IRB Review Points to Consider – September 2016

POINTS TO CONSIDER

Principal investigators

1. Does the principal investigator have the appropriate qualifications, experience, and facilities to ensure that all aspects of the project and follow-up will be conducted rigorously and with due regard for the safety and well-being of the subjects?
2. Are adequate procedures in place through which the researcher will monitor the project and report problems to the IRB?
3. What is the investigator's past record with regard to approved research?

Risk/benefit analysis

1. Are both risks and anticipated benefits accurately identified, evaluated, and described?
2. Are the risks greater than minimal risk? Has the IRB taken into account any special vulnerabilities among prospective subjects that might be relevant to evaluating the risk of participation?
3. If the research involves the evaluation of a therapeutic procedure, have the risks and benefits of the research interventions been evaluated separately from those of the therapeutic interventions?
4. Has due care been used to minimize risks and maximize the likelihood of benefits?
5. Are there adequate provisions for a continuing reassessment of the balance between risks and benefits? Should there be a data and safety monitoring committee?

Informed consent

1. Do the investigators plan to involve a particularly vulnerable subject population?
2. Do the proposed explanations of the research provide an accurate assessment of its risks and anticipated benefits? Is the possibility (or improbability) of direct benefit to the subjects fairly and clearly described?
3. Is the language and presentation of the information to be conveyed appropriate to the subject population? (Consider the level of complexity and the need for translation into a language other than English.)
4. Are the timing of and setting for the explanation of the research conducive to good decision making? Can anything more be done to enhance the prospective subjects' comprehension of the information and their ability to make a choice?
5. Who will be explaining the research to potential subjects? Should someone in addition to or other than the investigator be present?

6. Should subjects be reeducated and their consent required periodically?

7. Should the IRB monitor incoming data to determine whether new information should be conveyed to participating subjects? How often should this occur? Who is responsible for bringing new information to the attention of the IRB between scheduled reviews?

8. If a waiver of some or all of the consent requirements is requested, does the importance of the research justify such a waiver? Is more than minimal risk involved? Can the research design be modified to eliminate the need for deception or incomplete disclosure? Will subjects be given more information after completing their participation? Would the information to be withheld be something prospective subjects might reasonably want to know in making their decision about participation?

Selection of participants

1. Will the burdens of participating in the research fall on those most likely to benefit from the research?

2. Will the solicitation of subjects avoid placing a disproportionate share of the burdens of research on any single group?

3. Does the nature of the research require or justify using the proposed subject population?

4. Are there any groups of people who might be more susceptible to the risks presented by the study and who therefore ought to be excluded from the research? Are the procedures for identifying such individuals adequate?

5. To the extent that benefits to the subjects are anticipated, are they distributed fairly? Do other groups of potential subjects have a greater need to receive any of the anticipated benefits?

6. To the extent that participation in the study is burdensome, are these burdens distributed fairly? Is the proposed subject population already so burdened that it would be unfair to ask them to accept an extra burden?

7. Will any special physiological, psychological, or social characteristics of the subject group pose special risks for them?

8. Would it be possible to conduct the study with other, less vulnerable subjects? What additional expense or inconvenience would that entail? Does the convenience of the researcher or possible improvement in the quality of the research justify the involvement of subjects who may either be susceptible to pressure or who are already burdened?

9. Has the selection process *overprotected* potential subjects who are considered vulnerable (*e.g.*, children, cognitively impaired, economically or educationally disadvantaged persons, patients of researchers, seriously ill persons) so that they are denied opportunities to participate in research?

10. If the subjects are susceptible to pressures, are there mechanisms that might be used to reduce the pressures or minimize their impact?

Privacy and Confidentiality

1. Does the research involve observation or intrusion in situations where the subjects have a reasonable expectation of privacy? Would reasonable people be offended by such an intrusion? Can the research be redesigned to avoid the intrusion?

2. If privacy is to be invaded, does the importance of the research objective justify the intrusion? What if anything, will the subject be told later?

3. If the investigators want to review existing records to select subjects for further study, whose permission should be sought for access to those records (the physician, the institution maintaining the records, the subjects)? How should the subjects be approached (through their physician, the medical records department, the institution)?

4. Will the investigator(s) be collecting sensitive information about individuals? If so, have they made adequate provisions for protecting the confidentiality of the data through coding, destruction of identifying information, limiting access to the data, or whatever methods that may be appropriate to the study? If the information obtained about subjects might interest law enforcement or other government agencies to the extent that they might demand personally identifiable information, can a grant of confidentiality be sought from a federal or state agency to protect the research data and the identity of the subjects from subpoena or other legal process?

5. Are the investigator's disclosures to subjects about confidentiality adequate? Should documentation of consent be waived in order to protect confidentiality?

Monitoring and observation

1. How will the research data be recorded and maintained?

2. Considering the degree of risk, is the plan for monitoring the research adequate in terms of timeliness and thoroughness?

3. If the principal investigator is other than full-time on the project, is the oversight and monitoring time sufficient?

4. Is there a mechanism for providing information to the IRB in the event that unexpected results are discovered? (Unexpected results may raise the possibility of unanticipated risks to subjects.)

5. Does the institution have a data and safety monitoring board? If so, should it be asked to monitor the project under review? If the institution does not have a data and safety monitoring board, should the IRB request or recommend that one be appointed, either by the institution or the sponsor, for this project?

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Additional safeguards

1. Are recruitment procedures designed to assure that informed consent is freely given?
2. What special safeguards are included to protect the rights and welfare of subjects who are likely to be vulnerable to coercion or undue influence (*e.g.*, children, prisoners, pregnant women, persons with physical or mental illness, and persons who are economically or educationally disadvantaged)?
3. Does the nature of the disease or behavioral issue to be studied permit free consent?
4. Are any incentives offered for participation likely to unduly influence a prospective subject's decision to participate?
5. Is there an adequate procedure for monitoring the consent process, and should the IRB or its representative observe the process?

Incentives for participation

1. Are all conditions in keeping with standards for voluntary and informed consent?
2. Are the incentives offered reasonable, based upon the complexities and inconveniences of the study and the particular subject population?
3. Are there special standards that the IRB ought to apply to the review of research in which volunteers are asked to assume significant risk?
4. Should the IRB monitor subject recruitment to determine whether coercion or undue influence is a problem?

Continuing Review

1. Are the actual risks and benefits as anticipated?
2. Have any subjects been seriously harmed?
3. Has the IRB been informed of any unforeseen problems or accidents that may have occurred?
4. Should the IRB request that the investigator(s) submit scheduled progress reports?
5. Should the investigator(s) submit progress reports more often than annually?
6. Since the last IRB review, have subjects been informed of any important new information that might affect their willingness to continue participating in the research?
7. Have any new findings, knowledge, or adverse effects come to light that should be, but have not been, communicated to subjects?

8. Does the progress of the project together with the results of other new research indicate that the IRB should either impose special precautions or relax special requirements it had previously imposed?

9. Do the consent documents need to be revised?

10. Has due care been used to reduce risks and increase the likelihood of benefit?

11. Are the procedures agreed upon at the beginning of the research still being used?

12. Does the protocol adequately provide for continuing assessment of the balance between risks and benefits?

13. Should IRB approval be continued, or should approval be suspended or terminated?

14. When should the IRB next review the project (taking into account what has been learned about the actual risk to subjects since the project first received IRB approval)?

Research design

1. Does the study involve reviews of records, observation, surveys, or interviews? If so, does it qualify for exemption or expedited review under the federal regulations and institutional policy?

2. Is the scientific design adequate to answer the questions posed? Is the sample size (number of subjects) adequate? Is the method proposed for selecting and assigning subjects to treatment groups unbiased?

3. Does the investigator serve a dual role that may pose a conflict of interest?

4. Is any of the information to be collected sensitive (*e.g.*, related to sexual practices, substance abuse, or illegal behavior)?

5. Are there adequate plans to protect participants from the risks of breach of confidentiality and invasion of privacy?

6. Are there plans for approaching subjects in a way that will respect their privacy and their right to refuse? If the protocol involves an epidemiologic study, will subjects or their relatives be protected from learning inappropriate information?

7. Does the recruitment process protect subjects from being coerced or unduly influenced to participate? Are any payments to subjects reasonable in relation to the risks, discomfort, or inconvenience to which subjects will be exposed?

8. Are there adequate plans to exclude subjects who are vulnerable to injury during the period of withdrawal of active and effective therapy, if that is part of the research design?

9. Have the rights and interests of vulnerable subjects (*e.g.*, desperately ill persons) been adequately considered?

10. Are all appropriate elements of informed consent clearly provided for [Federal Policy §___.116], including:
    a. Do the consent documents describe the study design (including plans for randomization, use of placebos, and the probability that the subject will receive a given treatment) and conditions for breaking the code (if the study is masked)?
    b. Do the consent documents describe the risks and benefits of each of the proposed interventions and of alternative courses or actions available to the participants?
    c. Do the consent documents clearly describe the extent to which participation in the study precludes other therapeutic interventions?
    d. Are provisions made for supplying new information to subjects during the course of the study and for obtaining continuing consent, where appropriate?
    e. Must investigators obtain consent before reviewing records?
11. Will the consent process take place under conditions most likely to provide potential subjects an opportunity to make a decision about participation without undue pressure?
12. If the study is a clinical trial, how will the trial be monitored? What will be done with preliminary data? Should an independent data and safety monitoring board be established? How will decisions about stopping the trial be made? By whom? On what basis?
13. At what interval should the IRB perform continuing review of this project?

Women

1. Will women be appropriately represented in the study? Does the study need to be designed to allow evaluation of gender differences?

Children

1. Does the research have an identifiable prospect of direct benefit to the individual child participant? Can that benefit be achieved through alternative means?
2. Does the research have an identifiable prospect of risk to the individual child participant? What safeguards are proposed to minimize these risks? When procedures involving greater than minimal risk to children are anticipated, are convincing scientific and ethical justifications given?
3. Is the inclusion of normal volunteers justified?
4. Do studies involving placebo controls place the child at greater risk by withholding from selected subjects potentially therapeutic research drugs or interventions?

5. When possible, have appropriate studies been conducted on animals and adults first? Will older children be enrolled before younger ones?

6. What is the age of majority in the state? Can a child consent to medical care for certain conditions, and, if so, at what age? What legal limits are there on the right of parents to consent on behalf of their children?

7. Is permission of both parents necessary? Under what conditions may one of the parents be considered "not reasonably available?"

8. Will efforts be made to ensure that parents' permission to involve their children in research studies is free from coercion, exploitation, and/or unrealistic promises?

9. Are mechanisms in place to ensure that children are involved as research subjects in ways that do not undermine their dignity as young persons? Are provisions made that show respect for the developing rights of children, such as: (a) obtaining their assent, and, where appropriate, honoring their dissent; and (b) protecting their need for privacy and the confidentiality of information regarding them?

10. Are there special problems that call for the presence of a monitor or advocate during consent procedures?

11. Are special needs of adolescents such as counseling and confidentiality accounted for in the research design?

12. Are there any special problems such as confidentiality and reporting that might arise in sensitive research about child abuse or sexual practices of teenagers?

13. If conditions present in children have implications for other family members' health statuses, are appropriate mechanisms proposed for dealing with the larger family unit (*e.g.*, genetic risks or HIV infection)?

14. Should parents be required to be present during the conduct of the research? (Are proposed subjects to be very young? Are the procedures involved painful? Must subjects stay overnight in the hospital when they otherwise would not have to?)

Cognitively impaired persons

1. Does the IRB need to include a member knowledgeable about and experienced with the mentally disabled or cognitively impaired?

2. Does the research pertain to mental disabilities so that it is necessary to involve persons who are mentally disabled as subjects?

3. If the investigator proposes to involve institutionalized individuals, has he or she provided sufficient justification for using that population? Are noninstitutionalized subjects appropriate for the research and reasonably available? Does the research pertain to aspects of institutionalization?

4. Are adequate procedures proposed for evaluating the mental status of prospective subjects to determine whether they are capable of consenting? Are these procedures appropriate both to the subject population and the nature of the proposed research?

5. Is more than minimal risk involved? If so, is the risk justified by anticipated benefits to the participating subjects and the importance of the knowledge that may reasonably be expected to result?

6. Is it possible to identify persons authorized to give legally valid consent on behalf of any individuals judged incapable of consenting on their own behalf? Should assent of the prospective subjects also be required? If incapable of giving valid consent, can subjects' objection to participation be overridden? Under what circumstances?

7. Should an advocate or consent auditor be appointed to ensure that the preferences of potential subjects are elicited and respected? Should someone ensure the continuing agreement of subjects to participate, as the research progresses?

8. Should the patient's physician or other health care provider be consulted before any individual is invited to participate in the research? Is the research likely to interfere with ongoing therapy or regimens? Is it possible that the request to participate itself might provoke anxiety, stress, or other serious negative response?

Prisoners

1. Does the IRB have the necessary prisoner-related members?

2. Does the proposed research fall within one of the permissible categories of research with prisoners?

3. Is the use of prisoners as subjects justified?

4. Is there any evidence of duress, coercion, or undue influence in the particular prison(s) from which subjects will be recruited? (Does the prison facility meet all of the conditions set forth in applicable regulations?)

5. Are there any applicable state laws with which the IRB must comply?

Traumatized and unconscious participants

1. Does the research pose more than minimal risk to subjects?

2. Do the anticipated benefits to the subjects justify proceeding with the research even though it is not possible to obtain their prior informed consent? (Proceeding with research without prior informed consent is acceptable only for minimal risk research under DHHS regulations and in life-threatening situations under FDA regulations.)

3. Is consent from the patient's next-of-kin required? Is it sufficient? (Check if there are any applicable state laws on this subject.)
4. If a preliminary consent procedure is employed, what amount of time should reasonably be allowed to elapse before requiring that a valid consent be obtained or the subject be removed from the study?
5. Is there a need for additional monitoring, either of the consent process or the conduct of the research itself?

Terminally ill patients

1. Must the research involve terminally ill patients to achieve its objectives?
2. Is a clear explanation of the patient's eligibility for the study provided?
3. Are specific treatment alternatives, including the option of no treatment, described?
4. Are the potential benefits and risks (and their probability) realistically and simply stated?
5. Are the ways in which participation may affect the patient's lifestyle clearly described (*e.g.*, "You will be hospitalized each month for 5-7 days.")?
6. Is the patient assured that he or she can withdraw from the study at any time? If withdrawal from the research will result in a patient's discharge from a research unit or end the patient's access to health care that has been provided in conjunction with the research, is that fully explained?
7. Should a witness or patient advocate be present during consent negotiations?
8. Is there reason to require that the patient's physician not be the clinical investigator?
9. If the research is done under a Treatment IND or other expanded access mechanism, is the lack of conclusive effectiveness data made clear? Are all costs to subjects of receiving a drug or device under an expanded availability mechanism clearly specified?
10. If a drug is administered at the community level, does the subject's physician have access to information about the drug's potential usefulness and potential risks?

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Elderly Participants

1. Does the proposed consent process provide mechanisms for determining the adequacy of prospective subjects' comprehension and recall?
2. How will subjects' competence to consent be determined?
3. Will the research take place in an institutional setting? Has the possibility of coercion and undue influence been sufficiently minimized?

Minorities

1. Is the subject population appropriately drawn? Will minority subjects likely be appropriately and adequately represented? If not, is the homogeneity of the study population justified?
2. Does the study need to be designed to allow evaluation of racial/ethnic differences?
3. Are subject recruitment strategies appropriate for obtaining a diverse subject population?
4. Have the special needs of prospective subjects been addressed (e.g., child care, transportation)?
5. Has the possibility of undue influence or coercion been eliminated?
6. Does the proposed consent process ensure open and effective communication between the researcher and prospective subjects? Are the consent documents written in language that will be easily accessible to subjects? Are documents in foreign languages necessary? Is foreign language facility on the part of the research staff necessary (both for obtaining consent and conducting the research)?

These questions to consider were retrieved on 3/5/12 from the Office for Human Research Protections (OHRP) IRB Guidebook available at http://www.hhs.gov/ohrp/archive/irb/irb_guidebook.htm