

HUMAN SUBJECTS PROTECTION REVIEW
COMMITTEE (HSPRC)
POLICIES AND PROCEDURES MANUAL
FOR HUMAN SUBJECTS RESEARCH

October 1, 2016

Office of Sponsored Programs (OSP)
HSPRC

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1. INTRODUCTION

University of Holy Cross is committed to the protection of human research subjects. The University of Holy Cross Institutional Review Board (HSPRC) was established to protect the rights and welfare of human research subjects. This manual is designed to assist University of Holy Cross faculty, staff, and students who plan to perform research involving human subjects. The manual describes University of Holy Cross policies and procedures concerning the involvement of humans in research, and the requirements for submitting research protocols to the HSPRC for approval.

Prior to the initiation of any research activity involving human subjects, a research application must be submitted to the HSPRC and receive approval.

The HSPRC is a committee that determines and certifies that all research involving human subjects conforms to the regulations and policies set forth by the Department of Health and Human Services (DHHS), the Food and Drug Administration (FDA), Louisiana State regulations, and University of Holy Cross policies regarding the health, welfare, safety, rights, and privileges of human subjects. The HSPRC also assists investigators in conducting ethical research that complies with these regulations and policies.

The HSPRC is comprised of faculty representatives from various academic disciplines at University of Holy Cross, including scientists and non-scientists, as well as a community representative who is not affiliated with University of Holy Cross. The HSPRC operates within federal guidelines with respect to the review and approval of research applications involving human subjects. The welfare and dignity of individuals who participate in research is a central concern of everyone involved with the protection of human research participants. University of Holy Cross's primary goal is to have a fair and transparent process in which participants voluntarily decide to take part in a study based on intelligent and knowledgeable assessment of the risks and benefits of the research.

University of Holy Cross administrators, research investigators, and the HSPRC share the collective responsibility for the ethical conduct of research. This collaboration must exist in a culture of trust, complete openness, and honesty by upholding the highest standards; we build public support for the pursuit of greater knowledge in a safe research environment.

2. ACTIVITIES OF THE UNIVERSITY OF HOLY CROSS HSPRC AND FEDERAL REGULATIONS

The HSPRC is responsible for reviewing and overseeing research involving human beings. The HSPRC review process is designed to protect the rights and welfare of human subjects by ensuring equitable subject selection, assuring adequate informed consent, assessing and minimizing risks, and maintaining privacy and confidentiality.

Two agencies within the U.S. Department of Health and Human Services (DHHS) share responsibility for HSPRC oversight: the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA). Federal regulations for the protection of human research subjects are set forth in *45 Code of Federal Regulations (CFR) 46*. Part A of *45 CFR 46* covers

basic policies and is referred to as "the Common Rule." Parts B, C, and D of *45 CFR 46* address additional protections for pregnant women, fetuses, and neonates; prisoners; and children; involved as subjects in research, respectively. Many federal agencies and other funding sources have adopted "the Common rule."

The OHRP's main tool for oversight is the process of registration and the assurance document. Any institution that intends to conduct DHHS-funded research must have a registered HSPRC of its own or an association with a registered HSPRC. The Federal-Wide Assurance (FWA) is a commitment by the institution that it will comply with federal regulations. University of Holy Cross has an FWA and the University of Holy Cross HSPRC operates under this FWA. The OHRP also conducts a small number of site visits.

Additional regulations for research involving drugs and devices regulated by the FDA are set forth in *21 CFR 50, 56, 312, and 812*. The FDA's main mechanism for HSPRC oversight is the inspection process. The FDA also inspects research sponsors and research investigators.

Other federal agencies that adopt the Common Rule may add special requirements to these basic regulations. If you are proposing to apply for funding to those agencies, you should check with them and with the HSPRC Administration to get information about any such requirements.

3. ETHICAL PRINCIPLES

The federal regulations that protect human research subjects are grounded in fundamental ethical principles, as set forth by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*. The *Belmont Report* encompasses three key ethical principles: **respect for persons (autonomy), beneficence, and justice**. The University of Holy Cross HSPRC adheres to these ethical principles.

4. AUTHORITY OF THE HSPRC

The University of Holy Cross HSPRC has the authority to approve, disapprove, or require modifications in research activities that fall within its jurisdiction, as specified by federal regulations, state regulations and University of Holy Cross policies.

The University of Holy Cross HSPRC has the authority to:

- **Approve, disapprove, or modify studies based upon consideration of the protection of human research subjects.** Research that has been reviewed and approved by the University of Holy Cross HSPRC may be subject to further review and disapproval by officials of the Institution. However, those officials may not approve research if it has been disapproved by the HSPRC.

The HSPRC also functions independently of other committees and makes independent determinations to approve or disapprove the application based upon whether or not human subjects are adequately protected. The University of Holy Cross HSPRC has jurisdiction over all human subject research.

- **Require progress reports from investigators and oversee the conduct of the study.** Any approved non-exempt research is subject to continuing University of Holy Cross HSPRC review and must be reevaluated at least annually. The intent is not to interfere with ongoing research but to ensure that human participants are protected.
- **Suspend or terminate approval of a study.** University of Holy Cross has the authority to suspend or terminate approval of research not being conducted in accordance with the HSPRC's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the HSPRC's action and shall be reported promptly to the Principal Investigator (PI). The suspension or termination of an application will also be reported to the Institutional Official (IO) and any federal funding agency as required by regulations.
- **Conduct post-approval reviews.** The University of Holy Cross HSPRC has the authority to conduct post approval reviews on any applications for any reason. Review may consist of a review of documents and/or review of the activities to determine if the research is being conducted in accordance with the HSPRC's requirements (the approved application).

5. WHAT IS HUMAN SUBJECTS RESEARCH?

Federal, state, and University of Holy Cross regulations require the HSPRC to review and monitor **human subjects research**. Several terms are defined below to help investigators determine if HSPRC review of a project is required. In support of University of Holy Cross's mission to protect human research subjects, and the regulatory consequences of not obtaining HSPRC review and approval, investigators should consult with the HSPRC office if they have any doubt about whether or not a study involves human subjects research.

Research: Federal regulations define research as: "a systematic investigation... designed to develop or contribute to generalizable knowledge." [45 CFR 46.102(d)]

Human subjects: The DHHS regulations define a human subject as "a living individual about whom an investigator (whether professional or student) conducting research obtains:

1. Data through intervention or interaction with the individual.

Or

2. Identifiable private information." [45 CFR 46.102(f)]

Private information: Private information includes:

1. Information about behavior that occurs in a setting in which **the individual** can reasonably expect that no observation or recording is taking place.

2. Information that has been provided for specific purposes, other than research, where **the individual** can reasonably expect that it will not be made public (such as a medical record.) [45 CFR 46.102(f)].

Coded private information or biological specimens: DHHS Office of Human Research Protection (OHRP) policy considers private information or specimens to be individually identifiable when they can be linked to specific individuals either directly or indirectly through coding systems. The HSPRC must determine if coded specimen or data constitute research. Investigators do not have the authority to make an independent determination that research involving coded private information or specimens does not involve human subjects.

Clinical investigation: The Food and Drug Administration (FDA) defines clinical investigation as "any experiment that involves a test article and one or more human subjects and that either must meet the requirements for prior submission to the Food and Drug Administration... or need not meet the requirements for prior submission to the Food and Drug Administration... but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit." [21 CFR 56.102(c)]

6. RESPONSIBILITIES OF ALL INDIVIDUALS CONDUCTING HUMAN SUBJECTS RESEARCH

All faculty, staff, and students associated with University of Holy Cross who perform research involving human subjects are required to:

- Ensure that all research activities have HSPRC approval and other approvals required by the institution before human subjects are involved.
- Design and implement research in a manner that excludes or minimizes risks to human participants.
- Protect the rights and welfare of human subjects who participate in research.
- Understand the ethical standards and regulatory requirements governing research activities with human subjects.
- Personally conduct or supervise the research.
- Ensure that all staff, collaborators, and colleagues assisting in the conduct of the study are informed about the study, the regulations governing research, and the institutional policies.
- Implement the research activity as it was approved by the HSPRC.
- Obtain the informed consent of subjects before the subject is involved in the research and document consent as approved by the HSPRC.
- Maintain written records of HSPRC reviews and decisions and obtain and keep documented evidence of informed consent of the subjects or their legally authorized representatives.
- Obtain HSPRC approval for any proposed change to the research protocol prior to its implementation.

- Comply with the HSPRC requirements for timely reporting of unanticipated problems involving risks to subjects or others including adverse events, safety reports received from the sponsor, or data safety and monitoring summary reports.
- Obtain continuation approval from the HSPRC on the schedule prescribed by the HSPRC.
- Make provisions for the secured retention of complete research records and all research materials.
- Ensure the confidentiality and security of all information obtained from and about human subjects.
- Verify that HSPRC approval has been obtained from all participating institutions in collaborative activities with other institutions.
- Notify the HSPRC regarding the emergency use of an investigational drug or device within 3 working days of the administration of the test article.

Failure to follow HSPRC regulations may result in:

- Suspension of a research project.
- Suspension of all of a principal investigator's research projects.
- Inability to use data or publish results.
- Notification of sponsors, regulatory agencies, and funding agencies of noncompliance.
- Debarment by FDA from using investigational products.
- Inability to receive funding from federal grants.
- Additional monitoring and oversight by the HSPRC and/or third party monitoring of research activities.
- Termination of employment.
- Loss of licenses.
- Immediate shut-down of all research at University of Holy Cross.

Some or all of these consequences have occurred at institutions where research on human beings was conducted improperly or without HSPRC approval.

7. REQUIRED TRAINING FOR HUMAN SUBJECTS RESEARCH

University of Holy Cross policy requires all faculty, staff, and students who perform human-subjects research to be trained in the protection of human research subjects. The training can include enrollment in a class on research, completion of a terminal degree such as a Ph.D., Ed.D., or Psy.D., in which research is a requirement, or on-line training. The HSPRC will not grant approval of human subjects research applications until all investigators associated with the project have one of these requirements.

8. INFORMED CONSENT

Informed consent is one of the primary requirements of research involving human subjects. Informed consent is a demonstration of how investigators and those involved in human subjects research show respect to research subjects, and it is mandated by the DHHS and FDA.

It is important to remember that informed consent is an ongoing process, not a single event. Informed consent regulations were developed to:

- protect human subjects;
- ensure that potential study subjects clearly understand the benefits and risks associated with their participation in a study; and
- provide the potential study subjects with all information needed to reach a decision on whether or not to participate in a research study.

Investigators may seek informed consent only under circumstances that:

- provide the prospective subject or his/her representative sufficient opportunity to consider whether or not to participate, and
- minimize the possibility of coercion or undue influence.

Requirements for Informed Consent

The basic elements for legally appropriate informed consent, as specified in 45 CFR 46.116(a) and 21 CFR 50.25(a), includes the following elements:

1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.
2. A description of any reasonably foreseeable risks or discomforts to the subject.
3. A description of any benefits to the subject or to others which may reasonably be expected from the research.
4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records.
6. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
 - The University of Holy Cross injury compensation clause must be included: "University of Holy Cross has not provided for any payment if you are harmed as a result of taking part in this study. If such harm occurs, treatment will be provided. However, this treatment will not be provided free of charge."
 - In studies that involve greater than minimal risk and are sponsored, include a statement regarding the sponsor's injury compensation policy. The sponsor's injury compensation clause must be included if the sponsor will pay for compensation to injured research participants, or pay for treatment of research-related injuries (Note: Investigator must provide verification of sponsor's injury compensation clause when sponsor will pay.)

- If the sponsor will not provide any compensation for injuries related to the research, then include in the University of Holy Cross injury compensation clause, “University of Holy Cross and [name of sponsor] have not provided for any payment....”
7. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.
 8. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

In addition, if relevant to the research, legally effective informed consent will also include the following elements, as outlined in 45 CFR 46.116(b) and 21 CFR 50.25(b):

1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable. Examples of when the HSPRC requires this element are:
 - Phase I or Phase II clinical investigations;
 - Experimental procedures or treatments with limited available data on risks.
2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent. Examples of when the HSPRC requires this element are:
 - If the sponsor may stop the study;
 - If the investigator reserves discretion to remove the participant from the study;
 - If the investigator may remove the participant from the study should the investigator determine it is in the best interest of the participant;
 - If the participant does not follow study instructions.
3. Any additional costs to the subject that may result from participation in the research. Examples of when the HSPRC requires this element are:
 - If study procedures result in potential billing to the participant or third party payers;
 - If participants may have out-of-pocket costs from participation in the research (e.g., parking, meals, transportation);
 - If a possibility exists that a study drug becomes commercially available and no longer provided at no cost to the participant.
4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject. Examples of when the HSPRC requires this element are:
 - If drug dose tapering is required and has risks to participants;
 - When a follow-up visit or testing is required for safety reasons.

5. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.
6. The approximate number of subjects involved in the study.

University of Holy Cross Informed Consent Form

The following are required (when applicable) on the consent form:

1. Study title and name(s) of researcher(s) at the beginning of the consent form;
2. A statement that the study has been approved for human subject participation by the University of Holy Cross Institutional Review Board;
3. Consent document written at a reading and comprehension level appropriate for the age and/or background of the participant (6th-8th grade for most);
4. The language and its documentation (explanation of purpose, duration, experimental procedures, alternatives, risks, and benefits) written in "lay language," (i.e., understandable to the people being asked to participate);
5. Signature block to include participant, researcher(s), witness if appropriate, and date of signature;
6. When appropriate, check box or signature provided to indicate agreement to audio or videotape is included;
7. A statement that the participant will receive a copy of the consent form if appropriate; and
8. Consent form free of exculpatory language through which the subject is made to waive, or appear to waive, any of the subject's legal rights.

Assent

Assent is defined as an "agreement by an individual not competent to give legally valid informed consent (e.g., a child or cognitively impaired person) to participate in research."

Assent is generally required if:

1. subjects are minors between the ages of 7 and 17 (children below the age of 7 are generally not asked to provide assent); or
2. subjects are 18 or older and are intellectually or emotionally impaired and not legally competent to give their informed consent.

In cases where minor subjects are able to read and understand the informed consent document, they may provide assent on a form with a separate signature line for their parents/guardians.

The assent form must include:

1. Study title
2. Study purpose (provide a brief explanation of the purpose of the study)
3. Procedures (describe what the subject is being asked to do)

4. Withdrawal privilege (describe how a subject can stop participation later even if he/she agrees to start)
5. Voluntary participation (include a statement that the subject does not have to participate)
6. Confidentiality statement (indicate that the experimenter will not tell anyone – e.g., parents, teachers – what the subject says or does in the study)
7. Signature lines (include a signature line for the subject and for the investigator)
8. Date line

Requirement to Obtain Signatures

In most circumstances, the HSPRC will require that informed consent be documented by the use of a written consent form approved by the HSPRC and signed and dated by the subject or the subject's legally authorized representative. This consent form must contain the required elements of informed consent in language understandable to the subject. This form may be read to the subject or the subject's legally authorized representative. However, the investigator should allow the subject or the legally authorized representative adequate opportunity to read the consent document before it is signed.

Unless the HSPRC waives the requirement to document informed consent, an investigator must obtain the **written** legally effective informed consent of an individual (or, in certain circumstances, the individual's legally authorized representative) **before** the individual can participate or be involved in **any research activities** involving human subjects.

Because the signed document is a written record of the consent discussion,

- the investigator must retain the **original, signed** document, and
- each participant must be given a **copy of the signed** document.

Waiver of Documentation of Consent

In some situations (e.g., telephone survey or mailed survey, anonymous survey, internet research, certain international research), the HSPRC may waive the requirement for obtaining a signed informed consent form. Investigators can request a waiver on the HSPRC form.

As per 45 CFR 46.117(c), the HSPRC may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it determines either of the following:

1. The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research and the subject's wishes will govern. **NOTE:** Documentation of consent cannot be waived for FDA-regulated research that meets these conditions.
2. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. In cases in which the documentation requirement is waived, the HSPRC may

require the investigator to provide subjects with a written statement regarding the research.

Alteration or Waiver of Informed Consent

Some research studies (e.g., medical record review, deception research, collection of biological specimens) would not be possible if some/all elements of informed consent were required from participants. The HSPRC may consider waiving the requirements for some/all elements of informed consent when the research meets **all of the following conditions** (the researcher needs to explain for each condition how it applies to the research):

1. The research involves no more than minimal risk to the subject;
2. The rights and welfare of subjects will not be adversely affected;
3. The research could not practicably be carried out without the waiver or alteration; and
4. Whenever relevant, the subject will be provided with additional pertinent information after the subject has participated in the study.

NOTE: The investigator must describe which element(s) of consent will be altered and/or omitted, and justify the alteration/omission. The HSPRC does not approve waiver of informed consent for research that is subject to FDA regulations, except for planned emergency/acute care research as provided under FDA regulations.

Requirement to Use Understandable Language

The informed consent document must be in a language understandable to the participant. When the prospective participant is fluent in English, and the informed consent discussion is conducted in English, then the consent document should be in English. However, when and if the study population is to include non-English-speaking participants, so that the principal investigator or the HSPRC anticipates that the consent discussion is likely to be conducted in a language other than English, the investigator should address the following criteria in the description of the informed consent process:

1. Describe research and other personnel (e.g., PI, staff, translator) who will conduct the consent procedures/discussion, communicate other information, and be available to answer questions in a language understandable to the participant.
2. Submit translations and back translations of the informed consent documents for targeted populations for review and approval. The HSPRC strongly encourages the use of a full translation of the entire informed consent document.
 - For international research with local HSPRC review this requirement applies to locally approved documents.
 - For the University of Holy Cross HSPRC to grant approval, informed consent documents must include, at a minimum, the required elements of informed consent and the signatures of the participant, or legally authorized representative if applicable, and the person obtaining consent.
3. Provide certification that verifies that the informed consent document has been properly translated into the non-English language.

4. Provide the qualifications of the individual or the service that was used to translate the informed consent documents (e.g., credentials, certifications, education, or native language fluency).
5. Provide participants with the HSPRC-approved non-English-language informed consent document as part of the informed consent discussion and give them an opportunity to read and discuss the document with a fluent translator present.

9. PRIVACY AND CONFIDENTIALITY

The protection of privacy and confidentiality are important issues in the protection of human research subjects. Protection of human research subjects' privacy and confidentiality are extensions of the principles of autonomy (respect for persons) and beneficence from the Belmont Report.

Privacy can be defined in terms of having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others.

Confidentiality pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others in ways that are inconsistent with the understanding of the original disclosure without permission.

The investigator must describe plans to protect the subject's identity as well as the confidentiality of the research records. Care should be taken to explain the mechanisms that have been devised to protect the privacy of the subjects, for example, the use of numbering or code or safely locked files in private offices. Furthermore, the investigator should describe who has access to the data and under what circumstances a code may be broken. Without appropriate safeguards, problems may arise with long-term retention of records. In special circumstances requiring additional safeguards to prevent potential criminal civil prosecution of the participating human subject, the HSPRC may require the destruction of all data that can identify the subjects. Subjects should be informed of whether the data collected will be retained, and if so, for what purpose, what period of time, or whether and when data will be de-identified or destroyed.

A special situation arises for video or taped data and photographs since these media provide additional potential means for subject identification. Investigators must secure subject consent explicitly mentioning these practices. They should also explain plans for final disposition or destruction of such records.

Health Insurance Portability and Accountability Act (HIPAA)

The Health Insurance Portability and Accountability Act "Privacy Rule" (HIPAA) is a federal law that generally prohibits health care providers (such as physicians or other health care practitioners, hospitals, nursing facilities and clinics) from using or disclosing "protected health information" without written authorization from the patient.

If an investigator intends to use or release to others (e.g., sponsors, other investigators, collaborators) any identifiable health information in connection with their research, he/she must indicate that in the HSPRC application. Protected health information is health information transmitted or maintained in any form or medium that includes ALL of the three following characteristics:

- identifies or could be used to identify an individual; **and**
- is created or received by a healthcare provider, health plan, or healthcare clearinghouse; **and**
- relates to the past, present, or future physical or mental health or condition of an individual; the provision of healthcare to an individual; or the past, present, or future payment for the provision of healthcare to an individual.

10. TYPES OF HSPRC REVIEW

There are three categories of **human subjects research** reviewed by the University of Holy Cross HSPRC:

- Exempt Status Review**
- Expedited Review**
- Full Committee Review**

Projects that receive HSPRC approval following an Expedited Review or a Full Committee Review must also apply for a **Continuing Review** at least annually from the date of initial approval. The investigator is not permitted to make any revisions or amendments to an approved project without prior review and approval by the HSPRC.

Exempt Status Review

Although this category is called “Exempt,” this type of research requires HSPRC review and approval. Only the HSPRC can assign Exempt status to a project. The **determination of Exempt status by the HSPRC must be made prior to initiation of the research**; it cannot be made retroactively. After initial approval, an exempt research project does not require ongoing review by the HSPRC, unless it is amended in such a way that it no longer meets exemption status. Although a project may be granted Exempt status, no interaction with human participants is exempt from the ethical principles described in the *Belmont Report*. The principal investigator is responsible for ensuring that informed consent is obtained from human subjects participating in research determined to be exempt.

Exempt research is research with human subjects that falls under one or more of the following six exempt categories listed in the federal regulations (45 CFR 46.101b):

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:
 - a. Research on regular and special education instructional strategies.

- b. Research on the effectiveness or the comparison among instructional techniques, curricula, or classroom management methods.
- 2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures (of adults), interview procedures (of adults) or observation of public behavior, unless:
 - a. Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects. AND
 - b. Any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.
- 3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (2) if:
 - a. The human subjects are elected or appointed public officials or candidates for public office.
 - b. Or the research is conducted for the Department of Justice under Federal statute 42 U.S.C. 3789g, or for the National Center for Education Statistics under Federal statute 20 U.S.C. 12213-1, which provide certain legal protections and requirements for confidentiality.
- 4. Research involving the collection or study of existing data, documents, records, pathological or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
- 5. Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:
 - a. Public benefit or service programs.
 - b. Procedures for obtaining benefits or services under those programs.
 - c. Possible changes in or alternatives to those programs or procedures. OR
 - d. Possible changes in methods or levels of payment for benefits or services under those programs.
- 6. Taste and food quality evaluation and consumer acceptance studies, if:
 - a. Wholesome foods without additives are consumed. OR
 - b. A food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the U.S. Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

Federal regulations specify that the following research activities **CANNOT be exempt**:

- 1. Review of records if the information gathered from those records is recorded in such a way that it can be linked back to the subject either directly or indirectly through the use of a code.

2. Research involving prisoners.
3. Surveys or interviews given to children (individuals younger than 18 in TN).
4. Observations of public behavior when the investigator participates in the activities being observed.
5. Research involving deception. In some research projects it may be important to withhold the theoretical purpose of the research from subjects, so as to not bias their opinions. If done in a neutral way, withholding such information would not be considered deceptive. If subjects are intentionally led to believe that the research is for a purpose different than the actual purpose, this would be considered deceptive.

Expedited Review

If the research presents no more than minimal risk to human participants and it falls under one of nine expedited categories listed in the federal regulations, the HSPRC may determine that it qualifies for an expedited review.

Minimal risk means that "the probability and magnitude of harm or discomfort anticipated in the 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." ([45 CFR 46.102(i)] and [21 CFR 56.102(i)])

Expedited research is research with human subjects that falls under one or more of the following nine expedited categories in the federal regulations [45 CFR 46.110]:

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
 - a. Research on drugs for which an investigational new drug application (21 CFR 312) is not required.
 - b. Research on medical devices for which:
 - i. An investigational device exemption application (21 CFR 812) is not required.
 - ii. Or, the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
 - a. From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week.
 - b. Or from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.
3. Prospective collection of biological specimens for research purposes by noninvasive means.

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications). Examples in this category include:
 - a. Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy.
 - b. Weighing or testing sensory acuity.
 - c. Magnetic resonance imaging.
 - d. Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography.
 - e. Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.
5. Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects [45 CFR 46.101(b)(4)]. This listing refers only to research that is not exempt.)
6. Collection of data from voice, video, digital, or image recordings made for research purposes.
7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects [45 CFR 46.101(b)(4)]. This listing refers only to research that is not exempt.)
8. Continuing review of research previously approved by the convened HSPRC as follows:
 - a. Where (i) the research is permanently closed to the enrollment of new subjects, (ii) all subjects have completed all research-related interventions, and (iii) the research remains active only for long-term follow-up of subjects.
 - b. Or where no subjects have been enrolled and no additional risks have been identified.
 - c. Or where the remaining research activities are limited to data analysis.
9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where the following conditions apply:
 - a. Categories two (2) through eight (8) do not apply, and
 - b. The HSPRC has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

Full Committee Review

Research projects that involve more than minimal risk require full board review at a convened meeting at which a quorum of HSPRC members is present. For the research to be approved, it must receive the approval of a majority of those members present. Categories of research that require a Full Committee review include:

1. Studies with procedures that present more than minimal risk to human subjects.
2. Studies involving vulnerable populations, such as prisoners, pregnant women, fetuses, neonates, or cognitively impaired individuals.
3. Studies taking place internationally (particularly those with little or no provisions for protection of human subjects).
4. Studies where information may be disclosed that could require mandatory legal reporting (e.g., child/elder abuse, drugs, etc.), or damage the participant's social standing, financial standing, or employability.
5. Studies involving deception, which raises the risk level of the subjects.
6. Studies that fall under the jurisdiction of the Food and Drug Administration.

Continuing Review

Continuing Review of all projects initially approved by Expedited Review and Full Committee Review is required at least annually. The HSPRC may require more frequent review of a project depending on the risks to human subjects. All investigators must apply for Continuing Review at least annually

- even if no changes have been made in the project,
- even if the only project activity is participant follow-up, and
- even if the only project activity is data analysis.

The Continuing Review may occur via the Expedited or Full Committee Review process.

Projects that receive Exempt Status are not required to apply for Continuing Review after initial approval by the HSPRC.

As a courtesy, the HSPRC will send Continuing Review reminders to investigators approximately 90, 60, and 30 days before a project expires. However, it is ultimately the investigator's responsibility to initiate a Continuing Review application and to allow sufficient time for the review and re-approval process to be completed before the current approval expires.

If an HSPRC approved project expires, all research activities involving human subjects must stop. These activities involve subject contact, data collection, and data analysis.

Revisions and Amendments

All revisions and amendments to a project need HSPRC approval before they are implemented.

If the investigator wants to **change anything** in the research that would impact the subjects, such as recruitment procedures, key personnel, inclusion/exclusion criteria, research procedures, the informed consent document/process, or data elements collected, the investigator must obtain HSPRC review and approval prior to implementation of the changes. The only exceptions are changes necessary to immediately protect the safety of subjects.

Student Research Projects

University of Holy Cross HSPRC policy requires that the principal investigator (PI) on an HSPRC application be an University of Holy Cross faculty, student, or staff member. The PI is responsible for the content.

HSPRC review and final approval must be given prior to any research activity/study procedures. There is no retroactive approval for data previously collected for the current study. **Failure to seek approval for student research may invalidate the study and/or result in a delayed graduation.** If it comes to the attention of the HSPRC that HSPRC approval has not been obtained for student research prior to initiation of research involving human subjects, the HSPRC will refer the student researcher and advisor(s) to the Institutional Official.

11. STEPS IN THE HSPRC APPLICATION AND REVIEW PROCESS

To obtain HSPRC approval for a human subjects research project, researchers should take the following steps:

1. **Select the type of HSPRC review that is required for the project.** Refer to Section 10 (Types of HSPRC Review) and determine if the project fits the definition of Exempt Status Review, Expedited Review, or Full Committee Review. If the investigator has any doubt about the appropriate level of review for a project (Exempt, Expedited, or Full Committee Review), the HSPRC staff is available to aid applicants in making this determination. The final determination of whether the proposed research meets federal criteria for the requested review category will be made by the HSPRC.
2. **Complete the appropriate HSPRC application form.** The **Human Subjects Research Protocol: Exempt Review** form will be used for projects requesting Exempt Status Review. The **Human Subjects Research Protocol: Expedited or Full Review** form will be used for projects requesting Expedited Review or requiring Full Committee Review. The forms may be downloaded from the University of Holy Cross HSPRC website. A student performing research must complete the HSPRC application under the guidance of his/her faculty advisor. The faculty advisor must serve as the principal investigator on the HSPRC application form. The student's advisor is responsible for guiding the student investigator in the development of the research plan as well as the conduct of the research project.
3. **Submit the application to the HSPRC for review.** Upon receipt of the application, the HSPRC Coordinator will pre-review the application for completion before it is submitted

to the HSPRC Chair for review. An HSPRC application may be submitted to the HSPRC office at any time. The HSPRC will attempt to complete Exempt and Expedited Reviews within 10 business days of the receipt of the application. Full Committee Reviews occur when the full committee convenes on the last Wednesday of each month. To receive review of a project requiring Full Committee Review, the application must be complete and received by the HSPRC office a minimum of two weeks before the scheduled meeting.

4. **The HSPRC will notify the researcher with the outcome of the review.** The HSPRC will attempt to notify the researcher of the outcome within 5 business days of completion of the review. The HSPRC will notify the researcher in writing with one of the following outcomes after the application has been reviewed:
 - **Approved.** The application is complete, the risks to subjects are minimal/minimized, and the procedures are appropriate. The HSPRC gives approval for the research to be conducted. Although a project has been approved by the HSPRC, institutional administrative officials may disapprove a project for considerations outside the scope of the HSPRC.
 - **Approved Pending Modifications.** The application is complete but there are minor issues/changes that must be addressed before the project can begin. Once a satisfactory response to these contingencies is received and approved by the HSPRC, the review is complete.
 - **Deferred for Re-review.** Applications that are found to have deficiencies (risk to subjects, unclear procedures, serious omissions, ethical issues, or major contingencies) will be deferred. The researcher is sent a memorandum listing the concerns that must be addressed for approval to proceed. The researcher's response is reviewed by the HSPRC and will be approved or deferred until all issues are addressed satisfactorily.
 - **Disapproved.** Criteria for HSPRC approval are not met. Only the Full Committee may disapprove a study. Institutional administrative officials may not override this decision.
 - **Not Human Subjects Research.** Projects that do not meet the definition of *research* and/or do not involve *human subjects*.

5. **Conduct the research and report to the HSPRC as necessary.** Once the application is approved, the researcher may begin recruiting subjects and conducting study procedures. The researcher must verify that HSPRC approval has been obtained from all participating institutions in collaborative activities with other institutions. During the course of the study, the researcher must submit reports to the HSPRC if any of the following occurs:
 - **Revisions and amendments to the approved protocol.** Changes to the original submitted study must be reviewed and approved by the HSPRC before they are implemented.

- **Adverse events/effects and unanticipated problems involving risks to subjects or others.** The HSPRC must be notified immediately if any undue harms result from the study.
 - **Complaints regarding human subjects research.** The HSPRC must be notified immediately if any complaints, either from the subjects or the study staff, are made regarding the research study.
 - **Breach of confidentiality.** If any personal/confidential data has been inappropriately disclosed by any member of the study staff, the HSPRC must be notified immediately.
 - Refer to Section 13 (Reporting Project Revisions and Amendments) and Section 14 (Reporting Research-Related Problems) for additional reporting requirements.
6. **Submit an application for Continuing Review to the HSPRC.** Projects that received approval following an Expedited Review or a Full Committee Review must apply for Continuing Review at least once every 365 days from the date of initial approval. The HSPRC may require the Continuing Review to occur more frequently depending on the risk to participants compared to the potential benefits.

If an HSPRC approved project expires, all research activities involving human subjects must stop. These activities involve subject contact, data collection, and data analysis. As a courtesy, the HSPRC will send continuing review reminders to investigators approximately 90, 60, and 30 days before a project expires. However, it is ultimately the investigator's responsibility to initiate a continuing review application and to allow sufficient time for the review and re-approval process to be completed before the current approval expires.

7. **Maintain secure records of the study.** The investigator will ensure the confidentiality and security of all information obtained from and about human subjects, both during the study and after the study. The investigator will make provisions for the secured retention of complete research records and all research materials for at least three years after the completion of the study.

12. CRITERIA FOR HSPRC APPROVAL

Federal policy lists criteria [45 CFR 46.111 and 21 CFR 56.111] that the HSPRC must apply when reviewing research involving human subjects. To approve a research project, the HSPRC must determine that the following conditions exist at the time of initial review and at each subsequent review conducted by the HSPRC:

1. **Study design.** The HSPRC will consider the scientific design of a study to determine that risks to subjects are minimized by using procedures that are consistent with sound research design and the benefits of the research justify the potential risks. The HSPRC must assess whether the study design will produce reliable and valid information of

sufficient value and importance to justify the risks. Where appropriate, the HSPRC will determine if the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects.

2. **Risks and benefits.** The HSPRC will assess whether the risks to subjects are minimized. The HSPRC will further assess whether the risks are reasonable in relation to any anticipated benefits to the subject. The HSPRC will consider only those immediate risks and benefits to subjects that may result from research. The federal regulations do not allow the HSPRC to evaluate the possible long range effect of applying the knowledge gained through the research.
3. **Equitable selection of subjects.** The selection of subjects should be equitable and free of coercion or undue influence. The HSPRC will consider the purpose of the research and the setting of the research. The HSPRC will closely examine research that is conducted on Native American tribal lands or that targets vulnerable subject populations, such as prisoners, pregnant women, fetuses or neonates, children, subjects with cognitive disorders, or economically or educationally disadvantaged subjects.
4. **Identification of subjects and confidentiality.** The HSPRC will determine if there are adequate provisions to protect the privacy of subjects and to maintain confidentiality of data.
5. **The informed consent process.** Informed consent is a process, not a document. The consent form is the written documentation of the consent process. The HSPRC will carefully review the informed consent process: when, where and how consent is obtained and any provisions for the ongoing consent of subjects (see Section 8, Informed Consent, for additional information).
6. **Additional review.** The HSPRC will determine whether the research requires more than annual review and may require an appropriate monitoring procedure that could include monitoring of the consent process, observation of the research procedures, and review of research related records.

13. REPORTING PROJECT REVISIONS AND AMENDMENTS

No protocol, informed consent process, or informed consent document may be modified without prior approval from the HSPRC unless it is necessary to eliminate an apparent and immediate hazard to one or more of the participants.

Modification means any change. It encompasses two commonly used terms: A *revision* is a change in something that exists, such as increasing the number of participants. An *amendment* adds something new, such as a person who will obtain informed consent.

Commonly Reviewed Modifications

The list below includes some common modifications that the University of Holy Cross HSPRC reviews:

1. A change in the procedures of the protocol, such as:
 - when the inclusion/exclusion criteria change,

- when a genetic or sample-storage component is added or changed,
 - when the protocol is no longer open for enrollment of new participants,
 - when a sponsor temporarily suspends enrollment,
 - when the protocol ends.
2. A change in the procedures used to recruit or enroll participants, such as:
 - new or newly revised advertisements,
 - new or newly revised script or questionnaire for screening
 - a change in the circumstances under which informed consent is discussed or obtained,
 - a change in the wording or format of the informed consent document.
 3. Changes in study personnel, such as:
 - adding or removing an investigator,
 - adding or removing key personnel,
 - adding or removing persons who are involved in the informed consent process,
 - changing the Principal Investigator.

Application Procedures for Modifications

Any planned modification must be submitted to the HSPRC for review and approval before being implemented or used with participants.

Change in principal investigator. In this case,

1. The current Principal Investigator notifies the HSPRC that he or she has relinquished the responsibilities of Principal Investigator to the person named, or will do so on a specified date.
2. The newly named Principal Investigator notifies the HSPRC that he or she has read the protocol and agrees to accept the responsibilities of Principal Investigator.

Changes in the informed consent document. When a modification makes it necessary to change the informed consent document, regardless of whether any participants are enrolled, include two copies of the revised consent form:

1. One “mark-up” copy showing all changes from the previous version (e.g., highlighting all additions and striking-through all the deletions). You may use the “track changes” function available in most word processing software.
2. One “clean” copy for the HSPRC-approval stamp, without highlighting or outdated text.

Addendum informed consent documents. If participants have already signed a consent document and it becomes necessary to inform them of modifications or new information, an addendum informed consent document may be necessary when:

1. The protocol is open for recruitment and enrollment,

2. some participants are already enrolled, **and**
3. the change might be related to the participants' willingness to continue their participation in the study.

OR

1. The protocol is closed to enrollment, **and**
2. the change might be related to the participants' willingness to allow the continued use of data from their participation.

The FDA does not require re-consenting of participants who have completed their active participation in the study, or who are still actively participating when the change will not affect their participation, for example when the change will be implemented only for subsequently enrolled participants.

Modifications to eliminate apparent immediate hazards to human subjects. There are situations where a serious unanticipated event or adverse event requires an immediate change to an application in order to relieve an apparent immediate hazard to research subjects. In these situations, the principal investigator may implement a change necessary to protect the welfare of the research subjects. Investigators are encouraged to contact the HSPRC if this type of situation arises prior to implementation of the application change, if the time taken for notification does not place the subject in danger.

Investigators are required to notify the HSPRC in writing of the change within 5 working days and include a written description of the change and the events that necessitated immediate implementation of a modification to the approved protocol.

Further information. Please direct any questions about modifications to the protocol, informed consent process, or informed consent document to the HSPRC.

14. REPORTING RESEARCH-RELATED PROBLEMS

Reportable Problems

University of Holy Cross policy requires that "unanticipated problems involving risks to research subjects or others" be promptly reported to the HSPRC, the Institutional Official, the sponsor, and appropriate federal agencies. *Others*, in "research subjects or others," includes investigators, research staff, or other individuals affected by the research project.

In accord with this policy, the HSPRC has published a list of problems (below) that investigators must report to the HSPRC. The Principal Investigator must report the problems listed to the

HSPRC within the timeframes indicated. The HSPRC may request further information as necessary and will determine whether any research project that has been associated with unexpected serious harm to the participants must be terminated.

Investigators are responsible for meeting all reporting requirements that apply to their projects. For example, investigators have reporting responsibilities to sponsors of FDA-regulated research. Investigators serving as sponsors of FDA-regulated research have additional reporting responsibilities (see FDA-Regulated Research).

Investigator Reports to the HSPRC

Adverse events and safety reports that require prompt reporting should be submitted to the HSPRC.

Within 5 working days. As soon as possible but in all cases within 5 working days, the investigator must report to the HSPRC:

- Any changes to the protocol that were taken to eliminate an apparent hazard to a participant in an emergency.
- Any deviations from the investigational plan for an investigational device taken to protect the life or physical well-being of a participant in an emergency.
- Any emergency use of an FDA-regulated test article or Humanitarian Use Device prior to HSPRC approval.
- Any serious adverse event that is related or possibly related to the research, regardless of whether the event occurred at a University of Holy Cross site or non-University of Holy Cross performance site.

Within 10 working days. As soon as possible but in all cases within 10 working days, the investigator must report to the HSPRC:

- Any adverse event occurring at a performance site under University of Holy Cross HSPRC oversight that, in the opinion of the principal investigator, is both unexpected and related or possibly related to the research.
- Information that indicates a change to the risks or potential benefits of the research. For example:
 - An interim analysis or safety monitoring report indicates that frequency or magnitude of harms or benefits may be different from those initially presented to the HSPRC.
 - A paper is published from another study that shows the risks or potential benefits of the research might be different from those initially presented to the HSPRC.
- A breach of confidentiality.
- Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
- Change to the protocol taken without prior HSPRC review to eliminate an apparent immediate hazard to a research subject.
- Incarceration of a subject enrolled in a protocol not approved to enroll prisoners.

- Event that requires prompt reporting to the sponsor.
- Sponsor-imposed suspension for risk.
- Complaint of a subject when the complaint indicates unexpected risks or cannot be resolved by the research team.
- Protocol violation (i.e., an accidental or unintentional change to the HSPRC-approved protocol) that harmed subjects or others or that indicates subjects or others may be at increased risk of harm.
- Safety monitoring reports and DSMB reports from the sponsor.

HSPRC and Institutional Reporting

If the HSPRC determines that a reported event constitutes an unanticipated problem that alters the risk of the research, it promptly reports its determination and actions to the investigator and the Institutional Official. The Institutional Official, in turn, is responsible for promptly reporting the HSPRC findings to the sponsor and applicable federal agencies.

Definitions Related to Research-Related Problems

The "correct" terminology for an event can vary because different agencies use different terms. For example, a "serious adverse drug experience" under FDA regulations may or may not be an "unanticipated problem involving risks to subjects or others" under DHHS regulations. To help investigators plan their strategies for reporting, this section defines these terms in relation to University of Holy Cross requirements.

Unanticipated problems involving risks to research subjects or others includes any incident, experience, or outcome that meets **all** of the criteria below:

1. Is unexpected in terms of nature, severity, or frequency given
 - a. the research procedures that are described in the protocol-related documents, such as the HSPRC-approved Human Subjects Protocol and informed consent documents; **and**
 - b. the characteristics of the subject population being studied; **and**
2. Is related or possibly related to participation in the research (*possibly related* means there is some likelihood in the judgment of a reasonable investigator that the incident, experience, or outcome may have been caused by the procedures involved in the research); **and**
3. Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Adverse event is any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory findings), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subjects' participation in research. Adverse events encompass both physical and psychological harms.

Serious adverse event (includes *serious adverse drug or biological experience* and *unanticipated adverse device experiences* under FDA regulations) is any adverse event temporally associated with the subject's participation in research that meets **any** of the following criteria:

- Results in death.
- Is life-threatening (places the subject at immediate risk of death from the event as it occurred).
- Requires inpatient hospitalization or prolongation of existing hospitalization.
- Results in a persistent or significant disability/incapacity.
- Results in a congenital anomaly/birth defect.
- Any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition. Examples include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, and the development of drug dependency or drug abuse.

IND Safety Reports

The phrase “IND safety reports” originates in FDA regulations 21 CFR 312 Investigational New Drug Application. The regulations require a **sponsor**, not a study investigator, to submit IND safety reports to the FDA and to participating investigators.

HSPRCs are required by FDA and DHHS human subjects protection regulations to review “unanticipated problems involving risks to participants or others.” IND safety does not necessarily meet the definition of an unanticipated problem. Often, however, sponsors send IND safety reports to investigators and instruct the investigators to submit them to the HSPRC. The IND safety reports concern a product under study and such reports may not necessarily apply to events that occurred in the protocol conducted at University of Holy Cross.

The University of Holy Cross principal investigator must submit IND safety reports to the University of Holy Cross HSPRC only in the following cases:

1. When the report meets the definition of an unanticipated problem, OR
2. When an IND safety report triggers a sponsor-required change in the research protocol or consent form, OR
3. When the sponsor indicates the safety information must be reviewed by the HSPRC to determine that either a change in research is required or currently enrolled subjects should be informed of the new information.

15. HSPRC MEMBERSHIP AND MANAGEMENT

Number of members. The HSPRC will have a minimum of five members with varying expertise and backgrounds required to review and monitor the human subjects research activities commonly conducted at University of Holy Cross.

Qualification of members. The HSPRC will have sufficient expertise among its members to be able to comprehend the nature of the research, as well as other competencies necessary to interpret regulations, applicable law, ethical standards, and standards of professional practice.

Diversity of members. The HSPRC will be sufficiently qualified through the experience, expertise, and diversity of its members, to promote respect for its authority and counsel in safeguarding the rights and welfare of human subjects.

The HSPRC will include both men and women, at least one member whose primary concerns are in scientific areas, at least one member whose primary concerns are in nonscientific areas, and at least one member from the community who is not otherwise affiliated (either directly or through immediate family) with University of Holy Cross.

Every effort will be made to ensure that at least two of the following disciplines/fields of expertise will be represented on the HSPRC: Business, Education, Legal Studies, Nursing, Pharmacy, Physician Assistant Studies, and Science.

The Director of the University of Holy Cross Office of Sponsored Programs (OSP) and the HSPRC Coordinator will serve on the HSPRC as ex-officio members without voting privileges.

HSPRC membership roster. The HSPRC Coordinator will submit a copy of the HSPRC membership roster to the U.S. Department of Health and Human Services' Office for Human Research Protections along with registration renewals or updates as necessary. The membership of the HSPRC is also maintained by the University of Holy Cross Office of Sponsored Programs.

HSPRC management. The HSPRC functions administratively through the OSP.

The HSPRC Chair

Selection and Appointment. The HSPRC members are appointed by the Provost, the Chair is elected for one year. Members and chair may serve additional terms terms.

Duties. The Chair directs the HSPRC meetings in accordance with Institutional, state, and federal requirements. The Chair works closely with the HSPRC members, the OSP Director, Institutional officials, and investigators to ensure the rights and welfare of research participants are protected. The Chair designates the reviewers for expedited and full-board applications and may delegate in writing the ability to assign reviewers to the HSPRC Coordinator and others in the OSP. Such requests should be in writing, signed by the Chair, and for a period not to exceed one year. The Chair also designates the HSPRC Coordinator to send official letters and some HSPRC related correspondence on behalf of the Chair.

The Chair carries broad responsibilities and an obligation to:

1. Determine the type of HSPRC review appropriate for initial review of projects, continuing review of projects, and review of project modifications based on regulatory criteria.
2. Participate in pre-HSPRC planning meetings with the HSPRC Coordinator and the OSP to ensure optimal review procedures, assignment of duties, and preparation of convened meeting agendas.
3. Conduct expedited reviews and approvals.
4. Assign primary reviewers for full committee reviews and run the convened meetings.
5. Review revisions to protocols and other documents that are required as conditions of project approvals.
6. Sign the application form certifying project approval.
7. Document suspension of research procedures.
8. Refer to the full HSPRC research projects considered for termination of HSPRC approval.
9. Review and sign reports of unanticipated problems involving risks to research subjects or others, adverse events, complaints, or suspension or termination of a research project.
10. Assist in communications with federal agencies.
11. Assist in communicating with faculty and Institutional administration regarding HSPRC resources and functionality.
12. Assist in orientating new members to the board.
13. Delegate responsibilities to HSPRC committee members as needed.

Removal. The Chair may be removed or replaced by the provost.

HSPRC members

Selection and Appointment. University of Holy Cross faculty members are appointed by the provost and serve on the board for a three-year term. Faculty appointments to the committee begin August 1st of the year appointed and end July 30th of the final year of the appointment.

Community and/or non-affiliated HSPRC members will be appointed to the board for a three-year term and appointments have the same schedule as the University of Holy Cross faculty HSPRC members.

At the conclusion of a term, a committee member may (or may not) be appointed to an additional term.

Duties. HSPRC members are responsible for protecting the rights and welfare of human research subjects by reviewing, approving, and monitoring human subject research in a manner consistent with federal regulations, state and local laws, and Institutional guidelines and policies. Members must complete the HSPRC member training through CITI.

Removal. HSPRC members may be removed or replaced by the provost. Additionally, HSPRC members may be recused from participation in matters being decided by the HSPRC for reasons of conflict of interest or other reasons.

Use of Consultants by the HSPRC

The HSPRC is encouraged to use non-member consultants for advice and information in specialized areas as needed. These consultants may be University of Holy Cross faculty or staff, affiliates, or experts not affiliated with University of Holy Cross. The consultants may present their assessments in writing, by telephone, or in person.

The HSPRC Coordinator

Selection and Appointment. HSPRC Members will elect an HSPRC Coordinator.

Duties. The HSPRC Coordinator will coordinate the privileged and confidential institutional review and approval process of proposed research activities involving human subjects.

The HSPRC Coordinator:

1. Assists the HSPRC in complying with federal and state laws, regulations, and Institutional policies and guidelines relevant to the use of human subjects in research.
2. Communicates committee requests to investigators for additional information and revisions and review responses.
3. Prepares correspondence, reports, agendas, and certifications of review for funding agencies related to review and approval process.
4. Facilitates approval for emergency or unique opportunity situations.
5. Advises faculty, staff, and students in preparation of applications for research involving human subjects and consent documents.
6. Provides education to the University of Holy Cross community about the human subject protection process.
7. Completes the pre-review of applications.
8. Takes minutes at convened HSPRC meetings.

Removal. The HSPRC Coordinator may be removed or replaced by the HSPRC Committee.

16. CONFLICT OF INTEREST POLICY

When an investigator involved in research enrolling human subjects has disclosed a potential financial conflict of interest the Director of the Office of Sponsored Programs may refer the case to the University of Holy Cross Conflict of Interest Committee as appropriate. The Conflict of Interest Committee will review the financial disclosure, and consider the potential conflict of interest. The HSPRC will collect the information necessary to fully inform the rest of the HSPRC as recommended in Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection (DHHS, May 5, 2004).

The HSPRC will carefully consider specific mechanisms to minimize the potential adverse consequences of the conflict in an effort to optimally protect the interests of the research subjects. In general, if there are any conflict of interest issues on the part of the researcher, he/she should not be directly engaged in aspects of the trial that could be influenced inappropriately by that conflict. These could include: the design of the trial, monitoring the trial, obtaining the informed consent, adverse event reporting, or analyzing the data. The HSPRC will also consider if the source of funding and funding arrangements should be included in the consent form.

In all cases good judgment, openness of process and reliance upon objective, third party oversight can effectively minimize the potential for harm to subjects and safeguard the integrity of the research.

No selection of HSPRC members by investigators. Investigators are not allowed to select which HSPRC member will review their application.

Prohibition of participation in HSPRC deliberations and voting by investigators. Review of applications will be conducted with objectivity and in a manner to ensure the exercise of independent judgment of each member. Members may not participate in a vote by the HSPRC on actions concerning research in which they have an active role or conflict of interest related to any person or entity connected with the application. Failure to abide by these provisions may be cause for removal of a member from the HSPRC.

HSPRC members must not vote on an application if they are investigators on the application or have any other conflict of interest with any person or entity connected to an application. The HSPRC member must make any conflict of interest known to the Chair and HSPRC Coordinator. The member may provide information to the HSPRC if requested. The fact that an application is submitted by another investigator from an HSPRC member's department or area does not, in and of itself, constitute a conflict of interest.

The member is not required to identify the exact nature of the conflict of interest. They may simply inform the Chair and HSPRC Coordinator that one exists. If the member has been assigned to review an expedited application they should inform their unavailability to review the protocol to the HSPRC Coordinator as soon as they can so that the application can be reassigned to another reviewer. The member with the conflict of interest may participate in the discussion or deliberation to answer questions from the committee regarding the application under review to the same extent as any investigator when attending an HSPRC meeting. If there are no questions for the conflicted member, or after the conflicted member has answered any questions, he/she will be recused for the committee's deliberation and vote.

17. OPERATIONS OF THE HSPRC

Scheduling of Meetings

The HSPRC Coordinator will make meetings known and notify committee members of the meeting locations and times.

Receipt of Applications

Investigators may submit applications to the HSPRC office at any time. The types of HSPRC review are described in Section 10 (Types of HSPRC Review) and the review process is described in Section 11 (Steps in the HSPRC Application and Review Process). The HSPRC will attempt to review Exempt Status and Expedited Reviews within 10 business days of receipt of an application. Projects requiring Full Committee review must be submitted at least two weeks prior to the next convened meeting of the Full Committee.

Review of Applications

Pre-review. Upon receipt of all applications, the HSPRC Coordinator will pre-review the application for completeness before it is submitted to the HSPRC Chair for review. The HSPRC Chair will verify that the proposed research meets federal criteria for the requested review category. The HSPRC Coordinator will contact the investigator(s) in writing (email is acceptable) if any additional materials are required. The application will be assigned a registration number, YY-xxx, where YY indicates the last two digits of the year that the application was submitted, and xxx is the number given to the application in order of receipt.

Exempt Status Review. The HSPRC Chair, or any HSPRC member designated by the Chair, is authorized to independently review exempt status applications. If the reviewer needs additional information, he/she will communicate requests for additional information to the HSPRC Coordinator, who will ask the investigator for the information in writing. Upon receipt of the additional information, the reviewer determines whether the research activities qualify under one or more of the exemption categories. The reviewer will make a determination within 10 business days of receipt of the application. After review of the application, the reviewer will make one of the following determinations:

- *Certification of Exemption.* The reviewer determines that the protocol qualifies under one or more of the exemption categories; the project is certified exempt from HSPRC review with no changes required. An exemption notice is issued that specifies the exemption category(ies). The investigator is sent notification in writing that their project has been certified as exempt and does not require continuing HSPRC review.
- *Certification of Exemption Pending Modifications.* The reviewer determines that there are minor issues/changes that must be addressed before the project can begin. The HSPRC Coordinator will notify the investigator of the requested revisions in writing. Upon receipt of the investigator's response, the reviewer determines if the revisions are sufficient. If the reviewer determines the revisions are insufficient, the investigator may be asked to make additional modifications. This process will repeat until the reviewer determines whether the research activities qualify under one or more of the exemption categories.
- *Deferred for Re-review.* If the reviewer determines that the project does not qualify for exemption from HSPRC review, the HSPRC Coordinator will notify the investigator in

writing that the request for exemption status has been denied, and that the investigator must submit an application for either Expedited or Full Committee Review.

- *Not Human Subjects Research.* If the reviewer determines that the project does not meet the definition of *research* and/or does not involve *human subjects*, the HSPRC Coordinator will provide the investigator with a “Not Human Subjects Research” determination letter.

All members of the HSPRC committee will be informed of applications approved through Exempt Status Review at the next Full Committee meeting.

Expedited Review. The HSPRC Coordinator pre-reviews the application for completeness before it is submitted to the HSPRC Chair for review. The HSPRC Chair verifies that the proposed research meets federal criteria for Expedited Review. The Chair (or designee) selects a subcommittee of two members of the HSPRC to review the application. The HSPRC Chair may serve as one of the reviewers at his or her discretion. If the reviewers need additional information to make a determination of expedited status, they will communicate requests for additional information to the HSPRC Coordinator, who will ask the investigator for the information in writing. Upon receipt of the additional information, the reviewers will determine whether the research activities qualify under one or more of the expedited categories. The reviewers will make a determination with 10 business days of receipt of the application. After review of the application, the reviewers will make one of the following determinations:

- *Approved.* Both reviewers determine that the protocol qualifies under one or more of the expedited categories; no changes are required; all criteria for HSPRC approval are met. The approval letter will indicate if continuing review of the project is required more often than annually, based upon determination of the reviewers.
- *Approved Pending Modifications.* One or both reviewers determine that there are minor issues/changes that must be addressed before the project can begin. The HSPRC Coordinator will notify the investigator of the requested revisions in writing. Upon receipt of the investigator’s response, the reviewer(s) determine if the revisions are sufficient. If the reviewer(s) determine the revisions are insufficient, the investigator may be asked to make additional modifications. This process will repeat until the reviewer(s) determine whether the research activities qualify under one or more of the expedited categories.
- *Referred for Full Committee Review.* In the case of a split decision by the two reviewers, the application will be sent before the Full Committee for review. Only the Full Committee may disapprove a study if the criteria for HSPRC approval are not met. If one or both reviewers determine that the project does not qualify for Expedited Review, the HSPRC Coordinator will notify the investigator in writing that the application has been referred for Full Committee Review.
- *Not Human Subjects Research.* If the reviewer determines that the project does not meet the definition of *research* and/or does not involve *human subjects*, the HSPRC Coordinator will provide the investigator with a “Not Human Subjects Research” determination letter.

All members of the HSPRC committee will be informed of applications approved through Expedited Review at the next Full Committee meeting.

Full Committee Review. All human subjects research that does not qualify for Exempt or Expedited Review must receive Full Committee Review. Also evaluated by a Full Committee Review are reports of unanticipated problems, and allegations of serious and/or continuing noncompliance.

The HSPRC Coordinator conducts a pre-review of the application for completeness and forwards it to the HSPRC Chair, who determines that the project requires Full Committee Review. The Chair (or designee) selects three members of the HSPRC to serve as primary reviewers based on an appropriate balance of scientific and non-scientific expertise required for each application. If the Chair determines that the appropriate scientific expertise is not available within the HSPRC, the Chair may invite an internal or external consultant to serve as one of the primary reviewers. If the application involves vulnerable populations, such as children, cognitively impaired, or prisoner populations, the Chair may invite a special subject population representative to serve as one of the primary reviewers.

The HSPRC Coordinator distributes the application and related study materials to the primary reviewers and all other HSPRC members at least one week in advance of the scheduled meeting date to allow sufficient review of the materials. If the primary reviewers identify the need for additional information about an application, they will communicate these requests to the HSPRC Coordinator, who will ask the investigator for the information in writing. Any additional information needed for review of an application should be obtained before the full committee is convened at the scheduled meeting. All HSPRC members are expected to review and be familiar with all protocols prior to the Full Committee Review.

The Full Committee Review must be conducted at a convened meeting at which a quorum consisting of a majority of the members of the HSPRC is present, including at least one member whose primary concerns are in non-scientific areas. If an HSPRC Member is unable to attend a convened meeting, he/she is responsible for informing the HSPRC Coordinator with sufficient lead time so that an HSPRC Alternate Member may be assigned to review the proposal and attend the convened meeting. Approval of research is by a majority vote of the quorum. An HSPRC member with a conflicting interest on a project may be present to answer questions about the project, but must recuse himself/herself and may not participate in the subsequent discussion and voting. The HSPRC Coordinator is responsible for documenting a quorum in the meeting minutes and monitoring the maintenance of a quorum during the meeting. Should the quorum fail during a meeting (e.g., loss of a majority through recusal of members with conflicting interests or early departures, or absence of a non-scientist member), discussion of protocols may continue, but the HSPRC may not take further actions or votes unless the quorum can be restored. Each HSPRC member has one vote and no proxy votes are allowed.

At the discretion of the Chair and/or primary reviewers, the investigator may be invited to attend the Full Committee Review meeting (in person or by phone) for the purpose of

additional clarification or discussion. The investigator is required to leave the meeting for subsequent discussion and voting. The primary reviewers are each responsible for providing a brief summary of the project to the committee, identifying any concerns, and making a recommendation for the disposition of the application. All other HSPRC members are expected to have reviewed all materials in sufficient depth to discuss them at the convened meeting. After discussion of the application is completed, all HSPRC members will vote on one of the following determinations:

- *Approved.* A majority vote of the quorum determines that all criteria for HSPRC approval are met and that no changes are required. The approval letter will indicate if review of the project is required more often than annually, based upon determination of the committee.
- *Approved Pending Modifications.* A majority vote of the quorum determines that there are minor issues/changes that must be addressed before the project can begin. The HSPRC Coordinator will notify the investigator of the requested revisions in writing. Upon receipt of the investigator's response, the Chair will determine if the revisions are sufficient. If the Chair determines the revisions are insufficient, the investigator may be asked to make additional modifications. This process will repeat until the Chair determines that that issues/changes raised by the full committee have been adequately addressed.
- *Disapproved.* A majority vote of the quorum determines that criteria for HSPRC approval have not been met. Only the Full Committee may disapprove a study. Institutional administrative officials may not override this decision.
- *Tabled.* Criteria for a convened Full Committee Review are not met, and/or appropriate expertise is not available at the meeting.
- *Not Human Subjects Research.* If a majority vote of the quorum determines that the project does not meet the definition of *research* and/or does not involve *human subjects*, the HSPRC Coordinator will provide the investigator with a "Not Human Subjects Research" determination letter.

Continuing Review. Continuing Review of all projects initially approved by Expedited Review and Full Committee Review is required at least annually. The HSPRC may require more frequent review of a project depending on the nature of the study, the degree of risk involved to human subjects, and the vulnerability of the study population. The initial approval letter sent to investigators will include the date of approval and the date on which the project will expire. The Continuing Review may occur via the Expedited or Full Committee Review process. Projects that receive Exempt Status are not required to apply for Continuing Review after initial approval by the HSPRC.

It is the investigator's responsibility to initiate a continuing review and to allow sufficient time for the review and re-approval process to be completed before the current approval expires. If an HSPRC approved project expires, all research activities involving human subjects must stop. These activities involve subject contact and data collection.

Communication from the HSPRC to Investigators

HSPRC actions are communicated to investigators in writing by the HSPRC Coordinator within 5 business days of the rendered decision.

Stamping the Materials with HSPRC Approval

After the study materials have been reviewed and approved by the HSPRC, prior to sending the approval letter on non-exempt applications, the HSPRC Coordinator signs or stamps the English and non-English signed consent, parent permission and assent forms, and HIPAA authorization forms. The PI needs to submit these forms via e-mail to the HSPRC Coordinator to facilitate the process. The approval signature or stamp is placed on the Word version of the forms electronically and converted to PDF before sending out to the researchers. The approval includes the University of Holy Cross HSPRC number, along with the activity number, the word "Approved," the date of approval (MM/DD/YYYY), and valid until date (MM/DD/YYYY). Copies of the signed or stamped materials will be e-mailed to the researcher along with the approval. The approved materials should be used by the researchers during the consent process. This requirement does not apply when the consent process is via e-mail, verbal, or consent is embedded in a survey or questionnaire on the online system.

During continuing review, the investigator indicates if there are any changes on the forms, and submits the new forms to the HSPRC. The HSPRC will review the changes and authorize or not authorize the materials if necessary.

Appeal of HSPRC Decisions

If an HSPRC application receiving Full Committee Review is disapproved, the reasons for disapproval will be conveyed to the investigator in writing. The investigator may request the HSPRC to reconsider by responding in writing, and may request an opportunity to appear before the HSPRC. The application may be resubmitted if the reasons for disapproval have been corrected.

Cooperative Agreements and Individual Investigator Agreement

The University of Holy Cross HSPRC enters into written cooperative agreements or individual investigator agreements with the HSPRCs of other institutions when such agreements facilitate and streamline the HSPRC process while ensuring that the rights and welfare of human participants are fully protected. The cooperative agreements allow University of Holy Cross faculty, staff, and students to complete the review forms for the other institution's HSPRC and submit the form to the University of Holy Cross HSPRC. The University of Holy Cross HSPRC Coordinator documents the application form, completes administrative review, and forwards the material to the other institution's HSPRC for review. The University of Holy Cross HSPRC will receive documentation of actions taken on the application and subsequent reviews of the application from the other institution's HSPRC. This allows University of Holy Cross faculty, staff, and students to complete one HSPRC application and receive review from only one HSPRC, thus facilitating the review and approval of certain research covered by the appropriate cooperative agreement while simultaneously ensuring that human participants are fully protected.

Allegations of Non-compliance

The HSPRC will investigate any allegations of non-compliance as stipulated in the federal regulations. Any allegation will be discussed with the principal investigator of the HSPRC application in question. Any investigation of alleged non-compliance will require close cooperation and coordination with the principal investigator of the research.

If there appears to be credible evidence of non-compliance this situation will be presented to the Institutional Official. Any non-compliance based upon federal regulations will be reported to federal agencies and funding agencies as required. Based on the nature of any non-compliant activity, the HSPRC has the authority to suspend or terminate the project.

Complaints

The HSPRC Coordinator will communicate any research participants' complaints or concerns that may arise to the HSPRC Chair and OSP Director. In general the HSPRC can respond to complaints or concerns regarding the participant's rights as a paid participant or a volunteer participant in the research. The HSPRC Coordinator will assist the participant to get answers to any other complaints or concerns from the principal investigator.

Post-approval Review and Monitoring

The HSPRC may initiate reviews of approved HSPRC applications at any time. Post-approval reviews may be initiated for cause (request of the principal investigator, allegation of non-compliance, questions from research participants, post-approval monitoring, etc.) or for no cause (random sampling of approved applications, etc.). Post-approval review findings that indicate variances from approved applications, adverse events, or unanticipated events will be reported to the Institutional Official and federal agencies as required by the federal regulations. Based on the nature of any non-compliant activity, the HSPRC has the authority to suspend or terminate the project.

18. HSPRC RECORD REQUIREMENTS

The HSPRC will prepare and maintain adequate documentation of HSPRC activities, including:

1. Copies of all research proposals reviewed, scientific evaluations (if any) that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.
2. Minutes of HSPRC meetings that are in sufficient detail to show:
 - a. attendance at the meetings,
 - b. actions taken by the HSPRC,
 - c. the vote on these actions including the number of members voting for, against, and abstaining,
 - d. the basis for requiring changes in or disapproving research; and
 - e. a written summary of the discussion of controverted issues and their resolution.
3. Records of continuing review activities.
4. Copies of all correspondence between the HSPRC and the investigators.

5. A list of HSPRC members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to HSPRC deliberations; and any employment or other relationship between each member and the institution; for example: full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid consultant. Changes in HSPRC membership shall be reported to the department or agency head, unless the existence of an HHS-approved assurance is accepted. In this case, change in HSPRC membership shall be reported to the Office for Human Research Protections, HHS, or any successor office.
6. Written procedures that the HSPRC will follow:
 - a. for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution;
 - b. for determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous HSPRC review; and
 - c. for ensuring prompt reporting to the HSPRC of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which HSPRC approval has already been given, may not be initiated without HSPRC review and approval except when necessary to eliminate apparent immediate hazards to the subject.
7. Written procedures for ensuring prompt reporting to the HSPRC, appropriate institutional officials, and the department or agency head of:
 - a. any unanticipated problems involving risks to subjects or others or any serious or continuing non-compliance with this policy or the requirements or determinations of the HSPRC; and
 - b. any suspension or termination of HSPRC approval.
8. A statement in the informed consent documents that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject.

HSPRC records will be retained for at least 3 years. All records will be accessible for inspection and copying by authorized representatives of the federal department or agency at reasonable times and in a reasonable manner.

Meeting agenda, minutes, and HSPRC rosters will remain on file in the OSP as a permanent record of the committee's activities.

Policy guidance and forms will be disseminated from and stored at the OSP until replaced by new and/or revised documents.

19. DISCUSSION OF SPECIAL TOPICS AND ACTIVITIES

Alcohol

Consistent with the National Advisory Council on Alcohol Abuse and Alcoholism, University of Holy Cross recognizes the legitimate and important need for research involving the biological and behavioral effects of the ingestion of ethyl alcohol on human subjects.

It is essential that such research conform to the (ethical) principles that govern all research involving human subjects. These principles are elaborated upon in the latest report prepared for the National Institute on Alcohol Abuse and Alcoholism by the National Advisory Council on Alcohol Abuse and Alcoholism. The NIAAA website (<http://www.niaaa.nih.gov/>) provides information on research involving the administration of alcohol and also contains the latest NIAAA guidelines (<http://www.niaaa.nih.gov/Resources/ResearchResources/job22.htm>).

The HSPRC refers to and is guided by the NIAAA guidelines when reviewing research involving alcohol and researchers are strongly encouraged to review these guidelines prior to submitting applications to the HSPRC.

Depending on the nature of the research and the perceived risk to the participants the HSPRC may require frequent blood alcohol level (BAL) measurements, based on time intervals or numbers of participants. The HSPRC also may approve a limited number of initial human participants and require submission of BAL measurements for review before approving additional participants.

Certificate of Confidentiality

A certificate of Confidentiality helps researchers protect the privacy of human research participants enrolled in biomedical, behavioral, clinical, and other forms of sensitive research. These certificates are issued by the NIH. Certificates protect against compulsory legal demands, such as court orders, and subpoenas, for identifying information or identifying characteristics of a research participant. Any research that collects personally identifiable, sensitive information and that has been approved by an HSPRC is eligible for a Certificate. Federal funding is not a prerequisite for Certificate. For more information: <http://grants.nih.gov/grants/policy/coc/>

Children

University of Holy Cross adheres to Subpart D of the DHHS regulations (Additional Protections for Children Involved as Subjects in Research). Children are persons who have not attained the legal age of 18 years. The HSPRC will require that children approximately 3 years old and older provide their assent to participate in research activities. Verbal assent should be obtained from children who are approximately 3 to 6 years of age (a verbal assent script should be submitted to the HSPRC). Written assent should be obtained from children 7 through 17 years of age.

The regulations contain specific requirements and documentation for research involving children. Research that does not involve greater than minimal risk can be approved only if the HSPRC finds that adequate provisions are made for soliciting the assent of children and the permission of the parents. Research involving greater than minimal risk may be approved under three general conditions:

1. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects;
2. Research involving greater than minimal risk and no prospect of direct benefit to the individual subjects, but likely to yield generalized knowledge about the subject's disorder or condition; and
3. Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

In general, research involving children will be reviewed at the expedited or full board level. When the research involves observation of public behavior and the investigator does not participate in the activities being observed an exempt review may be utilized. Unless there are compelling reasons not to obtain parental permission and/or child assent the HSPRC will generally expect that both will be obtained.

Classroom Projects/Activities

The HSPRC does not review classroom projects/activities. Classroom projects/activities are generally considered to be conducted for a class assignment and turned in to the faculty/instructor. If the class assignment involves subjects from vulnerable populations or if the subjects are members of a certain population, the OSP should be contacted for. In certain situations where a class project will be used as part of larger research, HSPRC review and approval may be required. Contact the HSPRC Coordinator for help and assistance in determining the need for review and completing the appropriate application.

Confidentiality Agreements

Depending on the confidentiality of the material being collected, the HSPRC may request signed confidentiality agreements with certain study personnel (depending on the role in the research). Individuals with limited involvement (e.g., translator, transcriptionist, specific data analyses duties) may be asked to sign confidentiality agreements.

The HSPRC does not require confidentiality agreements in all situations except when the confidentiality (sensitivity of the material) warrants such consideration.

NOTE: Certificate of confidentiality is different from confidentiality agreement.

Facilities/Locations

Whenever University of Holy Cross faculty, staff, or students, will be conducting human subjects research at other facilities (such as hospitals, clinics, schools, school districts, factories, offices, etc.), the researcher must ensure that the outside entity is aware of the proposed research activity and has no objections (i.e., agrees to participate). Investigators are required to provide an assurance that this requirement has been met in the HSPRC application.

Genetic Research

Genetic testing and analysis is increasing and evolving rapidly. The HSPRC is concerned with protecting human participants, following OHRP/FDA advice and guidelines, and assisting researchers who are conducting genetic research.

In general, genetic research will require detailed and specific disclosure in the informed consent documents. Examples of items the HSPRC will look for:

1. Will samples be identified, confidential, or anonymous?
2. What tests/analyses will be performed on the material?
3. Will samples be destroyed (if so when) or will the samples be stored for future analyses?
4. If stored for future analyses, what type of research/analyses will be conducted? Any research study (open for any use), broad class of disease/study (diseases of the eye), or specific disease or genes only?
5. If samples will be stored for future use (data repository), how will the samples or identities remain protected?
6. If serious illnesses/diseases are detected/identified, will the participant be informed or not receive any tests results?
7. If results are given, how will the participant be counseled? More details from OHRP are available at: <http://www.hhs.gov/ohrp/policy/gina.html>

Internet (or On-line, Computer) Based Research

Use of the internet and other computer based research methods is evolving rapidly and offering many new methods for researchers to contact research participants and collect data for research (including opportunities for large numbers for participants, ease of data collection, possibilities for anonymity, etc.). All of the same HSPRC considerations and federal regulations apply; however, use of the internet also creates challenges for the HSPRC.

Recruitment. There are many methods of recruitment. Indirect recruitment would include using flyers and announcements which direct individuals to websites to participate in the research. Direct recruitment may include sending e-mails or letters directly to individuals whom the researcher would like to recruit. Researchers should ask themselves the following questions: For direct recruitment, would the participants reasonably expect the researcher to contact them regarding the research topic? Authentication can be a major challenge for the internet based research. How does the researcher know who the researcher is actually communicating with/recruiting?

Informed consent. Minimal risk research may qualify for a waiver of consent or a waiver of documentation of consent. The HSPRC would generally require the information normally contained in the consent be provided to participants so participants may make an informed decision as to whether to participate. Greater than minimal risk research may require more traditional methods, such as mailing an informed consent document and receiving the participant's signed copy, although, researchers may present suggestions to the HSPRC. Again, authentication may be a challenge for internet based consent.

Anonymity/confidentiality. The internet and computer based research can offer a “false sense” of anonymity/confidentiality. The researcher will be required to explain to the HSPRC how anonymity/confidentiality will be maintained. This will often rely on server administration/security. The use of encryption should be considered and may be encouraged or required by the HSPRC. Whenever possible, identifiable data should be de-identified. Any code linking data to identities should not be stored on the same server as the data.

Data collection. Depending on the type of data being collected, encryption may be suggested or required.

Data storage/disposal. Whenever possible, personal identifiers should be stored separately from the data and/or the codes linking the data to individuals. Back-up storage is always a consideration with electronic media. The HSPRC will be as concerned with the security of the back-up material as it is with the original material. Final data destruction of electronic media can be complex. The HSPRC will want assurance that the data deleted is truly not recoverable.

Pregnant Women, Fetuses and Neonates

The federal regulations have specific requirements for research involving pregnant women, human fetuses, and neonates. These requirements are found in Subpart B of the DHHS regulations (45 CFR Part 46):

<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartb>

Prisoners

The federal regulations have specific requirements for research involving prisoners. These requirements are found in Subpart C of the DHHS regulations (45 CFR Part 46). “Prisoner” means any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

Subpart C contains many specific requirements for research involving prisoners and should be reviewed by the researcher. In order to review research involving prisoners, the HSPRC is required to have a prisoner representative with appropriate background and expertise to serve in that capacity on the committee. The OHRP has specific guidance for involving prisoners in research at <http://www.hhs.gov/ohrp/policy/prisoner.html>

Recording (Photographs, Audio, Video)

Federal regulations require that whenever voice, video, digital, or image recordings are made, the application must be reviewed by Expedited or Full Committee Review. Expedited Reviews are possible if the research does not involve vulnerable participants and the information collected is not of a sensitive nature (e.g., sexual behavior, illegal activities, etc.).

The type of recording must be disclosed in the informed consent document. The investigator must clearly specify the steps taken to maintain the confidentiality of this identifiable information, both in the HSPRC application and in the informed consent documents. When the recording is deemed necessary to the research the informed consent must clearly indicate such. When recording is not absolutely necessary to the researcher a separate signature line for the recording acceptance should be included on the consent form so that the participant could choose to participate in the study but decline the recording of their participation.

The HSPRC considers recording for purposes of transcription only not to be part of the research that would automatically require Expedited Review.

Suicide/Depression

Research involving depression indices and scales can reveal information or disclosures that carry additional responsibilities for researchers. Studies with suicide or suicidal ideation related questions also require additional safeguards and responsibilities on the part of the researcher. The consent document will also need to contain specific information regarding the risks, resources for counseling, and reporting of certain information. The HSPRC will consider the following:

1. What is the level of risk? A brief depression index or a detailed questionnaire on suicidal ideations?
2. Is the individual obtaining consent or administering the survey/interview qualified to provide counseling? If not, how will counseling be made available?
3. Does the informed consent provide specific phone numbers or locations where counseling services can be accessed by other participants?
4. If a participant expresses the potential for self-harm or harm to others, how will the situation be handled? Who will be contacted? Such situations may require mandatory reporting to law enforcement (this should be disclosed in the informed consent).

20. SPECIAL APPROVALS

Placeholder for discussion. Radiation safety, recombinant DNA, gene therapy, vaccine trials.

21. DEFINITIONS

Anonymous: Subjects' identities are unknown to the investigator, not requested, and not given. If the only time the investigator asks for a name is for a signature on a consent form, the investigator should use implied consent, to preserve anonymity.

Application: The formal design or plan of a study's activity; specifically, the plan submitted to an HSPRC for review and to an agency for support. The application includes a description of the 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.

Assent: Agreement by subjects not competent to give legally valid informed consent (e.g., children or cognitively impaired people) to participate in the study. Refers to a child's affirmative agreement to participate in the research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

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.

Belmont Report: A statement of basic ethical principles governing research involving human subjects issued by the National Commission for the Protection of Human Subjects in 1979.

Benefit: A valued or desired outcome to the study that will be an advantage to the subjects participating. Compensation is not considered as a benefit.

Biomedical Research: Studies that are designed to evaluate the safety, effectiveness, or usefulness of an intervention including research on therapies (e.g., drugs, diet, exercise, surgical interventions, medical devices), diagnostic procedures (e.g., CAT scans, prenatal diagnosis through amniocentesis, chronic villi testing) and preventive measures (e.g., vaccines, diet, fluoridated toothpaste). It can also include normal human functioning and development, comparing the functioning of a particular physiological system at different stages of development (e.g., infancy, childhood, adolescence, adulthood, old age), or define normal childhood development. It includes research used to develop and refine hypotheses. Research on specific disease (e.g., research on the biochemical changes associated with AIDS or schizophrenia, the neurological changes associated with senile dementia of the Alzheimer type) and the human genome and genetic markers fall under biomedical research.

Biomedical research is focused on:

- Specific diseases and health conditions (mental or physical), including: detection, cause, treatment, prevention, and rehabilitation.
- Evaluation and testing of the safety, effectiveness, or usefulness of an intervention, treatment or therapy.
- Normal and abnormal physiology, human functioning, and development.
- Cognitive, emotional, and behavioral responses to real or potential health problems.
- The human genome and genetic markers.
- The incidence and prevalence of illness and injury among populations and strategies for prevention and health promotion.

Certificate of Confidentiality: A Certificate of Confidentiality helps researchers protect the privacy of human research participants enrolled in biomedical, behavioral, clinical and other forms of sensitive research. Certificates protect against compulsory legal demands, such as court orders and subpoenas, for identifying information or identifying characteristics of a research participant. Any research that collects personally identifiable, sensitive information

and that has been approved by an HSPRC is eligible for a Certificate. Federal funding is not a prerequisite for Certificate. For more information: <http://grants.nih.gov/grants/policy/coc/>

Certification: Official notification by the institution to the supporting department or agency, in accordance with the requirements of this policy, that a research or activity involving human subjects has been reviewed and approved by an HSPRC in accordance with an approved assurance.

Common Rule: A large majority of Federal Agencies simultaneously published a regulation or “Common Rule” on June 18, 1991 to regulate the conduct or support of human subject research. The rule is set forth in 45 CFR Part 46, Subpart A. Subpart A consists of 45 CFR 46.101 to 46.124.

Confidential: Subjects’ names are known to the investigator and are usually coded to a master list and/or kept separately from the data and results. This is usually used, for example, when the investigator must match test results with surveys or if there will be a follow-up survey. The investigator must know the subjects’ names.

Continuing Review: Approved research will undergo review until the completion or termination of the research, including scheduled continual reviews of research that will occur at least annually.

Crime: A crime is a wrongdoing which has been classified by the state or federal legislative body as a felony or misdemeanor.

Data: Refers to information that is collected for analysis or used to reason or make decisions.

Deception: Deception is the intentional misleading of subjects or the withholding of full information about the nature of the experiment. Misleading or omitted information might include the purpose of the research, the role of the researcher, or what procedures in the study are actually experimental. Deception increases ethical concerns because it interferes with the ability of the subject to give informed consent. However, deception is arguably necessary for certain types of behavioral research. Because humans act differently depending on circumstances, full knowledge by the subject might bias the results.

Directly or Indirectly Identifiable: Identities of individuals subjects are kept by the investigator. If subjects’ identities are inseparable from data, then data is directly identifiable. If subjects’ identities are kept separate from data with information connecting them maintained by codes and a master list, then the data is indirectly identifiable. In either case, the investigator must assure that confidentiality will be maintained, and must explain how subjects’ identities will be protected.

- **Direct identifiers:** Direct identifiers in research data or records includes names; postal address information (other than town or city, state and zip code); telephone numbers; fax numbers; e-mail addresses; social security numbers; medical record numbers; health plan

beneficiary numbers; account numbers; certificate/license numbers; vehicle identifiers and serial numbers; web universal resource locators (URLs); internet protocol (IP) address numbers; biometric identifiers, including finger and voice prints; and full face photographic images and any comparable images.

- **Identifiable data or records:** Contains information that reveals or can likely associate with the identity of the person or persons to whom the data or records pertain. Research data or records with direct identifiers removed, but which retain indirect identifiers, are still considered identifiable.
- **In-direct identifiers:** Indirect identifiers in research data or records include all geographic identifiers smaller than a state, including street address, city, county, precinct, zip code, and their equivalent postal codes, except for the initial three digits of a zip codes; all elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such age and elements may be aggregated into a single category of age 90 or older.

Educational Setting: Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (1) research on regular and special education instructional strategies, or (2) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management method.

Exempt: The Common Rule specifies that research activities may be classified as exempt in the policy if human subjects' involvement is limited to one of the listed scenarios, including studies involving the collection or study of existing data when those data either are publicly available or not personally identifiable. Exempt Status Reviews are evaluated by the HSPRC and will take approximately 10 working days for certification once they arrive at OSP.

Generalized Knowledge: Knowledge that could be applied to populations outside of the population served by the covered entity. This definition can vary. Examples of activities that typically are not generalized include:

- Biographies.
- Oral histories that are designed solely to a create record of specific historical events.
- Service or course evaluations, unless they can be generalized to other individuals.
- Services, or concepts where it is not the intention to share the results beyond University of Holy Cross or any agency supporting the research.
- Classroom exercises solely to fulfill course requirements or to train students in the use of particular methods or devices.
- Quality assurance activities designed to continuously improve the quality or performance of a department or program where it is not the intention to share the results beyond the University of Holy Cross community.

HIPAA: Health Insurance Portability and Accountability Act (HIPAA) of 1996 that protects certain health information. The Privacy Rule was issued to protect the privacy of health information that identifies individuals who are living or deceased.

Human Subject: A living individual about whom an investigator (whether professional or student) conducting research obtains:

- Data through intervention or interaction with the individual or
- Identifiable private information

Informed Consent: The knowing, legally effective consent of any individual or the individual's legally authorized representative; such consent can be obtained only under circumstances that provide the prospective subject or representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.

Interpreter/Translator: An agent of the researcher(s), who assists in the facilitation of communication between the researcher(s) and participants who are not fluent in the language of the researcher(s).

Institutional Review Board (HSPRC): A committee formed to facilitate the protection of human subjects in research.

Intentionally Identified: Subjects' names are identified in connection with the data when the research results are presented to the public. This procedure is common for journalistic-type interview studies, where subjects are public figures or in oral histories. In these cases, the investigator should seek explicit consent from the subjects for the use of their names in connection with their data

Interaction: Includes communication or interpersonal contact between investigator and subject.

Intervention: Includes both physical procedures by which data is gathered and manipulations of the subject or the subject's environment that are performed for research purposes.

HSPRC Approval: The determination by the HSPRC that the research has been reviewed and may be conducted within the constraints set forth by the HSPRC and other institutional and federal requirements.

Minimal Risk: A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed study is not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests. The definition of minimal risk for research involving prisoners differ somewhat from that given for non-institutionalized adults.

Neonate: Newborn.

Personally Identifiable Health Information: Health or medical data or information that can be linked manifestly or inferentially to an individual.

Population: A group of people in society meeting certain criteria to be eligible as subjects in a research protocol.

Principal Investigator: The individual with primary responsibility for the design and conduct of a research study.

Prisoner: A prisoner is defined by federal regulations as any individual involuntarily confined or detained in a penal institution and/or individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to incarceration.

Privacy: Control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others.

Private Information: Information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public. Private information must be individually identifiable in order for obtaining the information to constitute research involving human subjects.

Protected Health Information: Individually identifiable health information recorded in any form or medium that is created or received by a health care provider, health plan, public health authority, employer, life insurer, school or university, or health care clearinghouse and 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 for the provision of health care to an individual.

Publicly Available Data: Public sources of data, such as census data.

Research: Systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge. Activities which meet this definition constitute research for purposes of the HSPRC, whether or not the activities are conducted or supported under a program which is considered research for other purposes.

Risk: The probability of harm or injury (physical, psychological, social or economic) occurring as a result of participation in a study. Both the probability and magnitude of possible harm may vary from minimal to significant.

Significant Risk: A study's design that presents a potential for serious risk to the health, safety or welfare of the subjects.

Substance Abuse: Substance abuse refers to the use of substances when said use is causing detriment to the individual's physical health or cause the user legal, social, financial or other problems , up to, and including, endangering their lives or the lives of others. Substance abuse is not specific to illegal substances. Substance abuse also includes the abuse of legal substances which are legitimately purchased or prescribed.

Systematic: Step-by-step, methodical procedure presented or formulated as a coherent body of ideas or principles.

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