

Summary of Ten Steps Investigators Should Take in Preparing for Protocol Review by the Human Investigation Committee (HIC)*

1. Determine whether your proposed research is subject to HIC review. Research having the following attributes requires HIC approval:

- Research involving human subjects done on the premises of the Yale-New Haven Medical Center
- Research in which access to the human subject involves any records maintained by faculty or staff of the Yale-New Haven Medical Center
- Research involving human subjects conducted by faculty, students, or employees of the Yale-New Haven Medical Center regardless of where the research is undertaken.

Across all biomedical and behavioral disciplines, research includes (a) research development, testing, and evaluation; (b) therapeutic, diagnostic, or preventative procedures, if they are different from customary practice, (c) the comparison of two or more diagnostic, therapeutic, or preventative maneuvers or modalities, even if both are standard, (d) all investigational drug or device trials.

2. Obtain human subjects protection training for all study personnel. The HIC will not approve a protocol until all study personnel provide proof that they have completed the human subjects protection training requirement. Study personnel include all investigators involved in the design, performance, data acquisition, or analysis of the study. The definition also includes any person who may have significant contact with a human subject or identifiable information or data about the subject during the course of the study. These personnel may include student assistants, nurses, technicians, study coordinators, and general assistants. The training requirement can be met in any of the following ways:

- Complete the Yale web-based training program, accessible at <http://info.med.yale.edu/irbtraining/>.
- Complete the NIH web-based training program, accessible at <http://ohsr.od.nih.gov/cbt/nonNIHpeople.html>.
- Complete the Human Participation Protection Education for Research Teams training program, accessible at http://ohsr.od.nih.gov/extramural/extramural_training.html.
- Attend one of the monthly HIC Today sessions presented by the HIC office. Dates, times, and locations are posted on the Yale School of Medicine calendar, accessible at
- Provide documentation and certification of completion from some other training provider, such as another University's training program.

3. Begin considering the protocol, which consists of four parts. The four parts of a protocol are:

- Part I. Face Sheet. You will complete this “cover sheet” just before submitting the protocol for HIC review. See Step 5 for more information.
- Part II. Description of the Study.
- Part III. Human Subjects.
- Part IV. Consent Form.

* Investigators should refer to the HIC's website for a more detailed explanation of the guidelines and to access required forms. The HIC homepage can be accessed at <http://info.med.yale.edu/hic/guidelines/index.html>.

4. Write a description of the study (Part II of the protocol). In this section of your protocol, you should:
 - (a) State the purpose of the study; usually this will include a hypothesis to be tested.
 - (b) Describe relevant background findings, such as experimental or clinical findings that led to the plan for this protocol.
 - (c) Identify a specific location for the study (e.g., a hospital, out-patient facility, school, etc.).
 - (d) State the probable duration of the entire project.
 - (e) Describe the research plan, noting all procedures that directly affect human subjects.
 - (f) State an explicit plan for data and safety monitoring. Information about the requirements of a plan can be found on the HIC website.
 - (g) With the exception of pilot studies, all protocols must state the number of subjects expected to enter the study, its statistical power, and a summary of plans for statistical analysis.
 - (h) Describe any economic considerations of the protocol, including but not limited to, any material inducements that will be offered to subjects in return for participation.

5. Address the use of human subjects in the study (Part III of the protocol). In this section of your protocol, you should:
 - (a) Provide a detailed description of the characteristics of the proposed human subject population, including their anticipated number, their age range, and their health status. Explain the rationale for the involvement or exclusion of special classes of subjects, such as fetuses, pregnant women, children, prisoners, institutionalized individuals, or others who are likely to be vulnerable.
 - (b) Identify the sources of research material in the form of specimens, records, or data.
 - (c) Describe consent procedures, including how, where, and by whom consent will be obtained.
 - (d) Describe potential risks to the subject (physical, psychological, social, economic, legal, or other) and assess their likelihood and seriousness. Where appropriate, describe alternative treatments and procedures that might be advantageous to the subjects. If other methods of research present lesser risk, describe those that were considered and why they were not used.
 - (e) Describe the procedures for protecting against or minimizing potential risks, including risks to confidentiality. Also, where appropriate, discuss provisions for ensuring medical intervention in the event of adverse effects to the subjects.
 - (f) Reiterate, or refer to, the data and safety monitoring plan outlines in Part II, the description of the study.
 - (g) Explain the procedures that will be implemented to protect subject confidentiality.
 - (h) Discuss why the risks to the subject are reasonable in relation to the anticipated benefits to subjects and in relation to the importance of any knowledge that will result.
 - (i) Provide, as the investigator, an explanation of how you concluded that the risk-benefit ration was acceptable.

6. Prepare a proper consent form (Part IV of the protocol). Generally speaking, a consent form should be a statement addressed to the subject that gives him or her reasonable information about the study and its procedures, risks, benefits, and alternatives. The form should be worded in the second person, and should be written in language that the subject can easily understand. A sample consent form is available on the HIC website, at <http://info.med.yale.edu/hic/guidelines/index.html>. By law, all consent forms, however, must:
 - (a) Clearly invite the subject to participate in the study.
 - (b) Express the purpose of the study in lay terms, making it clear that the study is research.
 - (c) Inform the subject as to why he or she has been selected to participate.
 - (d) Inform the subject as to exactly what his or her participation will involve (e.g., frequency of hospitalizations, number of visits to the investigator, types of medication, types of tests, amount of blood to be withdrawn, etc.).
 - (e) Describe all reasonably foreseeable risks, discomforts, or inconveniences to the subject..

- (f) Explain the net financial consequences to the subject of participation in the study.
 - (g) Identify the subject's alternatives to participation in the protocol, and offer a brief discussion of the advantages and disadvantages to participation.
 - (h) State any steps taken to protect the subject's confidentiality as well as any limits on confidentiality (e.g., inspection of medical records by the HIC, the FDA, or the industrial sponsor).
 - (i) Describe whether any compensation or medical treatment exists if injury occurs.
 - (j) State that the subject's enrollment in the study should be voluntary, and that the subject may choose to withdraw at any time.
 - (k) Allow prospective subjects the opportunity to ask questions before making a decision about participation.
 - (l) Provide space for the subject's signature (or his authorized decision-maker) and space for the signature of the person who obtains the consent.
 - (m) Provide the name and telephone number of a person that the subject can contact if questions arise or the subject believes he or she has sustained a research-related injury.
7. Identify and consult with a primary reviewer. A primary reviewer is a member of the HIC who serves as an advisor throughout the preparation of the protocol. Any HIC member, other than a co-investigator, can serve as the primary reviewer, but it is to your advantage to select a reviewer whose field of expertise allows him or her to fully understand your research. If you have difficulty finding an appropriate reviewer, the HIC will help you locate one. The reviewer will help you determine, in advance, the kinds of issues the HIC is likely to raise regarding the protocol and consent form so that you can address those issues before submitting your protocol.
8. Complete the face sheet of the protocol (Part I), obtaining necessary signatures and additional approvals, if necessary. After the protocol is completed, but before it is submitted to the HIC for review, the reviewer and the chairperson of all departments involved in the research must sign the face sheet of the protocol. If your protocol involves the use of human biological materials, radioisotopes, recombinant DNA or gene transfers, the use of funds by the Department of Psychiatry, the use of Cancer Center personnel, or the use of a clinical research center, you must obtain additional approvals before the HIC will allow you to commence research activities. If your protocol is supported in whole or in part by grant funds, you must submit a copy of your grant application with the other materials submitted.
9. Duplicate the protocol, and deliver it to the HIC. Once the protocol is complete, and all necessary signatures have been obtained on the face sheet, deliver the original plus two copies to the HIC Office in time to meet applicable deadlines.
10. Await action by the HIC. The HIC assigns all submitted protocols to a secondary reviewer, who like the primary reviewer, has the responsibility of carefully studying the protocol and introducing its discussion at the HIC meeting. Copies of the protocol are sent to all members of the HIC to review before the meeting. At the HIC meeting the committee may take any of the following actions on a protocol:
- Approve the protocol as submitted
 - Approve the protocol subject to minor modification
 - Defer the decision pending substantive changes to the protocol and its resubmission to the entire committee
 - Disapprove the protocol.

You will receive notice of the committee's decision in writing promptly after the meeting.

Additional Procedures for Studies Involving HIV Antibody Testing

If your study utilizes HIV antibody testing to determine subject eligibility for participation, you must add the following to your protocol:

- (1) A satisfactory explanation as to why such testing is necessary.
- (2) A satisfactory statement as to which prospective subjects will be tested.
- (3) A description of all plans to safeguard confidentiality.
- (4) A statement that no results will be recorded in any identifiable records intended to be seen by persons other than investigators and those persons duly authorized by Yale-New Haven Hospital to read medical records.

You also must provide either a separate consent form for HIV antibody testing, or incorporate information about HIV antibody testing into a general consent form. The consent form should:

- (1) Inform subjects of items 1-3, above.
- (2) State that subjects will be informed of the results of the test, that counseling will be offered to those having positive results at the time they receive their results, that results will be given only orally in a face-to-face discussion with an investigator (not by telephone or mail), and (for those having medical records) that the results will be entered in the medical record. Prospective subjects should be advised that if they do not want to know the results of their test, they should refuse to be in the study.
- (3) State the social risks of having a positive HIV antibody test. This explanation should include at least a statement of potential limitations in one's employability, insurability, freedom to travel to some other countries, etc.

Note: Any of the preceding provisions may be waived by the HIC at the request of the investigators, but only based upon the HIC's decision that there is good cause to do so.