

Guide for Investigators



**Yale University
Human Subjects Committee**

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INTRODUCTION

Any research conducted by a Yale affiliated researcher which involves the use of *human subjects** must be reviewed by one of the four Yale institutional review boards (IRB). The IRBs were instituted to assure that all research involving *human subjects* is performed in an ethical manner. The IRBs have the authority to approve, recommend changes, disapprove, suspend or terminate research studies involving *human subjects* occurring under the auspices of Yale University. Review is required whether the study is conducted at Yale or at another location and whether or not federal funds are involved. Furthermore, Yale policy requires review of those studies which the investigator believes to be exempt under the federal regulations.

The four IRBs at Yale are (1) Human Investigation Committee I and II (HIC) which serve the School of Medicine, (2) the School of Nursing Human Subjects Research Review Committee which reviews protocols involving the School of Nursing, and (3) the Human Subjects Committee which serves the Faculty of Arts and Sciences. This document reflects the practices of the Human Subjects Committee which reviews protocols prepared by faculty, staff, and students affiliated with the Faculty of Arts and Sciences (FAS), School of Management, School of Forestry & Environmental Studies, School of Law, Divinity School, School of Architecture, School of Art, School of Drama, and School of Music. This Committee also reviews research which involves participants affiliated with these schools.

Federal policy requires that the IRB consist of at least five members with varying backgrounds to promote the complete and adequate review of research activities commonly conducted by that IRB's applicants. The members must be competent to assess the research in relation to applicable laws, institutional policies and standards of professional conduct. In addition, if the IRB regularly reviews research involving vulnerable categories of subjects, the IRB must also include a member who is knowledgeable in working with this subject group. To meet these requirements, the Human Subjects Committee is comprised of members from the major departments who apply to it as well as a member of the legal community, a member of the university administration, and a member who is not affiliated with Yale, such as a representative of a local school. The varied backgrounds of the committee members allow the research to be broadly assessed for the potential *risks* and benefits of the study.

The criteria for review and approval by the Human Subjects Committee are based on the federal regulations at 45 CFR 46. These regulations describe the requirements for working with *human subjects* in projects which are funded by the federal government. Yale policy requires that the Human Subjects Committee apply the federal regulations to all research occurring under its purview, regardless of the funding source. These guidelines are intended to clarify the federal regulations and University policy so that investigators will understand the requirements of the committee for approval. Furthermore, these guidelines, in conjunction with the attached application forms, describe the information needed for submission of a protocol to the committee.

* Please note that those italicized words indicate terms which are defined in the definitions section at the back of this document. The defined terms are italicized to highlight the fact that some of these terms, which may seem standard, in fact have specific legal meaning as dictated by the federal regulations.

APPLICATION PROCEDURES

Submission Requirements

The application to the Committee consists of a face page, description of the study and the subjects, and attachments including at least the following: (1) A complete set of proposed procedures and measures; (2) proposed informed consent procedure (including any proposed consent form and, if applicable, HIPAA authorization form); (3) a complete copy of any relevant grant application, if it has not yet been submitted to the agency via Grant and Contract Administration (copies of grant applications which have already been submitted will be made available to the Committee for review by Grant and Contract Administration); (4) any advertising intended to be seen or heard by potential subjects (5) documentation of training in the ethical conduct of research involving human subjects (see [Appendix C](#) or the Human Subjects Committee homepage at “www.yale.edu/hsc”). The checklist outlines the basic information which is needed for the Committee to review the protocol. This list is meant as a summary of the information contained here and is provided to remind the investigator of the most common items needed for a complete application. The information in the application should follow the instructions in the section "Elements of the Protocol," keeping in mind the review criteria as outlined in the section "Key Elements in Review."

Who May Submit A Protocol

Ethical standards require that studies be performed by scientifically qualified persons. To comply with this principle, Yale requires all projects involving *human subjects* be performed by or under the supervision of a faculty member or senior researcher. Studies performed by students, postdoctoral fellows and postdoctoral associates must be cosigned by the faculty member who will oversee the project. By signing the cover page, the faculty member takes responsibility for the project, including monitoring progress of the study to ensure that appropriate measures are taken to comply with HSC policy.

Time Constraints Of Review

The Human Subjects Committee generally meets once a month during the academic year and as needed during recess periods. Fifteen copies of the complete application must be submitted to the Human Subjects Committee, 155 Whitney Avenue, Room 210 at least 7 days prior to the Committee meeting. Applications should be submitted as early as possible before the anticipated start of a project. Since no project may begin prior to receiving full approval by the Committee, and since revisions to the protocol may be necessary, it is suggested that the application be submitted at least 2 months prior to the desired start date. For protocols related to grant applications, note that grant applications may be submitted to federal agencies prior to receiving *human subjects* approval.

ELEMENTS OF THE PROTOCOL

Project Description

Purpose, Background, and Significance: The purpose of the study should outline what questions the study hopes to answer. A clear statement of the goals of the research is necessary to evaluate the appropriateness of the proposed measures in achieving these purposes. The background information presented will be used to assess the significance of the study in relation

to any *risks* to the subject. In as concise a manner as possible, the background information provided should indicate the need for the study and what questions will be answered in relation to prior studies. The background need not include references to pertinent literature, but if it does, these references should include the complete citation for Committee reference.

Procedures: A full description of the procedures will allow the Committee to assess the potential *risks* to the subjects. Any written measures should be attached to the protocol in the form that they will be presented to the subject. This section should provide the investigator's assessment of potential *risks*, no matter how remote these *risks* may be. The description of each *risk* should include a description of how the *risk* has been minimized and what steps will be taken should adverse events arise as a result of the described *risk*.

Possible *risks* to the subject include physical, legal, social, psychological, and financial *risk*. In identifying the possible *risks* it can be helpful to reflect on both the procedures to be used and the data to be collected. Typical questions which the Committee asks related to *risks* are as follows:

- What aspects of the project might induce stress, either physical or emotional?
- Are there individuals who are more likely than others to experience the stress?
- What problems could arise for the subject should the data collected in the study be linked to the subject and made public?
- Could such a breach of confidentiality lead to social, emotional, legal or financial risk?
- How will the data be protected during the course of the study? Will paper records be under lock and key? Will computerized records be password protected or encrypted? Will a laptop used to store data be secured while at a research site?
- What steps will be taken if a subject shows signs of stress or other danger to him/herself or others?

Thoughtful and complete responses to questions such as these indicate to the Committee that the investigator has fully considered the study from the subject's point of view and made a best effort to reduce possible harm to the subject.

In a similar manner, any potential benefits to the subjects should be described in this section as well. Please note that compensation for participants' time is not considered a benefit of the research. Lastly, if in the opinion of the researcher the study may be exempt, a justification for the exemption may be presented. (See Studies Which May Be Exempt Under 45 CFR 46.)

In studies which pose more than minimal risk, as determined by the HSC, the investigator will be asked to submit a study specific conflict of interest disclosure to the HSC. The investigator is asked to provide details only on those financial relationships which could be affected by the proposed research study. If such conflicting interests exist, the HSC will determine the appropriate strategy to manage the conflict such as requiring disclosure in the consent form or increased safety monitoring. This disclosure is in addition to the annual disclosure required by the Conflict of Interest Committee.

Subject Population

Recruitment and Access: A complete description of the subject population which is to be recruited for the study should be provided and includes:

- the characteristics of the population such as Yale students, bilingual *children* ages X, couples married for more than 20 years, etc.
- how the subjects will be recruited such as advertisements in newspapers, posters on campus, acquisition of public records, etc.
- the number of subjects anticipated to be enrolled
- what compensation including gifts, cash or services, if any, will be provided.

Subject compensation is allowable when it serves to compensate participants for their time and effort. As such, any compensation to the subjects should not be so large as to appear coercive or be the focal point of any advertisement. Note also that “sweepstakes” systems, whereby study participants are entered into a drawing to win a prize are subject to state law requirements which do not allow advertisement in any form, including word of mouth, of such a sweepstakes unless the drawing is open to anyone irrespective of their agreement to participate.

Certain groups of subjects require additional safeguards for their protection. Investigators planning studies involving *children*, prisoners, or *decisionally impaired* individuals should refer to the section on "Special Populations" for further information and/or contact the Committee. Participants who will be recruited based on health status may have additional recruiting requirements as described in the section on HIPAA requirements.

The requirements for the use of the Yale Department of Psychology *Subject Pool* are the same as for any other protocol, with the additional caveats that the pool contains Yale College students, some of whom may be under 18. To ensure adequate review of the voluntariness of participation by Yale Students, studies involving the Psychology Pool are not eligible for exemption. Waiver of parental permission must be approved by the Committee in accordance with the federal regulations. (See Section on Special Populations for details.) In most cases, waiver of parental consent can not be justified under the regulations and investigators should be prepared to either exclude minors from the study or to obtain parental consent. Note also, that the Psychology Department has established its own additional requirements relating to the use of the Pool. For further information regarding the departmental requirements, the investigator should contact the Psychology Pool Coordinator.

Use of Populations Not at Yale: Access to previously assembled groups requires the consent not only of the individual participants but also the consent of the organization which has assembled the prospective subjects. Examples of such groups include schools, hospitals, other universities, social clubs, and places of employment. Studies involving pre-assembled groups will not be approved until the relevant official has approved access. In the special case of other universities, many of whom will have their own IRB, approval from that institution's *human subjects* review committee will be required. If the outside organization will be involved in the design, conduct or analysis of the research, the organization is considered to be engaged in the research study and must have an Assurance on file with the Department of Health and Human Services. An *assurance* insures that the administration of the project by the cooperating organization will be in compliance with federal regulations. The HSC will determine if an Assurance is necessary and will assist in providing the appropriate documentation.

Research projects which take place outside the United States require compliance with both Yale policies and the relevant laws of the host country. Compliance with local laws is most easily dealt with by collaborating with a foreign institution which is familiar with the regional

issues. In most cases, a special research visa will be required by the host country. Of primary concern to the Committee when reviewing projects which are to occur internationally is the protection of the subjects from physical or social harm arising from their participation. Care must be taken to insure that the cultural caveats of the host country are respected and that the participants will not be subjected to retaliation from local authorities or the local community. If possible, the study should be reviewed by a local IRB or Ethics Board and their approval should be submitted with the protocol. It is not uncommon however, that local ethics boards do not exist or do not review social science research. In this case, the application should indicate what local reviews have been done to assure protection of the participants relative to their culture.

Informed Consent: Freely given consent is one of the most important tenets of research involving *human subjects*. The principle is based on respect for the potential subjects and their ability to make an informed decision. In order for a subject to give truly *informed consent*, they must be given sufficient information as to the nature of the study. The information is to be provided to the participants using language which will be comprehensible to them. Depending on the subject population, this may mean translation of the information into a language other than English as well as removing technical jargon from the information presented. Note also that a copy of the signed consent form is to be given to the subjects for future reference. The basic requirements of consent are listed below:

- A description of the study which states that this is a research project and which indicates the goal of the research. The procedures which will be used are to be described and the expected duration of participation must be stated.
- A description of any foreseeable *risks* to the subject.
- A description of any benefits to the subject or to others.
- A statement describing the extent of *confidentiality* of the subjects' responses and how that confidentiality will be maintained.
- If the study involves more than *minimal risk*, a description of any medical treatment available to the subject or where they may obtain further information. Note that Yale provides only emergency care for subjects injured. Additional medical care is not provided by Yale.
- Contact information for both the investigator and the Committee.
- A statement that participation is *voluntary* and that the subject may decline or withdraw from participating at any time without penalty or loss of benefits to which the subject is otherwise entitled. Likewise, if the study may involve future contact with the subject, the intent to contact the subjects in the future should be stated and the ability of subjects to decline/withdraw at that time should also be clearly indicated.
- If the Subject may be dismissed from the study by the investigator, the conditions for dismissal are to be described.

The presentation of a written consent form in itself does not satisfy the requirements for *informed consent*. The information presented should be reinforced by a verbal presentation and the subject should be given sufficient opportunity to ask questions to clarify his or her understanding of the study. The participants are to be given sufficient time to decide if they wish to participate based on the information presented. No statements are to be written in a way

which could be construed to waive any of the subject's legal rights, including their right to seek restitution in cases of negligence.

For consent to be freely given, it is also necessary that the subjects be free from any perception of coercion. Hence, the consent form must indicate that refusal to participate will not lead to loss of benefits. More subtle forms of coercion must be removed as well. Some obvious examples of coercive practices include inordinately high subject payments and solicitations by individuals who hold power over the potential subject such as their physician, treating clinician, or teacher. Special care must be exercised to protect a subject's right to refuse when a physician, teacher or therapist is the *principal investigator* on a research study. Another subtle form of coercion involves participants recruited in classrooms or other public settings. In this case, those who do not want to participate may be hesitant to decline since non-participation will single them out from the rest of the group. Providing alternate activities for those who wish to decline can help to minimize this concern.

Studies Involving Deception: A special note should be made regarding *informed consent* in studies which involve deception. Clearly deception is not consistent with fully *informed consent*. Yet there are instances in which deception is necessary for the proper conduct of a study. Under those circumstances the investigator must fully justify the need for deception to the committee. The Committee must make specific findings in approving a study which involves deception and, therefore, the waiver of one or more elements of consent. The investigator must describe how the deception will be disclosed to the participants following the study. Lastly, it is imperative that the consent itself avoid any of the deception and that the information provided to the subjects is as free of deception as is possible without compromising the study.

Waiver of Consent Documentation: In certain circumstances, it is permissible for documented consent to be waived. The most frequent waiver of documented consent is in studies involving anonymous surveys where the consent form is the only record of participants' names. In these cases, the return of the survey implies the consent of the subject. Note, however, that the lack of a signed consent form does not negate the need to inform the participants fully of the nature of the study. All the information which would otherwise be provided in the consent form is to be provided to the participants. Frequently, this information is presented as a cover letter attached to the survey instrument or as an information sheet.

KEY ELEMENTS IN REVIEW

The Committee must receive a copy of the full application with all necessary attachments at least one week prior to the meeting at which the protocol will be reviewed. In conducting their initial review of these materials, there are seven principal areas on which the protocols are evaluated by the Committee. Information provided to the Committee should be of sufficient detail for the Committee to make informed judgments regarding these items.

Minimization of Risk to Subjects

It is important that any *risk* to the participants be minimized. To do so, the study should use procedures which are consistent with sound research design and do not unnecessarily expose subjects to risk. Whenever possible, procedures which are already being performed on the subjects for diagnostic or treatment purposes should be used. Any possible *risks* to the subjects,

and the steps taken to minimize these *risks*, need to be clearly described. Often, investigators try to downplay any associated *risks*. It is far better, however, to define all foreseeable *risks* and to be prepared with procedures for handling adverse events.

Please keep in mind, that the *risks* associated with being a research subject in the types of studies which are reviewed by the Human Subjects Committee are frequently not physical *risks*. As defined by the federal regulations, research *risks* also include psychological, social or economic *risk*. For example, participating in a study surveying HIV status is unlikely to cause *risk* of physical harm. However, such participation does pose a significant risk of social and economic harm should the participation of a given individual become public knowledge. Thus the security of the data during the course of the study may be paramount. Appropriate steps should be taken to minimize access to paper and electronic data such as locking up paper and hardware and password protecting or encrypting files. In some cases, it may be necessary to keep electronic databases off of computer networks.

Risk/Benefit Analysis

Any *risks* to the subjects are balanced by the benefits of the research. The *risks* must be reasonable in relation to the anticipated benefits to the subjects themselves and to the importance of the knowledge to be gained by the study.

In assessing the *risks*, the Committee is concerned that the benefits outweigh the *risks* and that the study design minimizes the *risks* to the subjects. Although there is no defined criteria as to what is considered "significant" research, some studies can clearly be seen to be of questionable significance. For example, studies which involve a high degree of risk to the subjects yet are performed only to replicate a prior accepted study would be of questionable significance. It is in the investigator's best interest to clearly indicate both the benefits to society as a whole as well as any benefits to the subjects. This is the only area of review which attempts to evaluate the scientific basis of the study. Studies which are poorly designed and thus lead to unnecessary *risk* cannot ethically be approved by the Committee. Usually such studies can be modified to reduce the *risk* and gain Committee approval. Occasionally, the Committee and the investigator working together cannot find a way to reduce the *risks* to a level which is commensurate with the prospective benefits of the research and a study will be disapproved.

Equitable Subject Selection

The selection of subjects must be equitable. Historically, certain populations, particularly the poor, have been used extensively for *human subject* research. While these populations as a group bore the *risks* of research, they often were not rewarded with the benefits of that research. More recently, public criticism has arisen over the lack of inclusion of women, ethnic and racial minorities, and children. In this case, the criticism involves the applicability of research findings to populations not included in the study, thus potentially denying women and children the benefits of the research. To this end, the National Institutes of Health have begun requiring investigators to justify the lack of inclusion of women and children in research studies. Similarly, the Committee requires investigators to justify the use of subsets of the local population or the need to perform studies in third world countries. Generally speaking, the subject selection should be equitable, reflecting a reasonable cross-section of the relevant demographic group. In studies which require the use of a more restricted population, the rationale for this need should be fully disclosed.

Certain populations have been defined as particularly vulnerable. These include *children*, prisoners, pregnant women, decisionally impaired persons, and economically or educationally disadvantaged persons. Use of such populations requires additional oversight and is described in section "Special Populations."

Informed Consent

Subjects must voluntarily agree to participate in the research. The investigator is required to obtain the *informed consent* of the participant or his or her *legally authorized representative*. In the latter case, the participant is required to *assent* to participating as well. Except in special cases, this consent is to be documented, usually by the signing of a consent form, a copy of which is to be given to the participant. The consent form used in obtaining consent must be clearly marked with the Committee's most recent approval date and the approval expiration date. The issues surrounding *informed consent* are described in more detail in section "Subject Population." The key features which the Committee looks for regarding consent are that the subjects are fully informed and not deceived as to the nature and procedures of the study and that the subjects will not be penalized for refusal to participate. The Committee may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided that the study meets certain federally mandated criteria.

Subject Safety

The researcher must make adequate provisions for monitoring the data to insure the safety of the subjects. Many of the studies examined by the Human Subjects Committee, such as anonymous surveys, do not collect the types of information which require data monitoring. Studies using diagnostic tests, however, may necessitate frequent data monitoring. As an example, measures which could reveal that a subject is at risk of harming himself or others, need to have the data analyzed in a reasonable time frame so that intervention procedures may be implemented. A second area which necessitates action for the safety of the subjects is instances of child abuse. Investigators in Connecticut are ethically, and in some cases, legally obligated to report suspected instances of current child abuse to the Department of Social Services. Because of the difficulties involved in properly recognizing and verifying such abuse, the Committee recommends that only studies by faculty investigators or closely supervised by faculty investigators address these issues.

Studies involving clinical interventions may require a data safety monitoring plan be developed. Such plans involve defining who will be responsible for reviewing the data for participant safety and at what interval. The complexity of the plan reflects the nature of the research study. In most cases, it is sufficient for the principal investigator to review the data quarterly or at any time there is a serious adverse event to evaluate whether the study should be modified to reduce the likelihood of future adverse events. For studies involving higher levels of risks to the participants, a more detailed plan for analyzing and categorizing the adverse events would be necessary and the HSC will assist in the development of an appropriate data safety monitoring plan.

Subject Privacy and Confidentiality

The privacy of the subjects must also be assured. Whenever possible, the data should be collected *anonymously*, thus removing any risk of an invasion of privacy. When the study design

requires names to be collected, the study data should be considered confidential. Sensitive information can be protected by coding the data such that subjects' names are not easily linked to their responses and by storing the key separately from the data. Note that *anonymous* data cannot reasonably be linked to a given subject. Even if names are not collected, if any of the information collected would allow one to deduce the subject's identity, the method is no longer *anonymous* and thus still poses a risk if disclosed. Instead, the data is considered *confidential*. Also note that video and audio taping of subjects can allow identification of the subjects and appropriate measures should be taken to restrict access to the tapes, to store such material in a secure location, and/or for their destruction following the study.

In some cases, it is in the investigator's and participants' best interest to pursue a *Certificate of Confidentiality* from the DHHS. This document insures that the investigator cannot be legally compelled to disclose subject identities under 42 CFR 2a. *Certificates of Confidentiality* are usually sought in studies which require disclosure of illegal behaviors but may also be issued for studies involving other sensitive topics such as mental health issues, genetic testing or HIV status. Following approval of the project by the Committee, the Committee can assist in obtaining a *certificate of confidentiality*.

Protection for Vulnerable Subjects

When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, students, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects. (See Section on Special Populations for more details.)

OUTCOMES OF REVIEW

Following the Committee's review, a letter indicating the findings and actions of the Committee will be sent to the investigator. A study may be approved, require modification (either minor or substantive revisions), disapproved, or exempt. Each of these categories is described below. Note that the study may not commence without the full approval of the Committee.

Approved: A protocol which has been approved by the Committee requires no further action from the investigator prior to commencing the study. Approval is for a period of time appropriate to the degree of risk as determined by the Committee, but not longer than one year from the date of Committee approval. If the study will continue beyond the approval period, a renewal application prior to the approval expiration date is required. In the course of the study, the investigator will be required to notify the Committee if any changes to the protocol are necessary or if any adverse events occur. (See also Responsibilities of the Principal Investigator Following Approval of a Study.)

Specific Minor Revisions Required: Specific Minor Revisions Required may be granted to projects requiring only minor changes, such as corrections to the language in the consent form. A protocol which requires minor revisions may not commence until the conditions for approval have been met to the Committee's satisfaction and the investigator so notified in writing. The investigator should submit the appropriate response(s) to the Committee for expedited review. The response will be reviewed between regular Committee meetings. Usually a full approval will be forthcoming in one week or less. Occasionally, the investigator's

response will be of a nature that necessitates review by the full Committee, in which case the response will be evaluated at the next meeting. Studies which involve multiple sites are frequently classified as requiring minor revisions as documentation of approval from the participating sites must be submitted. In this case, the entire study will require specific minor revisions, but full approval will be granted for individual sites as their documentation is received.

Substantive Revisions Required: Protocols which require substantive revisions usually require extensive clarification or additional information to be submitted to the Committee prior to approval. The notification letter will indicate the concerns of the Committee. The revised application should be submitted to the Committee clarifying the issues involved or adding the desired documentation. Applications deferred at a previous meeting are subject to full committee review of the investigator's response.

Disapproval: A protocol which has been denied approval by the Committee shall not be initiated by the investigator. The reasons for the denial will be indicated in the notification letter. Disapproval, in contrast to Substantive Revisions Required, indicates that the Committee finds the *risks* to research participants outweigh any benefit to society and the protocol must be extensively modified to reduce the risk.

Exempt: A study determined to be exempt requires no further action from the investigator prior to commencing the study. Exempt protocols also do not require annual renewal. The notification of exempt status will indicate the section of the federal regulations defining the exemption (such as 45 CFR 46.101 (b)(2)). This designation should be noted on grant proposals requesting support for the research. Occasionally, the notification from the Committee will include a suggested alteration in protocol in order for it to be exempt. The investigator is to respond in writing, modifying the protocol for such and exemption to be granted. Note that changes to exempt protocols may affect their status as exempt. Changes should be discussed with the Committee to verify that the study will remain exempt.

RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR FOLLOWING APPROVAL OF A STUDY

Renewals

Federal guidelines require that projects be reviewed at intervals appropriate to the degree of risk, but not less than once per year. Thus, the Committee will determine whether more frequent review is warranted to ensure adequate protection of the rights and welfare of research subjects. The initial letter of approval that the investigator receives from the Committee will specify the required frequency for review and re-approval of the protocol. Renewal applications are reviewed along with new applications at the monthly Committee meetings and must be delivered to the Committee at least 4 weeks before the expiration date.

Renewal applications must be submitted on the Review Report and Request For Reapproval Form and must include a copy of the current consent form and a progress report. The renewal form requests information on: (i) the number of subjects who have participated so far; (ii) withdrawal of subjects from research or complaints about the research; (iii) the number of subjects anticipated to be used in the coming year; (iv) a discussion of any adverse events or unanticipated problems involving risks to subjects or others occurring in the past year and how they were dealt with; (v) a summary of any recent literature, findings obtained thus far, amendments or modifications to the research since the last review, and any other relevant information especially information about risks associated with the research; (vi) a description of

any proposed changes in the existing protocol. The Committee will notify the investigator of its findings and actions. (See Outcomes of Review.)

Studies which have not been renewed prior to the expiration date will automatically be terminated and all research involving human subjects must stop until the project is renewed by the HSC.

Changes in Existing Protocols

The Committee must be promptly notified of any proposed changes to an existing protocol. Such proposed changes may include alterations of the procedures to be used, size or composition of the subject pool, etc. When such a change is anticipated, the Committee is to be notified by letter from the investigator indicating the nature and the rationale of the proposed change. All correspondence with the Committee should include the protocol number. The proposed changes will be reviewed at the next Committee meeting. Proposed changes in approved research may not be initiated without the Committee's review and approval except when necessary to eliminate apparent immediate hazards to the subjects. The amendment can also be used to "renew" the protocol, provided that the information necessary for renewal is provided as well. This procedure may be especially useful since a new approval period will begin on the review date.

Problems Occurring During the Course of the Study

Any serious or unexpected *adverse event* which occurs in the process of conducting research involving *human subjects* must be reported to the Committee as well as the Sponsor (if applicable). *Adverse events* include harm to the subject occurring during the study as well as the identification of subjects who may be at risk of harm to themselves or others. This latter category is one of the more common types of *adverse event* seen by the committee. For example, use of the diagnostic Beck Depression Inventory in a non-anonymous fashion allows the identification of individuals who are at risk of harm to themselves. Once these individuals are identified, the usual course of action is to provide further referral information to the participant. A *serious adverse event* is defined as any event that suggests a significant hazard, contraindication, side effect, or precaution.

An *unexpected event* is any *adverse event* that is not identified in severity or specificity in the current application. The Committee is also to be notified of any complaints about the research. The Committee is to be notified within 5 working days via letter, phone, or e-mail in emergencies, by the investigator describing the *adverse or unexpected event* or complaint which has occurred and any corrective actions or interventions which are being taken. All correspondence with the Committee should include the protocol number. Since many studies promise *confidentiality* of the subjects, the investigator should include only the subject number in the notification to the Committee. The investigator and institution shall receive written notice of any action taken by the Committee and the reasons for that action within 5 working days.

The Committee should be informed of any allegations of non-compliance with human subject regulations and/or the provisions and requirements of this Guide. The Chair will direct the review of all such allegations, report actual non-compliance, as appropriate, to DHHS and other entities.

Study Audits

The Human Subjects Committee is charged not only with prior review of research but also with monitoring study compliance with applicable University policy and federal regulations. A study could be audited in the case of reports of noncompliance, high incidence of adverse events, or as part of the Committee's research monitoring program. Such audits may involve review of study documents to verify consistency between HSC records and investigator records, interviews with research personnel, and interviews with participants. Studies subject to audit under the routine research monitoring program are meant to not only confirm that the study is being conducted as approved but also to identify areas where the interaction or performance of the HSC can be improved.

Completion or Withdrawal of a Study

When a study is completed or withdrawn, the investigator must notify the Committee in writing. Include a brief summary of experience with the project and reasons for its completion, termination or withdrawal when a protocol is terminated. The investigator should provide an account of any existing continuing obligations to subjects.

FAILURE TO COMPLY

Individuals who conduct research involving human subjects which does not comply with University policies and procedures may be subject to disciplinary procedures. Non-compliance includes, but is not limited to, failure to obtain IRB approval for research involving human subjects, failure to obtain approval for changes to the study, inadequate supervision of the research project, failure to report adverse events, and failure to adhere to the approved study. Any alleged violation will be reviewed by the Committee and, if warranted, referred for further investigation in accordance with the University IRB Operations Manual. Serious or continued non-compliance in projects which are funded through external grants are reported to the funding agency. Willful violation may lead to sanctions up to and including termination or expulsion.

PROTOCOLS RELATED TO GRANT APPLICATIONS

Research that will be included in a grant application should be submitted to the Committee prior to or at the time of submission of the funding application. Given the possibility that the Committee will require changes before issuing full approval, it is recommended that the protocol be submitted to the Committee as early as possible. For grant proposals which have already been submitted, the Committee will notify the Grant and Contact Office which will inform the agency of the approval date. In order to insure that the agency is notified, it is imperative that the cover page indicate as much information as possible regarding pending grant applications. However, the Committee does not submit a record of its deliberations. It is the responsibility of the principal investigator to inform the funding agency of any substantive changes to the protocol which arises from IRB review. Frequently, issues which arise for the Committee are raised by the reviewers as well. Thus, failure to notify the agency of these changes to the study can lead to delay or rejection of a grant. Many agencies will not review a grant proposal without evidence of IRB approval. Other granting agencies may not award a grant or contract until such evidence is provided. Regardless of the agency's policies, since

work with *human subjects* may not take place without Committee approval, such awards will not be available for expenditure until the research is fully approved.

SPECIAL POPULATIONS

The federal regulations define certain groups as having compromised capacity to give *informed consent* or are particularly vulnerable to undue influence and thus require additional safeguards to insure their proper treatment as research subjects. The populations include pregnant women, fetuses, prisoners, *children* and decisionally impaired individuals. Only under specific circumstances can studies involving these populations be ruled exempt. As the use of pregnant women and fetuses is rarely an issue with the types of studies occurring under the purview of the Human Subjects Committee, the regulations pertaining to them will not be discussed here. Should an investigator wish to use these individuals, the Committee should be contacted for further information.

Decisionally Impaired Individuals

Investigators must be especially careful when dealing with individuals who are legally incompetent. Legally incompetent individuals can never give legally binding consent. Proper procedure requires that the consent be sought from the court appointed representative of such an individual; the individual participant will be asked to *assent*. Such individuals may be encountered in studies of the mentally disabled, elderly or *children*. Children are defined as a special population according to 45 CFR 46 and the specific rules applying to work with *children* will be dealt with in the following section. Although not all elderly and *decisionally impaired* individuals are legally incompetent, the investigator should be aware that some fraction of these individuals will be. In the case of institutionalized individuals, investigators are advised to seek the agreement of the administrative body of the institution not only to allow the research but also to accept responsibility for identification of individuals who are legally incompetent so that they may be excluded from the study, or so that the appropriate legal representative can be contacted. Therefore, investigators using these populations should carefully design their studies to insure that proper consent is obtained and should consult the Committee for advice.

Other individuals, although considered competent under the law, may show limited ability to comprehend the risks and benefits of the research, making their ability to provide informed consent questionable. It is the responsibility of the investigator to assess that the potential participant has in fact understood the information presented. In studies where many of the participants to be solicited are likely to have limited cognitive capabilities or who may lose this ability during the course of the study, it may be necessary to have an unaffiliated investigator assess capacity to consent or to involve a subject advocate who assists in explaining the research to the participant.

Children

Studies involving *children* are more strictly regulated than those involving adults. The regulations define four categories of risk and the commensurate level of required protections. Most studies reviewed by the HSC involve only minimal risk research, in which case the only added requirement is to obtain both the permission of the child's parent or guardian and the child's assent to participate.

For older children, assent can be obtained via a written consent form similar to that used for the parent. With younger children, *assent* is usually verbal. In either case, the pertinent information is to be presented to the child in age-appropriate language. The child is then asked if he or she wishes to participate. In order to assess whether the child is truly giving informed *assent*, the Committee requires a script of the information which will be presented to the child to gain his or her *assent*. Only in very limited circumstances may the parental permission or child's *assent* be waived. Waivers of parental permission require that the conditions for waiver of elements of informed consent be satisfied.

The choice of an appropriate mechanism for obtaining the children's assent would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

Note that additional requirements apply to studies involving more than minimal risk or involving children who are wards of the state. Should an investigator wish to include these individuals or are proposing a study which poses more than minimal risk, the Committee should be contacted for further information.

Prisoners

Incarceration, by its very nature, raises the specter of coercion, hindering assessment that participation is truly *voluntary*. Because of this difficulty, state and federal penal authorities maintain procedures for gaining access to prisoners. The approval of the appropriate penal official will be required in addition to that of the Yale Committee. Furthermore, the types of research which may involve prisoners are limited to studies examining issues specific to prisoners. These include studies of incarceration and criminal behavior. Other studies may be approved under special circumstances, and the Committee should be contacted for advice prior to formulation of a study plan.

It should be noted that the definition of prisoner under the regulation is broader than individuals currently incarcerated. So participants who are detained pending trial, serving a sentence outside of a penal facility, or in juvenile detention are considered prisoners under the regulations. The requirements for prisoner research are also triggered by individuals who become incarcerated after recruitment regardless of whether or not the study is targeted to prisoner issues.

Most of the special precautions required for work with prisoners merely require the investigator to be particularly diligent in conforming to the regulations described above for standard research subjects. Investigators wishing to use prisoner populations should consult the Committee for more detail. In general, special attention should be given to the following:

- The benefits to the participants must not be of such a magnitude relative to the standard conditions of inmates that the benefits become coercive.
- The *risks* involved are no greater than that which would be expected of a non-incarcerated participant.
- Selection of subjects and their placement into control or experimental groups is to be fair to all subjects and free from arbitrary intervention by prison authorities or other prisoners.
- The information provided to the prisoners is presented in language which is understandable by the prisoners.

- Provisions are to be made such that parole boards, or other authorities with the power to make release decisions, will not use the inmate's participation in studies as a factor in parole decisions. The prisoners are to be informed that participation will in no way effect their parole, continued incarceration or sentence.
- If the Committee finds there may be a need for follow-up care of subjects, provisions have been made for such care, taking into account the varying lengths of subject prisoner's sentences and informing participants of this fact.

Studies Involving Yale Students

Use of Yale students presents a special set of concerns which are applicable in any study which could potentially recruit Yale undergraduates. This includes not only pools specifically recruiting undergraduates, such Psychology Pool studies, but also studies which are advertised on campus. Undergraduates at Yale may be below the age of consent in Connecticut. As such, the special requirements for studies involving children apply to studies involving Yale Students. This limits the studies which can involve Yale students and means that parental consent is required unless explicitly waived by the Committee. One solution is to limit inclusion to individuals over the age of 18. Please note that studies involving the Psychology Pool cannot be exempted by the Committee. An additional concern in studies which involve Yale students is the possibility of coercion. Obviously, recruitment of a subject by his or her advisor holds the potential for coercion. This also holds true whenever a student's participation will be made known to someone who holds power over that student's academic status. These issues must be addressed in studies involving Yale students.

STUDIES WHICH MAY BE EXEMPT UNDER 45 CFR 46

Certain types of research are classified in 45 CFR 46 as exempt. The six categories of research which qualify for exemption are described briefly in this section. Since Yale policy requires the Committee to determine if a study qualifies for exemption, this listing is presented only to allow the investigator to tailor a study so that it may possibly be ruled exempt. For example, editing many survey instruments can lead to an anonymous measure which is of *minimal risk* (see 2 below).

1. **Educational Research:** Research conducted in accepted educational settings using normal educational practices are exempt. This category includes research on regular and special education instructional strategies or research comparing the effectiveness of instructional techniques, curricula and classroom management.
2. **Surveys, Interviews, and Public Observation:** Studies involving surveys, interviews and observation of public behavior are exempt as long as they are either anonymous or any disclosure of the subjects' responses would not induce risk of criminal or civil liability, damage to financial standing, employability or reputation. The issue of *anonymity* requires more than just not recording the subject's name on collected data. Individuals can be identified through other means. For example, collection of extensive demographic data can allow one to surmise the identity of a given subject. Obviously, the ability to do so becomes easier as sample sizes are reduced. Given the potential to identify subjects from extensive data, the Committee carefully reviews survey instruments before approving a survey as exempt.

3. **Elected Officials or Federally Protected Confidentiality:** Studies which use the techniques described in number 2 above which are not otherwise exempt, are considered exempt when the subjects are elected or appointed public officials or candidates for public office.
0. **Existing Data:** The use of previously collected data, documents, records and pathological specimens are exempt as long as the data are publicly available or the subjects cannot be identified either directly or through identifiers linked to the subject. This category includes the use of archival material as well as tissue banks. Note, however, that tissue collected by the Yale University Cancer Center and the Department of Pathology does not constitute pre-existing tissue. This tissue is not necessarily previously collected and may be linked to identifying information. The use of this service requires review by the Human Investigation Committee at the Medical School.
0. **Research and Demonstration Projects:** Studies conducted by or under the approval of federal departments which study public benefit or service programs such as studies involving the Social Security Administration, are exempt.
0. **Taste and Food Quality:** Evaluation of food products are exempt if the food is wholesome and any additives to the food are at a level deemed safe by the FDA, EPA, or USDA.

STUDIES INVOLVING INFORMATION PROTECTED UNDER HIPAA

Studies which require access to protected health information (PHI) or which occur in the School of Medicine, School of Nursing, and the Psychology Department Clinics are subject to the requirements of the Health Insurance Portability and Accountability Act (HIPAA). PHI includes any identifiable information, whether oral or recorded in any form, that relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present or future payment of health care to an individual. Below is a summary of some of the research requirements under HIPAA. For more information see the Yale [Policy On Use And Disclosure Of Protected Health Information For Research Purposes](#) or The Researchers' Guide to HIPAA, both available on the HIPAA web site www.yale.edu/hipaa.

The Privacy Rule applies to the following types of research activities when they involve PHI:

- Research using or creating PHI about living or deceased individuals
- Activities preparatory to research such as reviewing health information in order to develop the study protocol
- Recruitment based on health status

HIPAA requires either a patient/research subject *authorization* or a *waiver* of the authorization requirement for the use, disclosure or creation of identifiable health information for research. An *authorization* is not required for research using only "*de-identified*" data. If a researcher uses health information from which direct identifiers have been removed, then no authorization is required but the researcher must enter a *data use agreement* covered with the entity that holds the records.

The *Yale University Research Authorization Form* has been designed to incorporate standard language for the statements required in the authorization. Investigators need only specify on the form to whom and where PHI will be sent and what type of PHI will be disclosed. Authorization forms which are not based on the Yale template or which modify or remove language from the template are subject to review by the Privacy Office. Authorization forms are generally separate from the Informed Consent document and are signed at the same time. In some cases, the authorization form can be merged into the Informed Consent, thereby creating one document for the research subject to sign.

A waiver of authorization is permitted only when the following conditions exist:

- The research could not be practicably conducted without the waiver.
- The research could not be practicably conducted without access and use of PHI.
- A written assurance to the IRB that the PHI will not be re-used or disclosed except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of PHI would be permitted by the Privacy Rule.
- Uses and disclosures of PHI will be limited to the minimum necessary standard.
- Disclosure involves no more than minimal privacy risk to the individuals.
- Reviewed by the IRB with specific approval regarding access to the PHI.

Researchers can request a waiver of authorization by completing the Yale University Request for HIPAA Waiver of Authorization for Research Form and submitting to the IRB for approval.

Recruitment

HIPAA also applies to recruitment and research activities conducted via medical records and medical registry reviews. Investigators must obtain either authorization from the subject or a *waiver of HIPAA Authorization* approved by an IRB prior to commencing research recruitment activities from these sources. The *Waiver of HIPAA Authorization* for recruitment purposes only is referred to as a partial waiver. Researchers are required to obtain a subject's authorization after recruiting and enrolling subjects via a partial waiver and prior to creating or using PHI during research procedures.

De-identified Data

De-identified data are data that contains none of the 18 identifiers on page 3 of the HIPAA at Yale Researchers' Guide to HIPAA. If all of the identifiers are removed, the information is considered to be no longer individually identifiable, no longer PHI, and no longer subject to HIPAA's requirements. A de-identified data set may be coded with a unique identifier that cannot be traced back to the individual for the purpose of being re-identified by the recipient at a later date. De-identified data may include gender, age, race or relevant information regarding disease or tissue source and can later be re-identified, by the original holder of the data, if necessary by means of a unique, non identifiable code for purposes of carrying out research. It is important to remember that re-identification will subject the information to HIPAA's requirements. A resubmission of the protocol to the IRB for approval is required when re-identification of the data is desired. Note that de-identification is more stringent under HIPAA

than is usually considered for anonymous data. All of the 18 identifiers must be removed from the data for it to be de-identified.

Exempt Studies

Note that exemption from IRB review for studies which involve existing data does not also mean that the study is exempt from HIPAA requirements. Access to the existing PHI would still require a HIPAA authorization or waiver of authorization.

FREQUENT PROBLEMS

The following are some of the most frequently occurring problems seen by the Committee:

Anonymous vs. Confidential Information: Frequently, participants are promised *anonymity* in the consent document when the information is being held *confidentially*. Please keep in mind that if there is a key linking subjects names to their responses or if the data are such that one could potentially identify the participant, then the data are *confidential* not *anonymous*. Removing direct identifiers such as name or e-mail address in and of itself also does not necessarily ensure anonymity. If the data contains sufficient demographic information, it may still be possible to identify the individuals and thus be considered confidential.

Inadequate Protection of Subject Identity: Investigators should try to protect subject identity to the maximum extent in all studies. Frequently this can be accomplished by coding the data and whenever possible, destroying the code as soon as possible following data collection. Note that locking data keys in a student's room is not considered adequate. Special care should be taken with regard to the storage of video tapes and other sensitive information.

Inadequate or Unspecified Data Storage Plans: Many studies address protection of participants' identities during publication but neglect to address protection of the data during collection. It is critical that the data be secured throughout the project. For example, harm to the participant in an international study is more likely to arise from their peers or local government gaining access to the raw data while the researcher is in the field. Appropriate steps need to be taken to secure the data on site such as encrypting or password protecting electronic data and locking up notes in a safe location.

Study Descriptions on Consent Forms: Even though the written consent form is complemented by a verbal presentation, the consent form should give a reasonably complete description of the study. This description should include the purpose and procedures involved as well as the expected time required for participation.

Contact Information: The federal regulations require that the participants be informed of whom to contact for answers to questions about the research and research subjects' rights. Since subjects who are concerned about a study they are participating in may be hesitant to contact the investigator to complain, it is necessary that the consent form or other informational documents containing contact information list both the investigator and the Human Subjects Committee and that the subjects given a copy of these documents for future reference. Both the address and phone number of the Committee should be listed (155 Whitney Avenue, Suite 210, New Haven, CT 06520; 203-436-3650; e-mail: human.subjects@yale.edu).

Plans for Adverse Events: Investigators need to be prepared to act should an adverse event occur. Thus, the plans for identifying and responding to any such events should be fully described.

Agreement of Organizations Involved in the Study: Written documentation of the approval of any participating organizations will be required prior to full approval. However, since participating organizations frequently wish to see that Yale has approved the project; protocols which are otherwise acceptable will be approved on condition, pending agreement of the participating organization. This status is usually sufficient to assure the participating organization of the forthcoming approval of the protocol.

Lack of Editing of Written Measures: Often published questionnaires include collection of participants' names and/or identifying information. When such measures are to be used in an anonymous study, the appropriate editing should be done prior to submission of the protocol.

Potential for Disclosure of Illegal Activities: Open ended interviews and surveys can occasionally solicit the disclosure of illegal activities. To protect the investigator from subpoena, the committee recommends that participants be reminded not to disclose such information during the interview/survey. Studies which by their very nature involve such disclosure should ideally be anonymous. If anonymity is not an option, arrangements can be made for the investigator to obtain a *certificate of confidentiality*.

Alternate Activities for Students: One subtle form of coercion which is frequently a concern in classroom studies is the ability of the children to decline to participate without their classmates being aware. In paper and pencil measures, students who do not wish to participate or whose parents have not consented to their child's participation may be instructed to not complete the forms and instead draw/doodle on the paper. In studies which involve removing individuals from the group, the committee recommends providing an alternative activity for the non-participants such that they may not participate discretely.

Disclosure Language on Consent Forms: The language used to describe conditions under which the investigator may be compelled to disclose the subjects' responses is frequently inaccessible to participants. The following statement is recommended: "I have been assured that my personal information and answers will be disclosed only to the investigator and his or her collaborators and to those responsible for research oversight. However, the confidentiality of this information is not protected under the law in the same manner as communications with my doctor or lawyer may be. The investigator can be compelled by a court to disclose this information."

DEFINITIONS

Adverse Event: An undesirable and unintended, although not necessarily unexpected, result of participation in the Study.

Anonymous: Data which are collected in such a way that the subject cannot be identified either by the name or by the descriptive information collected about the subject (*cf.* Confidential).

Assent: Agreement by an individual not competent to give legally valid *informed consent* to participate in research. Such individuals include *children* and *decisionally impaired* persons.

Assurance: A formal written, binding commitment that is submitted to a federal agency in which an institution promises to comply with applicable regulations governing research with *human subjects* and stipulates the procedures through which compliance will be achieved.

Authorization: A specific type of permission given by the individual to use and/or disclose protected health information about the individual. The requirements of a valid authorization are defined in the HIPAA regulations. Yale recommends use of the research authorization form found on the HIPAA web site. Use of a modified form other than addition of required information requires review and approval by the privacy office.

Certificate of Confidentiality: Authorization granted by the Department of Health and Human Services to withhold the names and other identifying characteristics of individuals who are subjects of research from any person or authority not connected with the conduct of such research. When issued a Certificate of Confidentiality, the researcher may not be compelled in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings to identify the individuals.

Children: Persons who have not attained the legal age for consent to treatment or procedures involved in the research as determined under the applicable law of the jurisdiction in which the research will be conducted. In Connecticut, the age of consent to participate in research is 18, while the age of consent for medical treatment is 16.

Common Rule: The regulations at 45 CFR 46 were adopted by 17 federal agencies for protection of human subjects in studies under their purview. The regulations have subsequently been known as the Common Rule.

Confidential: Data which is collected in such a way that the subjects may be identified but which will not be disclosed by the investigator without the permission of the subject except in limited circumstances such as for research oversight purposes or as required by law. Confidentiality may be maintained by coding the data and establishing a key which links the subjects' names to their responses or by separating descriptive personal data from sensitive data (*cf.* Anonymous).

Data use agreement: An agreement between a covered entity (the holder of the PHI) and the recipient of the PHI (such as a research investigator) in which the covered entity discloses a limited data set for purposes of research, public health or healthcare operations. Data use agreements are required to restrict the use of the PHI in the limited data set to a specified purpose, to safeguard the PHI, and to assure that the individuals whose PHI is included in the limited data set will not be identified by the recipient.

Decisionally Impaired: Having either a psychiatric disorder or a developmental disorder that affects cognitive or emotional functions to the extent that capacity for judgment, reasoning and decisions is significantly diminished. Others, including persons under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interests.

De-identified: Data is considered de-identified if the health information does not identify an individual and with respect to which there is no reasonable basis to believe that the information can be used to identify an individual. Health information is considered de-identified (1) if stripped of all of the 18 direct identifiers defined under HIPAA, or (2) if an expert in statistical and scientific method determines that there is a very small risk that

- the information could be used alone or in combination with other information to identify an individual. HIPAA does not apply to de-identified data.
- DHHS Regulations: The federal policy for the protection of *human subjects* as implemented by the Department of Health and Human Services, published in the Code of Federal Regulations, 45 CFR 46.
- FAS: Faculty of Arts and Sciences, a division of Yale University.
- FDA Regulations: The federal policy for the protection of *human subjects* as implemented by the Food and Drug Administration, published in the Code of Federal Regulations, 21 CFR 50 and 56.
- Human Subject: Living individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or about whom an investigator obtains identifiable private information.
- Informed Consent: A person's *voluntary* agreement, based on adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure. In giving informed consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the institution or agents thereof from liability for negligence.
- IRB: Institutional Review Board: A specially constituted review body established or designated by an entity to protect the welfare of *human subjects* recruited to participate in biomedical or behavioral research. Yale has three IRB's. This document reflects the policies of the Faculty of Arts and Sciences Human Subjects Committee. The School of Nursing and the Medical School have IRB's as well. The latter is referred to as the Human Investigation Committee (HIC).
- Legally Authorized Representative: A person authorized either by statute or by court appointment to make decisions on behalf of another person. In *human subjects* research, an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure involved in the research.
- Minimal Risk: A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
- Principal Investigator: The scientist or scholar with primary responsibility for the design and conduct of the research project. HSC policy requires that the principle investigator be or be directly overseen by a faculty member or a research scientist.
- Protocol: The formal design or plan of an experiment or research activity; specifically the plan submitted to an IRB for review. The protocol includes a description of the research design or methodology to be employed, the eligibility requirements for prospective subjects and controls, the treatment regimen(s), and the proposed methods of analysis that will be performed on the collected data.
- Research: A systematic investigation designed to develop or contribute to generalizable knowledge.
- Risk: The probability of harm or injury (including physical, psychological, social, or economic) occurring as a result of participation in a research study.

Special Population: Particularly vulnerable subjects including *children*, prisoners, pregnant women, *cognitively impaired* persons, or educationally disadvantaged persons who require special consideration to protect their welfare.

Subject: See human subject.

Subject Pool: Students in Introductory Psychology who participate as *human subjects* via the Psychology Participant Pool.

Voluntary: Free of coercion, duress, or undue inducement.

Yale Investigator: The member of the Yale faculty or staff who is primarily responsible for assuring that the study is performed as agreed to with the Committee and in a competent manor.

Yale Population: Individuals affiliated with Yale University who are to be recruited as subjects by virtue of their affiliation to Yale.

APPENDIX A

Supplemental Information for Investigators Working in Schools

Research conducted in schools raise a distinct set of concerns with regards to proper treatment of research participants. In addition to the usual requirements of IRB review, an investigator who intends to conduct research in a school needs to be aware of these issues when designing a research study. The discussion below describes some of the more common issues which have come to the attention of the IRB. The Committee is available to assist investigators in determining what issues are likely to arise in a particular study.

Student Concerns

Special caution must be taken when recruiting students. In most cases they are minors and by definition require special protection under the regulations. When recruiting in schools, investigators also must be sensitive to the influences of peer pressure and the desire to please teachers and parents. Studies performed in schools require special attention to consent and confidentiality.

Consent and Assent: Participants in school studies are likely to be minors and thus not able to give legally effective consent. The minimum age at which an individual can consent to research participation varies from state to state and may be distinct from other consent statutes such as ability to consent to medical treatment. The laws of the state in which the study is conducted are the ones to be followed. In Connecticut, only subjects over the age of 18 can legally consent to participate in research. Written parental consent is required for all participants under the age of 18 except in rare cases as determined by the HSC.

Despite their inability to legally consent, ethical standards require that the autonomy of minors be respected by requesting assent to participate. Assent is similar to consent although the information provided to gain assent must be tailored to the intellectual capacity of the children. For example, a form similar to the parental consent form may be appropriate for high school seniors whereas a less detailed verbal description may be most appropriate with kindergartners. Most research can only proceed when both the parent and the child have agreed to take part in the study.

Limits to Confidentiality: Most studies promise confidentiality of the student's responses. When this promise is made, it is absolute. The only instances in which it can be breached involve state-mandated reporting requirements (abuse, some infectious diseases, etc.), prevention of harm to the participant or others, and subpoena. The promise of confidentiality is to the student and their parent or legally authorized representative. Thus, in cases where there is a need to intervene, it is not considered a breach of confidentiality to contact the parents. The one exception would be circumstances in which it would be more damaging to the child for the parents to be informed, such as instances of child abuse. These limitations of confidentiality must be conveyed to the students, including under what circumstances their parents would be informed of their responses.

Providing information about an individual participant to anyone other than the student and parent/guardian is considered to be a breach of confidentiality. This includes providing individually identifiable information to the schools, whether or not it is in the student's best

interest. Although the school is often thought of as a partner in the research, they are nonetheless not privileged to see the individually identifiable data.

If the information to be collected in the study includes criminal activity (drug use/sale, violence to others), and it can not be collected anonymously, then the investigator may need to apply for a Certificate of Confidentiality from the DHHS. This document protects the identifiers from subpoena, and thus removes the risk of use in criminal proceedings in an identified manner. Receipt of a Certificate of Confidentiality does not alleviate legal or ethical requirements to report child abuse. It should be noted that even in cases where a Certificate of Confidentiality is not presumed to be needed; access to research data may be sought via subpoena. For example, one can imagine that the child's responses could be of value in the context of a custody dispute. Although the likelihood of a litigant wanting to look at your data is low, it remains a possibility. Thus, it is always in the best interest of the participants to have all of their information coded and the code destroyed upon completion of data collection.

School Concerns

One could argue that the concerns of the school are not within the purview of the IRB as a school is not a "subject" since it is not a "living individual." Nor is the school part of the research team since they will not be involved in the design and conduct of the research. However, since a school study can not, by definition, be conducted without the approval of the school, sensitivity to their concerns will facilitate your ability to complete the proposed data collection and produce valid results.

The primary function of a school is to educate students. Involvement in a research study will necessarily compete for the limited time that a school has to perform its primary function. The moment an investigator enters a school, the education function of the school has been disrupted. Such disruption will only be tolerated by the school if it anticipates receiving some benefit from participation. In agreeing to participate and to allow access to its students, the school must weigh the disruption of the study against the expected benefits. To do so, the school must be fully informed about the details of the study, much like the requirement for an individual participant's informed consent. It is imperative that the investigator clearly describes the roles of all parties, the risks and benefits of the study, as well as the purpose and procedures of the study.

Define who is responsible for what. There is a broad spectrum of the intrusiveness of a study. At one extreme are observational studies in which the investigator is interested in discreet observation and thus, only approval to enter the schools is needed. Purely observational studies would not require parental consent, although the school may require that the parents are informed of the research.

Most common, however, are studies in which the data is collected interactively on school grounds during the school day. The responsibility of the schools may include distribution and collection of parental consent documents. The testing session itself may occur during normal classroom time, either with the class being testing *en masse* or by individuals being excused from the class to meet with the investigator. When the data is collected *en masse*, it is the school's prerogative to determine appropriate alternate activities for those students who decline to participate. It should be noted, however, that in some cases it is preferable to have a "filler" activity for the non-participants. In this way, the confidentiality of those who chose not to participate can be respected by allowing the appearance of participation in front of their peers and teachers while completing an unrelated task.

In defining the roles of the research team and the schools, the research personnel who will be on site should be identified to the school along with their qualifications and role. The school should be forewarned about who will be present in the schools, when they will be present and in what capacity. This includes undergraduates on the project as well as graduate students and post-doctoral fellows. To facilitate the school's ability to monitor who is present in their facility, the Committee recommends that all research personnel wear a visible form of identification which indicates their name and their affiliation with the research project.

Define benefits to the school: As noted, schools are only willing to relinquish classroom time if they feel that the benefits of the study are worthwhile. A realistic description of the benefits for the school should include not only what benefits will be provided but also what the limitations of these benefits are. For example, the types of reports which will be provided to the schools must be outlined—will there be information specific to an individual school or to schools in general? Are there circumstances in which the study will be terminated early and thus reports not be provided? This latter instance must be addressed if a study commences prior to securing adequate funding. The Committee recommends that the school be provided with a timeline showing when the data will be collected and when the school can expect to see any promised reports or other benefits.

Define disclosure risks: Public schools in particular have legal and moral requirements which they must fulfill to ensure the safety of their students. For example, school personnel in Connecticut are mandated to report suspected child abuse to state authorities. Such reports are frequently followed by an investigation by DCF and have the potential to have a child removed from the home. The threshold of required reporting is low and schools are put into a difficult situation when informed of suspected abuse of an identified student.

Another area where the school would be expected to act include threats to student safety. Information suggesting that a student may harm another student or him/herself would require the school to further assess the threat. Should the threat be substantiated, the school would be expected to mitigate the situation. Although it would be difficult to identify all situations in which a response would be necessary, investigators should be prepared when the study queries about depression, possession of weapons, or threatening behavior, either directly or indirectly.

To protect the school from having to implement its mandated procedures, it is generally better for the investigator to take responsibility for information uncovered in a study and present the school with generalized results. Any reporting should be done by the investigator directly to the relevant authorities. Note that many reporting requirements are defined by each individual state. Investigators are urged to be aware of what they as researchers would be legally required to report, as well as what they as individuals may feel ethically required to report. In cases where it would be absolutely necessary to inform the school, the school and the participants must be informed from the start that this would be a potential risk involved in the study. This risk must be stated clearly and in writing, including what types of actions the school would be required to take and whether or not the information would become part of the student's school record. The Committee urges investigator to discuss reporting expectations with the school personnel prior to the initiation of a study.

Define other site -specific risks: Each school is a unique environment about which the school personnel are experts. Measures, which are of little concern in one school, may be of great

concern in another, based on the local culture. It is essential that investigators provide school administrators with a full set of the measures to be used so that they may assess the likelihood of problems for their school. The school should be asked if the measures are appropriate for their students and if any problems can be anticipated during or after the research procedure. Note that highly sensitive topics may promote discussion of these issues by the students during the remainder of the school day. Depending on the nature of the issues, the school may want to be prepared for any subsequent repercussions arising from the research participation. Hence, the school must be aware of what measures will be administered when.

Define appropriate contacts: Communication is essential to maintaining rapport with the schools. Not only does the school need to be informed as to whom they should contact with questions and concerns, but also, the investigator will need to know who the appropriate contacts are for various aspects of the study. The individual with authority to allow access to the students is usually different from the person who should be contacted about the logistics of data collection. In any case, these individuals should be defined up front to facilitate future communication.

Obtaining approval to work in the schools is a multi-step process. In the end, written approval should come from the highest level. In public schools this may be the superintendent. For private schools, the headmaster may be the appropriate official. This individual will be required to sign a letter indicating that they agree to allow access and have been shown all the required materials. To facilitate this process, the HSC will provide the investigator with a study specific checklist that is to be attached to the letter. This checklist will indicate all the relevant measures and responsibilities inherent in participation.

Study Administration:

HSC Review: In reviewing research studies, the HSC takes all of the above into account, in addition to the standard review requirements, to weigh the risks and benefits of the research. Once approval is granted, all subsequent changes to the study must be approved by the HSC to insure that the changes do not alter the risks for the participants. The HSC requires *all* proposed changes be submitted. This includes, but is not limited to, any change to the measures themselves, the way in which the measures will be presented, and the personnel on the project.

Adverse Event Reporting: Occasionally, there will be problems during data collection. Whether or not these problems were anticipated, they constitute an adverse event and must be reported to the HSC. Problems can range from complaints or distress of a participant to identification of participants at risk of harm. Note that an “adverse event” is viewed from either the participants or the researcher’s point of view. Whether or not the event is expected, if there is an outcome that is detrimental to the participant or perceived as detrimental, then an adverse event has occurred. If the event requires investigator intervention or alteration of procedures then the event must be reported within 5 working days. Otherwise, the events may be reported annually via the renewal application. Note that the HSC has experience in ways to handle adverse events and is available to assist the investigator to determine the appropriate course of action.

Schools as Research Partners: Occasionally, the study will call for a the school to play an active roll in the design and/or conduct of the research. Once the school moves beyond merely

providing access, it is considered to be “engaged in research” and must meet additional requirements under the regulations. In particular, the school would be required to file an assurance with OHRP, indicating their plans to comply with 45 CFR 46. The HSC will assist in determining when such an assurance is needed and how the school can comply with this requirement.

Exempt Studies: 45 CFR 46 exempts “research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special educational instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.” Thus, studies which focus on improving the educational experience of the students are not covered by the regulations. Yale policy, however, requires that the exempt status always be determined by the HSC. It is worth noting that few of the studies reviewed by HSC qualify for this exemption. To qualify the study must be limited exclusively to normal educational practices.

Checklist of Requirements for School Studies Involving Collection of Data from Students

Information to be provided to school officials:

- ✓ Full copy of protocol including all measures
- ✓ Logistics of data collection—when and where?
- ✓ Estimation of intrusiveness
- ✓ Length of individual sessions
- ✓ Length of entire study
- ✓ Handling of students who do not consent to participate. Who will be responsible for alternate activities?
- ✓ Listing of all research personnel, their roles on the project and qualifications
- ✓ Anticipated benefits to the school including timing and certainty of delivery
- ✓ Any risks of the study
- ✓ Possible disruptions to school both during and after data collection
- ✓ Identification of students at risk of harm
- ✓ Identification of other reportable information
- ✓ Any responsibilities of the school—collecting consents, monitoring, interventions, etc.
- ✓ What, if any, individual student information will be provided to the school and if none, so state
- ✓ Ability to withdraw participation or request an individual measure be withdrawn. If school cannot participate without inclusion of all measures, so state.
- ✓ Contact information for the Principal Investigator and HSC

Items to be ascertained from the schools

- ✓ Appropriate contact(s) for day to day issues
- ✓ Authorized official for the school
- ✓ Assessment of local context and related issues which the investigator must be sensitive to
- ✓ Appropriateness of study measures for the local population

Information to be provided to parents/guardians and students:

- ✓ Description of the study and clear statement that this is research
- ✓ Confidentiality of responses
- ✓ What information will be shared with school
- ✓ What information would be reported to other authorities
- ✓ What information will be shared with parent and/or student
- ✓ Ability to decline/withdraw
- ✓ Both parent and child can withdraw individually
- ✓ Impact of study on students who decline to participate
- ✓ Duration of study
- ✓ Risks of participation
- ✓ Benefits
- ✓ Contact information for PI and HSC

Information to be provided to HSC, in addition to standard requirements

- ✓ Listing of all research personnel, their roles/responsibilities, and qualifications
- ✓ Approval of the study by appropriate school official

- ✓ Description of procedures for mitigating consequences of adverse events
- ✓ Availability of appropriate level of funding for duration of project
- ✓ Assurance that full scope of study is within PI's area of expertise and if not, provide signed agreement from appropriately trained collaborator
- ✓ Continuing review items
 - ✓ Adverse event reporting
 - ✓ Reporting of all adverse events whether or not they were anticipated
 - ✓ Reporting of any complaints about the study
 - ✓ Reporting of any difficulties encountered by the investigator or participants
 - ✓ Copies of any new measures/procedures
 - ✓ Justification for addition
 - ✓ Description of how change will effect the risks and benefits of the study
 - ✓ Description of how new measure will be administered
 - ✓ Approval of the school for additional measure
 - ✓ Description of any changes in procedures from initial submission including revised measures with changes highlighted
 - ✓ Copies of all correspondence with school including relevant letters, reports, and e-mails

Agreement to Participate in a Research Study

As the authorized official of _____ school, I am agreeing to the participation of _____ school in the study entitled “_____” under the direction of Professor _____.

I have been given a full description of the project and have reviewed the following items and discussed their appropriateness with Professor _____:

Measure 1

Measure 2

Listing of all research personnel who will be working in the schools

I understand that school personnel will be asked to perform the following functions: (as applicable)

Distribution and collection of parental consent forms

Providing alternate activities for those students who decline to participate

I understand I will be provided with a report on the outcome of the study within X months of completion as well as annual progress reports. The school system will also receive _____ as a thank-you gift for our participation.

I understand that I will not be provided with any information that individually identifies students and their responses except in cases where the student is found to pose a risk of harm to another student. I understand that the investigator will take responsibility for any other findings that require follow-up with the student, their parents or appropriate state authorities.

I understand that I may withdraw the school’s participation at any time or prohibit the inclusion of any of the measures listed above.

If I have any questions about this research study I may contact Professor _____ at 432-_____.

If I have any concerns about the conduct of this study I can contact the Human Subjects Committee at 203-436-3650, human.subjects@yale.edu.

Name authorized official: _____

Title: _____

Phone: _____

Signature _____

Alternate school contact for routine study administration issues: _____

Title: _____

Phone: _____

APPENDIX B
Sample Informed Consent

The following is intended as a sample. It should be modified to fit the specific study, both in content as well as format.

Research Informed Consent

Study Title
Investigator

Purpose:

We are conducting a research study to examine describe the purpose and goals of the study.

Procedures:

Participation in this study will involve description of tasks (completing a survey, interview, etc.)
We anticipate that your involvement will require x minutes/hours. You will receive x dollars for participating (as applicable).

Risks and Benefits:

Participants in this study may experience description of risks (distress over the nature of the questions, etc.) Although this study will not benefit you personally, we hope that our results will add to the knowledge about describe public good. If there is a benefit to participants, so state.

For studies which involve more than minimal risk of harm to subjects include: If you are hurt or injured as a result of your participation in this study, [indicate whether treatment will be made available, and who will be responsible for its cost.]

Confidentiality:

All of your responses will be held in confidence / anonymous—chose only one. Only the researchers involved in this study and those responsible for research oversight will have access to the information you provide. You're responses will be numbered and the code linking your number with your name will be stored in a separate locked file cabinet (if applicable). Please note, however, that unlike information you provide to your doctor or lawyer, the investigator can be compelled by a court to disclose this information (if applicable – that is if the data would have any value in court proceedings).

For HIPAA covered studies involving PHI include: Except as permitted by law, your health information will not be released in an identifiable form outside of the Yale University research team, collaborating researcher's institution and describe any other groups who would have access (if applicable). Note, however, that your records may be reviewed by those responsible for the proper conduct of research such as the Yale University Human Subjects Committee or representatives of the U.S. Department of Health and Human Services or the name of research sponsor (if applicable). Information may be re-disclosed if the recipients are not required by law to protect the privacy of the information. At the conclusion of this study, any identifying

information related to your research participation will be destroyed, rendering the data anonymous OR will be retained indefinitely.

Voluntary Participation:

Participation in this study is completely voluntary. You are free to decline to participate, to end participation at any time for any reason, or to refuse to answer any individual question without penalty or loss of compensation (*if applicable*).

For studies involving the psychology subject pool include: Your participation in this study is extremely valuable for our research, and we hope that participating will prove to be an educational experience for you. In addition, however, please remember that this is only one of the ways in which you can fulfill your “experimental participation” credits for Introduction to Psychology. Other ways, as detailed in the form handed out to you in class, include serving as an observer of 5 experiments, or arranging for other options of equivalent educational value (e.g., writing essays) through your instructor.

Questions:

If you have any questions about this study, you may contact the investigator, investigator name and contact information.

If you have any questions about your rights as a research participant or concerns about the conduct of this study, you may contact the Yale University Human Subjects Committee, Box 208252, New Haven, CT 06520-8252, 203-436-3650, human.subjects@yale.edu.

For studies involving the psychology subject pool include: If you have questions about the Psychology Subject Pool, you may contact the coordinator at 432-4518, or psychsubject.pool@yale.edu

Agreement to Participate:

I have read the above information, have had the opportunity to have any questions about this study answered and agree to participate in this study.

(printed name)

(date)

(signature)

APPENDIX C

Guidance on the Involvement of Undergraduates in Human Subjects Research Projects

Researchers who propose to involve undergraduate research assistants in the conduct of the research must ensure that the student is properly qualified and is subject to the appropriate level of oversight. All personnel, including undergraduates, must complete training in the ethical treatment of research participants and, if the study will be performed in one of the HIPAA covered components, they must also complete HIPAA training.

Student qualifications

All research personnel must be qualified in accordance with their role in the project. The necessary level of experience will depend on the student's function such that students involved in data entry need only demonstrate that they can preserve data integrity. Students who will directly interact with participants should be qualified to answer any questions that could arise. In studies where there is a potential for participants to express distress in the course of the study, the prospective research assistant must have experience in or be trained in the appropriate responses and when to involve more experienced investigators in the response.

Anonymous studies, coded data sets or studies involving minimal risk of social harm

Studies which pose little or no risk from disclosure either by the innocuous nature of the questions or by steps taken to minimize potential for identification of the participants, may involve undergraduate research assistants with minimal selection criteria. Thus, involving students in data entry using coded data sheets is perfectly appropriate.

Studies involving the collection of identifiable sensitive information

Studies that involve the collection of sensitive information would include, for example, data on mental health, sexual behavior, drug and alcohol use, or illegal activities. The involvement of other undergraduates as participants can compound the issue since the participants may also be fellow students or dorm residents of the undergraduate research assistant. For these projects, the prospective research assistants should be screened by the faculty member overseeing the project and queried regarding their understanding of the need to maintain participant confidentiality. Some projects may be sufficiently sensitive that only senior level students be involved or that students be excluded from either handling any identified data or from administering assessments.

Sample Confidentiality Pledge for Use of Sensitive Data

Pledge of Confidentiality

I _____, through my involvement with and work on {*Title of Research Project*} will have access to data which contains confidential information which respondents generally perceived as personal and private. I understand that access to this confidential information and data carries with it responsibility to guard against unauthorized use and to abide by the data security plan. To treat information as confidential means not to divulge it or make it accessible to anyone who is not a project member. Such a disclosure would violate the confidentiality promised to participants and would violate University ethics policies.

I agree to fulfill my responsibilities on this project in accordance with the following

0. I agree to not permit non-project personnel access to the data, either electronically in hard copy or orally.
0. I agree to not attempt to identify individuals, families, households, schools, or institutions {*Select only those categories relevant to the nature of the study*} except in those cases where it is necessary in accordance with my role on the research project.
0. I agree that in the event I inadvertently uncover the identity of an individual, family, household, school or institution, I will maintain the highest level of confidentiality of this information, make no use of the knowledge and inform the study's Principal Investigator.

Name

Signature

Date

APPENDIX D
Committee Forms