

AAHRPP DOCUMENT # 76
UNIVERSITY OF ALABAMA
HUMAN RESEARCH PROTECTION PROGRAM
GUIDANCE: IRB APPLICATION GUIDE

GENERAL REMARKS

1. This guidance applies to any level of application (exempt, expedited, full-board review), any type of application (medical, non-medical, initial, continuing, or modification of an approved protocol), and to both electronic and non-electronic submissions.
2. Not all issues addressed here will apply to every application. It is also possible that e-PROTOCOL may not ask about an issue that is a factor in your study. In that case, please label and raise the issue in a logical place in the application.
3. E-PROTOCOL individualizes the nature and sequence of questions for users depending on the level and type of application. Therefore, elements of this application guide may appear in different places on different electronic applications. Also, investigators may have to decide where to place requested information within e-PROTOCOL.
4. Review the FORM: IRB Checklist for Reviewers and Investigators. Knowing what reviewers are looking for will help you prepare a complete application and reduce requests from the research compliance staff or IRB for additional information.
5. Consult the IRB website for policies, forms, templates, and guidance documents that are relevant to your study. Some are identified within this document but many more are available online. These documents provide many helpful details and give you suggestions for handling various issues, thus reducing the need for the IRB to request additional information.
6. The University of Alabama expects investigators to comply with Alabama state law, federal regulations for research (protection of human subjects, FERPA, PPRA, HIPAA, and other relevant statutes) and sponsor requirements, such as those of NIH, the Department of Defense, the Department of Energy, or corporate entities.

7. It is highly recommended that faculty supervisors review student IRB applications before submission. This will avoid adviser surprises in communications from IRB and often reduces the need for revisions and requests for additional information.
8. Investigators must evaluate and report conflicts of interest to their departments, the IRB, and often on the consent form for prospective participants. See UA POLICY: The University of Alabama Policy on Conflict of Interest/Financial Disclosure in Research and Other Sponsored Programs and the IRB POLICY: IRB and Investigator Responsibility for Applications Involving Declared or Undeclared Investigator Conflict of Interest.
9. For non-electronic submissions: Applications MUST be typed, using font size 12. Please number the pages of the entire application, including appendices, consecutively. This is very helpful to reviewers in discussing the material.
10. Both electronic and non-electronic applications should include appendices and attachments as described immediately below in #11.
11. NON-ELECTRONIC APPLICATIONS: Please arrange in this order:
 - a. Face Sheets. These are the Request for Approval of Research Involving Human Subjects (Page 1 of the application) and the IRB Application Study Personnel Sheet (Page 2 of the application).
 - b. Any cover letter to the IRB.
 - c. FORM: Signature Assurance Sheet or other document used by your department for this purpose
 - d. For continuing review insert FORM: IRB Renewal Application. For modification of approved protocols, insert FORM: Modification of Approved Protocol. If applying for both renewal and modification, insert both forms.
 - e. Research Description (explained in detail later in this document)
 - f. Appendices (Not all relevant to every application. Please label and paginate.
 - i. Consent and Assent forms
 - ii. The DHHS-approved sample consent document and the complete DHHS-approved protocol (when they exist) and also if you are engaged in DHHS multi-site research.
 - iii. Advertising/recruitment materials

- iv. Any supplementary forms as for vulnerable populations or HIPAA releases
 - v. Scientific portion of research grant application, thesis, or dissertation proposal (if applicable)
 - vi. Letters of access, permission, collaboration, or IRB approval from other sites. This includes letters from UA facilities used in the research but not controlled by the investigator's department.
 - vii. Instruments—include in entirety. *University Legal Counsel has stated that IRB review is a fair and expected use of an instrument.*
 - viii. Any FDA or Sponsor forms
 - ix. Current certificates of training for investigators and project staff in contact with participants, if not already on file with IRB.
12. Please spell check and proofread your application and especially the informed consent documents. Frequent errors cast doubt on scholarship and reflect poorly on the university when distributed.
13. Research conducted at sites not owned or operated by the University of Alabama or in other states or countries is subject to special procedures for coordination of research review. See POLICY: Review and Oversight of Research Conducted at Multiple Sites and GUIDANCE: International Research.
14. You are welcome to consult with a Research Compliance Specialist at 348-8461 or an IRB member about preparation of your application.
- a. If you are not sure whether your research involves human subjects or whether you need an application, please contact a compliance specialist who will assist you with this decision.

BASIC INFORMATION ABOUT THE APPLICATION

Face Sheets—Pages 1 and 2

1. Please provide the following information:
 - a. Page 1: Request for Approval for Research Involving Human Subjects
 - i. At UA students may be principal investigators.
 - ii. For student research, the faculty supervisor must be the second investigator.
 - iii. Provide contact information for both, including an e-mail address. Attach a continuation page if more than three persons are classified as investigators.
 - iv. Give the COMPLETE title of the research project.

- v. If the research involves several components that will be reviewed separately, please distinguish among the parts, e.g., Phase I, Qualitative Phase.
- vi. If a study is federally funded, the title of the IRB study and the title of the funding application must match.
- vii. Name the actual or potential funding agency, whether intramural (UA funds) or extramural (non-UA funds). State "NONE" if there is no external financial support.

COVER LETTER (OPTIONAL)

You may write a cover letter to the IRB if you wish. Possible reasons for doing so include requesting that the proposal be considered for Exempt or Expedited review (identify the relevant federal criterion/ia for that status) or to provide unique or preliminary information about some aspect of the study. On non-electronic submissions, put this immediately after the face pages. E-PROTOCOL allows you to check which level of review you believe may be applicable.

SIGNATURE ASSURANCE SHEET or DEPARTMENTAL EQUIVALENT (Required for all applications)

Please obtain the necessary signatures and attach. If absolutely necessary, you may submit the application without this page in order to get it entered within IRB, but the completed sheet must be submitted before the application will be sent to reviewers.

RESEARCH DESCRIPTION

IRB recognizes that some proposals require more description than others, but as general rule the description of the research (not including appendixes) needs to be approximately 5-10 single-spaced pages long to ensure adequacy for IRB purposes. IRB sees many applications that are simply too brief to provide an adequate description of the research.

As with grant applications, your IRB application should be understandable to all IRB members, both professional and lay. Include simplified examples and explanations to achieve this goal.

Include some references. Grant or dissertation-level document is not expected but provision of key references is often helpful and instills confidence in the quality of the work. It is essential to include references for conclusions about the state of the art, such as "Scientists agree that A is superior to B", "C" is the gold standard for measuring "D", "E" is the standard of care for this condition, "The

complication rate for this procedure is 30%”, and “Subjects prefer “X” approach over “Y” approach when discussing depression and suicidal thoughts.

Please describe the requested information within the research description. For example, describe the elements of consent within the description and do not refer reviewers to the consent form for all information about consent, privacy, or confidentiality. The justification to an IRB and the information provided to prospective participants are different and serve two different purposes.

Please do not submit the funding proposal or a thesis or dissertation prospectus to the IRB as an IRB application. Again, the purposes are different, and IRB members do not have time to read pages and pages of need, significance, and other literature. Prepare a separate IRB application and submit it in the recommended format. The scientific portion of the funding proposal, thesis, or dissertation should be appended for reviewer reference but does not suffice for an IRB application.

You may scan in or cut and paste passages from the sponsor’s protocol, thesis, or dissertation that address requested information rather than retyping blocks of material. However, please review your application to verify that irrelevant wording from an earlier or related proposal does not appear. For example, old references to “Incarcerated” or “mentally ill” participants in a proposal that does not otherwise speak of them causes the IRB to wonder whether an investigator is not fully disclosing the nature of the research. This will lead to a request for clarification and a delay in the approval of your application.

SECTIONS OF THE IRB APPLICATION

Purpose, Objectives, Design

1. Provide a 3-5 sentence lay summary of the purpose of the study.
2. List your objectives/aims/hypotheses/research questions/study questions. This is a new request from IRB. IRB needs this information in order to determine that the research has scientific validity, that the variables are measured and measurable, that the research questions can be answered, and to assess subject risk and burden.
 - a. (If aims, hypotheses, etc. are lengthy and repetitive, shorten them by combining variables and saying “The effects of A, B, and C on D, E, and F on G, H, and I will be assessed through 5 surveys and 3 observation periods.” The ensuing method description will then describe these in detail.

3. Name the approach and/or design of the study—ethnographic interviews, randomized Phase III clinical trial, one-time telephone survey, one group pre- and post-design, etc.
4. What do you hope to learn from the study—why is it important? What will it add to knowledge? (The IRB acknowledges that some studies are more exploratory than others and also that replications are useful contributions to knowledge.)

Study Procedures

1. Do NOT describe the sample criteria and selection here.
2. Describe all procedures in chronological order, from screening through closeout (or by study phase) that human subjects will undergo in the study. Define any key terms. How long will each procedure take? NOTE: *The IRB finds tables showing timing of interventions and assessments very helpful for understanding complex studies.*
3. Describe the setting(s) and major essential equipment to be used. (NOTE: *If you are using University sites or resources that are not controlled by your department, such as the Recreation Center or Ferguson Center, please supply a letter of support from the director of that resource/site. Some departments or facilities have their own internal coordination routing sheets that cover outside or research use of their facilities that you must complete and attach.*)
4. Describe the number, level, and expertise of study personnel (GRAs, registered nurses, licensed clinical psychologists, lab assistants trained in CPR, statistician, etc.
5. Describe any needed training and supervision of personnel, especially if the investigator or research staff are students. Be sure to explain how staff will be trained to recognize signs of participant distress, such as resistance to assent or risk of suicidality and how they will respond. How will the supervising professor of a student investigator be available to them? How will the integrity of the study be monitored and assured? Explain how staff will be instructed about the importance of responding to, referring, or noting questions or complaints from participants and about their responsibility to report protocol deviations, unanticipated or adverse events, or scientific misconduct.
6. If deception is used, explain the nature of the deception, justify the need for it, and explain any debriefing process. Attach the debriefing script and FORM: Request for Waiver/Alteration of Informed Consent.

Study Background

1. Problem, Purpose, Significance: Provide the IRB with a concise introduction and background information. What is the problem that gives rise to this research—what scientific, social, or medical problem led to this study? What is not known about this problem? What exactly do you want to learn (purpose). What will your study contribute to knowledge about this problem—why is it significant? (For example, this study may lead to the development of a device for reading blood glucose levels through the skin without any needle stick—or this study may reduce the incidence of juvenile repeat offenders—or it may improve the theory of X.) Provide some references.
2. What is your background in this research area? Where does this study fit in your research trajectory? For example, “This study will be the third in the PI’s program on supportive interventions for home caregivers of persons with dementia” or “This study is the PI’s master’s thesis.” The IRB recognizes that many UA investigators are new investigators and that established investigators pursue new lines of research at times. These are not negative circumstances.

Subject Population

1. Describe the characteristics of the study population: age, race, gender, ethnic background, health status, etc.
2. Describe the anticipated or desired sample size. If it is based on a power calculation, describe it. If it is based on literature or personal knowledge of the population, describe. (Hint: Providing a number or a range that is somewhat larger than your actual need or expectation, particularly for survey research, may save you a later application to modify your proposal for a larger sample size. Do, however, avoid “sky-high” estimates.
3. State whether subjects are a vulnerable population. If so, attach the supplementary application form for that population and describe why that population must be used. Note that some subjects may be a member of more than one vulnerable population (pregnant women may be incarcerated and cognitively impaired). In that case, complete the supplementary form for each population attribute.
4. State the exclusion and inclusion criteria. If women or minorities are excluded, please explain why their exclusion is appropriate to the purposes of the study. NOTE: Cost is not an acceptable reason for exclusion except when the study would be duplicating already available information. Women of childbearing potential and children should not automatically be excluded from participation in clinical research.

Subject Recruitment Methods

1. Describe plans for identifying and recruiting the needed subjects. How will the population be identified and by whom? How will initial contact be made with prospective subjects and by whom? What measures will be used to reach any group that is likely to be difficult to access—for example, recruiting rural African American males for prostate screening has often been found difficult.
2. Describe any advertising to be used (see GUIDANCE: IRB Advertising Guidelines) and append copies. Advertising must be approved by IRB before use.
3. Identifying and recruiting subjects may involve protected health or personal information and HIPAA, FERPA, or PPRA legislation or special requirements of sponsors like the Department of Defense or the Department of Energy. Address this issue and attach any supplementary forms. (See IRB website for policies and forms).
4. If non-English speaking subjects from a foreign culture will be involved, please explain how you will communicate with them in terms they can understand and in an appropriate manner for their culture. For example, in some culture unrelated males—the research staff—may not converse with female participants unless a related adult male is present. Will an interpreter or translator be used? If so, how will that person's familiarity with the culture and the appropriateness of a translated document be assessed?
5. NOTE: Recruitment of vulnerable subjects, those with protected health information, or those of different cultures is highly relevant to the informed consent process.
6. NOTE: *UA does not routinely allow finder's fees for recruiting participants. However, if a sponsor's protocol allows it or the literature strongly supports this means of recruitment for a certain problem, IRB will consider their use and determine whether the consent document should disclose them.*

Risks

1. Describe any physical, psychological, social, economic, or legal risks and assess their likelihood and seriousness. If quantitative or experiential information is available about the likelihood of a risk, please provide it and a reference. State whether the procedures to be used represent the least risk to participants; if not, explain why more risky procedures must be used.
2. For medical studies, assess any potential risks or likely adverse effects of any drugs, biologics, devices, or procedures subjects may experience during the study.

3. If international research is involved, describe any qualifications or preparations that enable you to estimate and minimize risks to subjects.
4. If community-based participatory research is involved, what risks may accrue to the community? Might the community be stigmatized in some way or deprived of some new resource?

Evaluation of Level of Risk

1. Identify the level of risk as Low, Medium, or High. (NOTE: *Categories greater than minimal risk are not defined in federal regulations; the PI and then IRB must assign a label.*)

Special Precautions/Safeguards Against Risk

1. Describe all efforts to prevent, minimize, and detect risk to participants, including communities. Describe any measures and resources to provide professional or medical intervention in case of adverse events or unanticipated problems, whether medical or psychological. How will participants be monitored to ensure their safety?
2. If the study is clinical research, funded by NIH or FDA-regulated, or is of greater than minimal risk (sponsored or not), a Data Safety Monitoring Plan (DSMP) must be presented. Some studies also require a Data Safety Monitoring Board (DSM). Both DSMPs and DSMBs must be approved by the IRB.
3. Describe and justify any Data Safety Monitoring Plan or Board. Identify persons who will carry out procedures to monitor the progress of the study and the safety of participants. How often will the Plan be reviewed? How often will a Board meet? What reporting procedures are to be used for unanticipated problems or adverse events?
4. Assure the IRB that any action resulting in a temporary or permanent suspension of the study is reported to the appropriate entities.
5. For more help, see IRB POLICY: Data Safety Monitoring in Proposed Research and GUIDANCE: Developing a Data Safety Monitoring Plan or Data Safety Monitoring Board.

Benefits

1. What benefits, if any, are likely to accrue to subjects? Do not “reach” for benefits; in many cases the most accurate statement is that “There are no direct benefits to you”. You may identify altruism as a possible benefit.
2. What benefits may accrue to science or society? How important is the knowledge that is likely to result?
3. Compensation may not be identified as a benefit.
4. If you are using vulnerable populations, relate the benefits to the participants’ vulnerable status if possible.
5. If the study involves community-based participatory research or foreign countries, describe any benefits that may accrue to the community or country.
6. Consider the risks and benefits of the study jointly and select one of the following risk-benefit categories for participants:
 - a. Minimal risk, no direct benefit to participant. *This means that potential harm/risk is not greater than that encountered in everyday life or during routine physical or psychological examinations and the only likely benefit to the participant may be feelings of altruism.*
 - b. Minimal risk, potential for direct benefit to participant. *This means benefits to participants are more tangible than feelings of altruism, such as increased knowledge of how to care for one’s illness or actual improvement in symptoms.*
 - c. Greater than minimal risk (state “Moderate” or “High”) but potential for direct benefits.
 - d. Greater than minimal risk (state “Moderate” or “High”), no direct benefit to participant, with potential to yield generalizeable knowledge about the participant’s disorder or condition.
7. Explain why risks are reasonable in relation to the benefits to the participant, science, or society.