Is assent required?
2. If yes, is a separate assent form required? Is a witness signature or an attestation to the assent required?
3. For parental consent, if the subject is unable to consent, is the signature of one or both parents/guardians required?

3) Process of obtaining informed consent/assent. Although the regulations require the inclusion of certain elements in the informed consent document, they do not provide rules or requirements for the process of obtaining informed consent. Investigators and reviewers are urged to consider the following general recommendations and suggestions when proposing or reviewing a method of obtaining consent.

- **Who?**
It is important to consider what type of relationship exists between the subject and the person approaching the subject for consent.
- **When?**
When potential subjects are being educated or informed about the research opportunity available to them, timing is very important. The IRB should consider when subjects would be approached regarding participation in a research study.
- **Where and How?**
The IRB should consider where the informed consent process will take place and how it will be conducted.

Worksheet Questions

1. Is the consent process well defined?
2. Does the consent process provide sufficient time, privacy, and an adequate setting for the subject to consider participation?
3. Does the consent process minimize the possibility of coercion or undue influence?
4. Is the individual obtaining consent/assent appropriate to do so?

5. Are the issues of subject's comprehension and autonomy considered?

4) Waiver or modification of informed consent. Federal regulations permit the waiver or alteration of the informed consent document if a protocol meets very specific criteria. In order for the IRB to determine whether a protocol meets the criteria, it is essential that investigators seeking the waiver or alteration provide adequate justification for the request. The worksheet questions here help IRB reviewers to look for the appropriate justification if a waiver or alteration is requested.

Worksheet Questions

Consider when appropriate:

1. Have **one** of the criteria for a waiver/modification of informed consent documentation (outlined below) been met? **Note, a *waiver* in this context refers to the documentation of consent, not to the need to obtain informed consent itself.**
 - a. The consent form would be the only record linking the subject with the research, and a potential risk would be a breach in confidentiality. In such case, it is up to the subject when asked if they want documentation, or
 - b. The study presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context.
 - c. If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, and the research presents no more than minimal risk of harm to subjects, and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.
2. If informed consent documentation is waived, should the investigator be required to provide subjects with a written statement regarding the research?
3. If children are included, have **all** the criteria for waiver of parental/guardian consent (outlined below) been met?
 - a. The IRB must determine whether parental/guardian permission is not a reasonable requirement to protect subjects.
 - b. Appropriate mechanisms must be implemented to protect children as subjects.
4. If a waiver or modification to required consent elements was proposed, have **all** the criteria (outlined below) been met? **Note, a *waiver* in this context refers to some or all of the elements of informed consent itself.**
 - a. The research involves no more than minimal risk to the subjects.
 - b. The waiver/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.

d. When appropriate, the subject will be provided with pertinent information after participation.

Other Issues and Considerations

Other issues that may be useful to ask are provided in this section of the reviewer worksheet. The interval between reviews must be determined on an individualized, per-protocol basis and must consider the degree of risk associated with the protocol. 45 CFR 46 states that IRBs are required to conduct continuing review of research at intervals appropriate to the degree of risk and, at a minimum, review must occur once annually for full review protocols. More frequent review may be necessary and is recommended for high-risk protocols.

Worksheet Questions

1. When should the next review occur? Should it occur before the required annual review of the study? If frequent reviews are necessary, how should the interval be determined?
2. Are there any notable conflicts of interest?
3. Are there appropriate resources (such as equipment, space, funding, staff) to conduct this research safely?
4. Has the investigator assured appropriate monitoring of subjects during and after the research?
5. If applicable, will counseling referrals or other support services be provided?
6. If applicable, are there provisions included for research-related injuries?