

The Intelligent Scholar's Guide to the Use of Human Subjects in Research

Since its inception, the Standing Committee on the Use of Human Subjects has tried to keep its procedures simple and unbureaucratic. An unanticipated result has been to persuade some of you that its workings are inscrutable and hence potentially threatening. This brief manual (which does not pretend to be exhaustive) is an attempt to allay such apprehensions. We want to be, and to appear to be, both scrupulous *and* scrutable.

When does the Committee meet and who are its members?

The CUHS is a Standing Committee of the Faculty of Arts and Sciences, which also serves Harvard's other non-medical professional schools, the Radcliffe Institute, and the University Health Services. Membership includes faculty and administrative members from FAS and several other schools.

The Committee meets monthly during the academic year, on Thursdays at 4:10 p.m. Our meetings are not “open” in the sense that anyone can drop in any time, because there are some aspects of some projects that have a legitimate claim to confidentiality.

Committee staff members:

Jane Calhoun, Senior Research Officer, (jcalhoun@fas), 495-5459

Elizabeth Bowie, Research Officer, (ebowie@fas), 496-6087

Rachel Krebs, Research Officer, (rkrebs@fas), 496-1185

Emiko Saito, Research Officer, (esaito@fas), 496-2618;

Betsy Draper, Protocol Coordinator, (bdraper@fas), 496-3137

Committee Offices are at 50 Church St. Fifth Floor; phone 496-CUHS, fax 496-7400, email cuhs@fas.

What is the application procedure?

Applications to be considered at scheduled meetings are circulated to members for study in advance and we ask you, therefore, to email your application to cuhs@fas.harvard.edu or to deliver your request for approval to the Committee Office, 50 Church St. Fifth Floor, according to the schedule posted on the web site at <http://cuhs.harvard.edu/#schedule>. In addition to the application form, you should include copies of the proposed recruiting letter or advertisement, the consent form and/or written instructions to subjects (if any), and any questionnaires, interview outlines, or reproducible test instruments.

Some research is exempt from prior review or may be approved by “expedited review” (i.e., review by Committee staff). If your project appears to offer no risk of harm to the subjects, we urge that you discuss it with a Committee Officer; it may be that no formal application for approval is necessary, or that approval can be granted before the next scheduled meeting of the Committee.

It is also very helpful to talk with a Committee Officer before you submit your application if your research procedures are complex and their effects on the subjects difficult to perceive, or if the subjects are minors, or patients, or if participation in your study will put subjects at risk.

Investigators applying for funding to support their research should know that granting agencies require that our Committee review and approve the subject procedures before any funds are disbursed, and some may require approval at the time the proposal is submitted. Thus if you hope to commence the use of human subjects in mid-January you must get your procedures for subject use reviewed at our December meeting, which means submitting your application to the Committee at the beginning of December. (Alas, no one has claimed that this whole process is designed to make research easier!) Because the timing gets complicated, the Committee is willing to issue a certification of “pending review” (in some cases) or even act ad hoc (in some others) when investigators get caught in a squeeze not of their own making. However, we cannot function if we have to do this often and you are likely to find us surly indeed if, simply for lack of alertness on your own part, you ask us to act out of season.

Research in a foreign country may require the approval of a government board or committee. You should find out whether this additional approval is necessary well in advance. The committee cannot approve research if foreign government clearance is lacking.

Finally, research carried out by students or staff is always done under the supervision of a member of the Faculty. Thus, our Committee insists that a faculty member approve such proposals before they come to us, and staff and students must anticipate the time needed to complete that step. If the proposed study is the basis for a doctoral dissertation and the department concerned uses prospectus committees, we prefer that the prospectus committee complete its work before the project comes to us.

What is the source and scope of the Committee's authority?

By vote of the President and Fellows on 22 September 2003, reprinted here as Appendix B, the Committee is “authorized to review and to approve or disapprove, or state conditions for, the conduct of any research involving a human subject or subjects, in accordance with the policies stated herein.” The wide discretion given the Committee (“any research. . .”) is intended to make clear its authority to intervene as necessary to protect research subjects.

What is the rationale for the system of independent Committee review?

At least three parties have legitimate interests in any research venture involving human subjects: the investigator who initiates it, the society that provides the conditions for it, and the subjects who participate in it. Ultimately, if the study is important, their interests do not conflict, but in the short range they can and often do. Sad experience has demonstrated that able and conscientious scholars sometimes fail to give proper weight to considerations that are salient to the interests of either the public or the subjects. To leave all the decisions solely in the hands of one of the parties involved is not wise. For this reason the Faculty of Arts and Sciences set up its committee review system early in

the sixties. Since then, for the same reason, most federal agencies have mandated similar review systems for grantees.

No one has illusions that the committee system—or any other set of institutionalized procedures—is a substitute for ethically alert scientists who are sensitive to the well-being of their subjects. That is the *sine qua non* of meaningful protection and no system relieves the investigator of the *primary* responsibility for securing subject's rights and welfare. The committees serve only to remind all concerned of the network of interdependence that exists and to interpose a disinterested judgment where necessary.

What does the Committee need to know about a proposed study?

In the application form we have tried to provide an outline that will elicit the information we need to make an intelligent judgment. It is important that you respond to each question, if only to say “not applicable,” and that the information be presented in this format. Please use the latest version of the application, available on our web site, <http://www.cuhs.harvard.edu> (We have tried to use copies of grant applications in order to spare you an extra step, but we quickly discovered that they were unmanageable—they told us both too much and too little.)

As you complete the application, consider that the members of the Committee come from a variety of disciplines, and some members are not academics at all. Vis-à-vis your specialty, most of us are laymen and need to be addressed in non-technical language if we are to understand what you are trying to convey. Like much of the public we are committed to the proposition that scientific research is valuable and important; but like most of the public (and most of the scientific community) we also believe that research should not be done at the expense of subjects who are unaware of or misled about how they are being used.

Our questions are aimed at finding out (1) whether there is anything about the study that is likely to harm the subject, either grossly or subtly; (2) if so, whether the risk of such harm is at the absolute minimum level consistent with pursuing the work; and (3) whether the benefits anticipated are sufficient to justify exposing the subject to any risk that may be involved. We believe the questions to be reasonable, and in most cases they elicit what we need to know; however, we still depend on you to volunteer other information (unique, perhaps, to your project) that a committee like ours should have if it is to act wisely.

Much of the mystery, and perhaps even resentment, that some feel about the Committee would dissipate, we believe, if investigators would look at their plans from the point of view of a wary subject, or a disinterested observer concerned about responsible research. Who are the subjects? How are they recruited? Is it through an institution that may have responsibilities toward them and should be consulted? Might they feel under undue pressure to volunteer? Do they understand, in advance, what participation entails? What will they actually do, and what is done to them, during the study? Is it conceivable that the experience might be injurious, painful, uncomfortable, needlessly boring, embarrassing, offensive, or otherwise stressful? Might there be long-term consequences? Could the subject be endangered or compromised if information collected leaked out?

The possible considerations are myriad, but not difficult to perceive in any particular case if one assumes the subject's perspective.

The need for consideration does not imply—nor does it excuse—timidity on the part of scholars or the institution. In many areas the advance of knowledge requires the use of human subjects, just as their humanity requires procedures for their protection. It is the responsibility of (first) the investigator and (second) the Committee to ensure that good research proceeds and that it proceeds without unnecessary risk to its subjects. If this is sometimes difficult it is rarely impossible, and the difficulty is insufficient reason to back off from work that should be done.

What about “informed consent?”

The belief that people should not exploit other people makes the concept of informed consent prominent in any consideration of subject protection. Based on widely shared ideas about human dignity, the need for voluntary, informed consent strikes most of us as self-evident, but its implementation quickly runs into practical difficulties. Many scientific studies involve considerations so technical in nature that the subject may find it difficult to weigh their implications. In such a case how can consent be truly “informed?” (Perhaps this is seen most clearly when the subject is also a patient in treatment and lacks the medical training that would be helpful in weighing the physician's advice). A second difficulty occurs when studies depend on the use of subjects who are naïve or are deliberately misled about the research. Fully informed consent is then inconsistent with obtaining the desired results. How is one to weigh the value of the putative findings against such an affront to the individual subject?

Tangential to the necessity of ensuring that subjects participate voluntarily and with full understanding is the problem of documenting their consent—a matter of considerable self-interest to investigators in today's climate. It is important to remember that the consent form is simply a written confirmation of the agreement between investigator and the subject concerning the content and terms of the proposed activity. Our Committee insists upon such documentation only when the study appears to involve some degree of risk (though we strongly advise written parental consent for *all* studies of infants or minors), and when written consent is required by regulation. Otherwise we are content with an oral exchange.

When written consent is indicated, the form the subject signs must include a brief, clear statement of exactly what is involved so that there can be no question later as to whether the individual was properly informed. (See Appendix A.) The form itself should be written in the second person (“You will be asked to complete the following tests...”) so that it accurately reflects the exchange between investigator and subject. The written consent form should make it clear, also, that the subject is free to withdraw from the study at any time and without prejudice. It must not include “exculpatory” language suggesting that the subject waives any rights—the right, for instance, to sue!

How can one weigh the “benefits” against the “risks?”

Always a problem, this becomes especially difficult when the potential benefits devolve on “science,” or the general public, whereas the risks fall on the individual subject.

Fortunately the research typically conducted outside the medical setting seldom poses risk of harm—though we hope it is of some benefit. But, unfortunately, that which *is* risky rarely promises immediate, obvious benefits. In actual practice our Committee shrinks from making judgments about the substantive merit of the projects it considers; whatever the field only some of us will be expert in it and, for the most part, we accept the implied judgment of the sponsoring faculty member that the work is worthwhile. Still, we are bound both legally and logically to make the calculus whenever the research holds the possibility of harm for its subjects: legally because Harvard's rules and those of most funding agencies impose the responsibility on us; logically because, unless the research promises discernible benefit, how can one justify asking subjects to suffer inconvenience, let alone the risk of significant damage?

Let us dwell on this a bit. It is rare for any scholar to confront the critical experiment: “Eureka! If x, then y, and the planet is saved!” Very rare. More commonly, knowledge grows organically and the ripe fruit appears only as the result of the cumulative effect of many efforts. Few investigators can assert, in conscience, that their work will produce a certain benefit, nor do we expect them to. All that is needed is reasonable evidence that the study proposed may add an iota to our knowledge in some area of demonstrable interest. In most cases the benefits (if modest) are apparent and the risk (if any) so minor that the Committee has little difficulty approving. As the seriousness of the risk increases, however, our concern for establishing the likelihood of significant benefit must increase also. We must satisfy ourselves that the knowledge sought is important to someone other than the investigator and that the study is well designed to elicit it. When necessary we seek advice beyond our own membership, among specialists in the area with no vested interest in the particular project. (In the analogous case of studies involving special subject populations that the Committee is not well constituted to represent, we do likewise.) Armed with such advice we consult our own consciences and decide.

A difficult problem is posed by studies that require subjects who are naïve or are purposely misled about the aims and procedures of the research. Although there may be little risk of lasting injury, the possibility of offending or upsetting subjects may be increased when deception is used. The Committee is reluctant to approve research involving deception that is likely to be significant to subjects unless the risks appear to be negligible, the potential findings are important, no other method available, and appropriate plans are in place to debrief subjects after their participation.

The hardest ethical question arises when an experienced investigator encounters an important problem that cannot be resolved except by using subjects who may be hurt in the process, who will themselves gain no benefit, and who cannot be fully informed and therefore freely consenting. Is anyone competent to decide for them that they will accept the risk?

* * * * *

So brief a guide can only scratch the surface and a multitude of questions that might be raised remain unanswered here. Please feel free to call the Research Officers or any member of the Committee about particular problems that may occur to you. The Research Officers' contact information is given at the beginning of this document and the extensions of other members can be found in the Directory or through Harvard Information.

Appendix A

SUGGESTIONS FOR CONSENT FORMS, INFORMATION SHEETS, and ORAL CONSENT SCRIPTS

The Committee on the Use of Human Subjects requires written evidence of informed consent whenever the research may involve a risk of harm to subjects; in addition, we ordinarily require written parental consent for studies of infants or minors. (Otherwise an oral exchange is sufficient. It should, however include the information that would be contained on a written form.) The following paragraphs suggest some language that may be appropriate for studies where written consent is indicated. *A sample consent form, completed for a psychology experiment, follows.*

There are two major parts to a written consent form, the description section and the signatures and names.

1. Description

Try to be succinct. Begin with a description—in layman's language—of what participation will involve. The essential elements in the description are:

- a. A brief summary of the research objectives, e.g., "This research may help us learn more about how babies think at age 6 months and a year."
- b. A clear explanation of the procedures to be followed. Write as though you were speaking to your subjects, not as if they were speaking to you, i.e., use the second person singular voice: "You will be asked to come to our laboratory on three different occasions, for about half an hour each time, and fill out a questionnaire about" Remember, it is you who are the expert doing the explaining here! Also, be sure to take your subjects' age and reading and comprehension skills into account. In general, consent forms should be written at the eighth grade level or below. (Most word processing programs include a utility for determining reading level.)
- c. A description of any possible discomforts or risks that may exist. Explain how confidentiality will be assured if that is a potential problem. Explain what will happen to data collected, including any video or audio recordings, once the study is completed.
- d. A description of benefits that the subject may receive.
- e. A description of any payment, credit, or other compensation the subject will receive for participation.

2. Signatures and names (for consent forms only)

In this section, you may write as though you and your subject were each speaking for yourselves, i.e., in the first person singular, "I".

- a. In addition to what is written on the form you should discuss the procedures with each subject and be in a position to add the following countersignature:

I have discussed with _____ the above procedures, explicitly pointing out potential risks or discomforts. I have asked whether any questions remain and have answered these questions to the best of my ability.

(date) (investigator's signature)

b. Subject's signature:

The nature and purpose of this research have been satisfactorily explained to me and I agree to become a participant in the study as described above. I understand that I am free to discontinue participation at any time if I so choose, and that the investigator will gladly answer any questions that arise during the course of the research.

(date) (subject's signature) (print name)

c. The investigator's name and contact information, and the name of any assistant(s) who may be actually working with the subjects, should be included on the form. Both the investigator and the subject should keep a copy of the signed form.

3. If not using the template displayed in the attached example, we suggest that you add this paragraph at the bottom of the form:

Whom to contact about your rights in this research, for questions, concerns, suggestions, or complaints that are not being addressed by the researcher, or research-related harm: Jane Calhoun, Harvard University Committee on the Use of Human Subjects in Research, 50 Church St., Room 533, Cambridge, MA 02138. Phone: 617-495-5459. E-mail: jcalhoun@fas.harvard.edu

4. Under Federal regulations, when the Committee has ruled that there is risk of physical harm to subjects, the following statement shall be included on the consent form:

If you are injured during the course of the study and as a direct result of this study, you should contact the investigator at the number provided. Although compensation is not available, Harvard will assist you in obtaining medical treatment, including first aid, emergency treatment, and follow-up care as needed. Your insurance carrier should be billed for the cost of such treatment. If your insurance carrier denies coverage, Harvard is under no obligation to pay for the treatment but may do so in its sole discretion. By providing financial or other assistance, neither Harvard nor the researchers are stating that they are legally responsible for the injury.

Further information regarding compensation for injured research subjects may be obtained from Jane Calhoun, Research Officer for the Committee at the above number.

5. Finally, here are things to avoid:

- a. The consent form should not be deceptive in any way. There may be legitimate reasons for withholding information from subjects until the debriefing session, but the consent form itself must neither deceive nor mislead subjects.
- b. The letterhead should not imply that the consent form is a Harvard University consent form, nor that the study is sponsored by Harvard University. (See Item 14 of "The Vote.") Department letterhead may be used with permission, but in that case the "consent form" heading should be clearly separate.
- c. The form should not include any "exculpatory" language, i.e., anything that suggests that the subjects waive their rights by signing.

1/13/09

Sample Consent Form (3/6/09 version)

Please consider this information carefully before deciding whether to participate in this research.

Purpose of the research:

To examine how performing multiple tasks affects performance.

What you will do in this research:

You will view a moving object on a computer display and you will do your best to track that object using either a mouse or a joystick. You will also respond by pressing a button whenever another event occurs on the computer display. While you are performing this task, you will be asked to also perform a second task such as counting backwards or repeating words that are read to you.

Time required:

Participation will take approximately 60 minutes to complete.

Risks:

There are no anticipated risks associated with participating in this study. The effects of participating should be comparable to those you would experience from viewing a computer monitor for 60 minutes and using a mouse or keyboard.

Benefits:

At the end of the study, we will provide a thorough explanation of the study and of our hypotheses. We will describe the potential implications of the results of the study both if our hypotheses are supported and if they are disconfirmed. If you wish, you can send an email message to [investigator's name (email address)] and we will send you a copy of any manuscripts based on the research (or summaries of our results).

Compensation:

You will receive \$10 for participating in this study.

Confidentiality:

Your participation in this study will remain confidential, *[if relevant, and an accurate description of what you are going to do]* and your identity will not be stored with your data. Your responses will be assigned a code number, and the list connecting your name with this number will be kept in a locked room and will be destroyed once all the data have been collected and analyzed.

Participation and withdrawal:

Your participation in this study is completely voluntary, and you may withdraw at any time without penalty. You will receive payment based on the proportion of the study you completed. You may withdraw by informing the researcher that you no longer wish to participate (no questions will be asked).

Contact:

If you have questions about this research, please contact [investigator's name, title, address, phone number, and email address]. You may also contact the faculty member supervising this work: [adviser's name, title, address, phone number, and email address]

Whom to contact about your rights in this research, for questions, concerns, suggestions, or complaints that are not being addressed by the researcher, or research-related harm:

Jane Calhoun, Harvard University Committee on the Use of Human Subjects in Research, 50 Church St. Room 533, Cambridge, MA 02138. Phone: 617-495-5459. E-mail: jcalhoun@fas.harvard.edu

Agreement:

The nature and purpose of this research have been sufficiently explained and I agree to participate in this study. I understand that I am free to withdraw at any time without incurring any penalty.

Signature: _____ Date: _____

Name (print): _____

Appendix B

HARVARD UNIVERSITY

STATEMENT OF POLICIES AND PROCEDURES

GOVERNING THE USE OF HUMAN SUBJECTS IN RESEARCH

As voted by the President and Fellows of Harvard College, September 22, 2003

Harvard University is guided by the ethical principles regarding research involving human subjects set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (*Ethical Principles and Guidelines for the Protection of Human Subjects of Research* [the “Belmont Report”]). The minimum standard is set by the Department of Health and Human Services regulations at 45 CFR 46 (the “Common Rule”). Harvard University has additional provisions beyond that standard, which help to establish the highest expectations for performance and oversight by investigators, Institutional Review Boards (IRBs), and the University. The following policies and procedures outline these expectations.

Policies

1. Research that exposes human subjects to the unreasonable risk of harm shall not be conducted.
2. Subjects must not be exposed to any risk that can practicably be avoided without impairing the research design.
3. Individuals who propose to conduct research involving human subjects must be qualified by experience and/or training to safeguard the well-being of the subjects of their research.
4. Investigators under whose aegis research is to be conducted have primary responsibility for determining whether subjects might be exposed to a risk of harm. In making this determination, investigators shall seek advice from the appropriate IRB. Principal investigators also have primary responsibility for protecting subjects from being harmed by their participation in a study. All others involved in the study share this responsibility.
5. Each IRB shall be authorized to review and to approve or disapprove, and to state conditions for, the conduct of any research involving a human subject or subjects, in accordance with the policies outlined herein. In addition to membership requirements stipulated by federal laws and regulations, the membership of each IRB shall be chosen with a view to its ability to represent credibly the varying perspectives of subjects, investigators, and society at large. In appropriate circumstances, the IRB shall solicit advice from others who are especially qualified to represent the views of a particular subject population. IRB members shall not participate in the approval of projects in which they are involved or have a conflicting interest.
6. Although the typical issues dealt with by IRBs that oversee human subject research in different Faculties differ greatly, the Chairs of the IRBs shall confer as needed to assure that similar issues are treated similarly across the University.
7. Investigators shall explain to subjects, prior to their participation, the objectives of the research, the procedures to be followed, and the potential risks and benefits. Investigators shall not use individuals as subjects unless satisfied that they, or others legally responsible for their well-being, consent to participation freely and with understanding of the consequences. Ordinarily, investigators shall also obtain the assent of subjects who are not legally capable of consenting to participation. The IRB may waive some or all of these requirements only when persuaded that the research could not practicably be conducted otherwise, that the potential value of the research outweighs the indignity to the subject, and that the subject risks no other harm in participating. If

appropriate, the IRB may also stipulate that additional information about the study will be provided to subjects after their participation.

8. Investigators shall respect the privacy of subjects. They shall protect confidential information given them, advising subjects in advance of any limits upon their ability to ensure that the information will remain confidential.
9. Subjects shall not be induced to participate by means or in circumstances that might affect their ability to decide freely.
10. Investigators shall address the equitable selection of subjects, taking into account the purposes of the research, the setting in which the research will be conducted, and any special vulnerabilities of the subject population.
11. It shall be made clear to subjects that they are free to withdraw from active participation in the research at any time and without prejudice to their legitimate interests. Subjects who indicate a desire to withdraw shall be allowed to do so promptly.
12. An investigator shall disclose to a subject, upon request, the source of support for the research.
13. Instructors who assign or supervise research projects and exercises conducted by students are responsible for ensuring that the student is qualified to safeguard adequately the well-being of the subjects.
14. Investigators may indicate their position at Harvard, but shall not represent that the research is sponsored by the University or a department within the University except by explicit arrangement with appropriate administrative authorities.

Procedures

- A. An investigator proposing to conduct, direct, or supervise research involving human subjects shall make certain that the research is consistent with the policies and procedures stated herein, and that the appropriate IRB has been informed of existing knowledge of any risks involved.
- B. Regardless of funding source, all investigations that meet the definition of research involving human subjects as specified in the Common Rule shall be reviewed according to the standards therein, as well as any other applicable laws or regulations.
- C. Whether or not the Common Rule mandates review, proposed research involving human subjects must be submitted to the IRB for review and approval, or determination of exemption, if the research presents more than minimal risk to subjects or if the research involves any of the following:
 1. Procedures that might harm the subjects physically;
 2. Procedures that deprive the subjects of necessary, or accustomed, resources;
 3. Hypnosis or unusual degrees of mental stress;
 4. The use of subjects who are not able to give free and informed consent, including minors, prisoners, and individuals of diminished mental capacity;
 5. Explicit or implicit deception of the subjects in any aspect likely to be significant to them;
 6. The use of subjects who are available because they need the investigator's professional services;
 7. Activities that may be illegal, or are likely to offend prevailing standards of morality.

- D. Each IRB shall develop guidelines for investigations involving human subjects that do not meet the definition of research as specified in the Common Rule or the conditions elaborated in part C of these Procedures. The guidelines should provide procedures to be employed for the review and approval of such studies. Investigations in this category might include, for example, those designed to train individuals in research techniques, such as student exercises assigned during the course of classroom instruction or other pedagogical programs.
- E. Investigators shall submit their plans for using human subjects to the appropriate IRB in the form, and according to the timetable, established by that IRB to ensure orderly handling of its business. IRB approval is ordinarily limited to the specific research plan submitted to the IRB. Approval shall be for a definite period of time up to one year. A new application must be approved for research continuing for more than a year. Extensions of the specified time that subjects participate, and changes in plan that subjects might consider significant, require further IRB approval.
- F. If investigators detect an adverse change in the health or behavior of a subject that may be attributable to a study, or if they identify new risks that may result from subject participation in that study, they shall exercise judgment as to whether to suspend the study immediately. In any event, they shall immediately report the incident to the IRB. Regardless of the investigators' decision about whether to suspend the study, the IRB independently shall determine whether suspension of the study is in order, and, if so, under what conditions it may be resumed. Study participants must be informed of any findings developed during the course of the research that may relate to their willingness to continue participation.
- G. This Statement of Policies and Procedures shall be distributed annually to all faculty and administrative officers who might bear responsibility for studies involving human subjects. They, in turn, shall take appropriate steps to assure that their students and staff associates are aware of its contents.