



**UNIVERSITY OF KANSAS MEDICAL CENTER
HUMAN SUBJECTS COMMITTEE
INSTRUCTIONS FOR THE **FULL-COMMITTEE APPLICATION**
TO CONDUCT HUMAN SUBJECT RESEARCH**

These instructions outline the information that the Human Subjects Committee (HSC) will use in evaluating proposed human subjects research. In its review, the HSC must determine that the proposed research meets federal standards for the protection of human subjects. Those regulations, enforced by the federal Office for Human Research Protections (OHRP), are found in 45 CFR 46 at: <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm>

The federal regulations list eight criteria that must be met for research to be approved. The criteria are summarized as follows:

- **Risks to subjects are minimized: (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.** Note that all risks should be considered, including the potential for economic, legal, physical, psychological, and social harm.
- **Risks to subjects are reasonable in relation to anticipated benefits**, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.
- **Selection of subjects is equitable.**
- **Informed consent will be sought** from each prospective subject or the subject's legally authorized representative, except in cases where the requirement is waived.
- **Informed consent will be appropriately documented** as required.
- When appropriate, the research plan makes adequate provision for **monitoring the data** collected to ensure the safety of subjects.
- When appropriate, there are adequate provisions to **protect the privacy of subjects** and to maintain the confidentiality of data.
- When some or all of the subjects are likely to be **vulnerable to coercion or undue influence**, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, **additional safeguards** have been included in the study to protect the rights and welfare of these subjects.

The HSC application is designed to facilitate the review process and demonstrate that federal criteria are met. In addition to the regulations, OHRP has published an IRB Guidebook at http://www.hhs.gov/ohrp/irb/irb_guidebook.htm which provides helpful information about research ethics and the research review process.

It is important to understand that the review process is conducted on a case-by-case basis and is specifically tailored to the proposed methodology. Additional supportive information may be requested at the discretion of the HSC in an effort to assure regulatory compliance and protection of research subjects. If you have questions, please contact the KUMC HSC at (913) 588-1240.

SECTION I: STUDY INFORMATION

Please provide all requested information about the Principal Investigator (PI) who will be conducting the human subject research. Note that students, residents, and fellows must have a faculty mentor as principal investigator. Ensure accurate contact information so that the HSC office can communicate with the PI in a timely manner.

In addition to Protocol Title, provide protocol number/version and date.

SECTION II: STUDY PERSONNEL

List all individuals who have any role in the design or conduct of the study. The personnel section has two purposes. First, it assists the HSC in evaluating whether the principal investigator and other study personnel have the appropriate qualifications, experience, and facilities to properly conduct the study and provide for the safety and welfare of subjects. Second, HSC office staff reviews the list of study personnel to ensure that the named individuals have completed training in human subjects and HIPAA training and have filed an annual Conflict of Interest disclosure. Study approval will be withheld if the training and disclosure requirements are not met.

SECTION III: FUNDING INFORMATION

State whether the study is funded or unfunded or if the investigator is seeking funding. Funding information is used to identify potential data recipients, to determine whether there are adequate resources to conduct the study, and to evaluate available resources in the event of a subject's injury. NOTE: When the proposal is part of a federal or non-federal grant application, investigators must submit the entire grant application for HSC review.

SECTION IV: LOCATION OF THE STUDY

Provide information about the location(s) for which the KUMC investigator is responsible. If KUMC is the coordinating site for a multi-center trial, the study protocol must address the PI's plan to manage data collection for all study sites.

If the KUMC investigator is entering a non-KUMC healthcare facility, a classroom and/or any other non-KUMC site, they must provide a letter of permission from that site reflecting permission for the KUMC investigator to conduct the proposed research.

For studies at non-KUMC facilities, the protocol must outline the study procedures and the potential involvement (if applicable) of employees of the non-KUMC facility. If those employees have a role in the research, then documentation is required to demonstrate regulatory compliance at the facility. Additional information is available from the HSC Office.

Studies conducted at international sites must meet additional ethical and compliance standards. The HSC Office can provide further information.

The investigator may not change the location of the research site(s) without the prior written approval of the HSC.

SECTION V: CONFLICT OF INTEREST

This section asks *study-specific* questions on conflict of interest. Requirements for this information are separate from the requirement to complete the annual Conflict of Interest Form that is required of all KUMC employees.

In addition to reporting his/her own financial interest, the principal investigator is responsible for conferring with the study team to determine whether *any* team member has a reportable financial interest *related to the study*. Team members are not required to disclose confidential details of their interest to the principal investigator; they may simply inform the principal investigator that their interest is reportable. Financial interests are not necessarily prohibited, and not all financial interests impact the welfare of human subjects. If the principal investigator or a study team member has a reportable interest, the study will be referred to the KUMC Conflict of Interest (COI) Committee. The COI Committee will work with the team member on a confidential basis, to determine whether the financial interest requires a management plan. If the committee requires a management plan, HSC approval for the project will remain pending until the plan is implemented.

SECTION VI: PROJECT INFORMATION

(a) Protocol

A research protocol must accompany the application. The full protocol will be reviewed by at least two primary reviewers. Researchers should provide as much information as possible to avoid unnecessary delays in the review process.

The protocol should cover the purpose, results of similar or related studies, rationale and specific aims, hypotheses, study design, participant selection criteria, recruitment strategies, informed consent, assignment to study groups (if applicable), study procedures, risks and benefits, confidentiality protections, statistical analyses, safety monitoring (if applicable) and record retention. The protocol should include a list of any instruments used in the study (i.e., surveys, questionnaires, inventories, etc.) as well as the instruments themselves. Also required are consent forms, instruction sheets and any other information provided to the subject. If available at the time of initial submission, include proposed advertising and recruitment materials. Proposals using investigational drugs, biologics or devices should include an investigator's brochure or study plan.

(b) Study Summary

The study summary is reviewed by all members of the HSC. The HSC is comprised of scientists with varied backgrounds, non-scientists and community members. Describe the specific scientific objectives in language that can be understood by persons who are unfamiliar with your area of research, as follows:

What is your research question (hypothesis)?

State your research question (i.e., hypothesis) so that the HSC can understand your research intent.

What study design will you use?

The study design should demonstrate how you will answer your research question. Describe the study design (e.g., single/double blind, parallel, crossover, randomized, placebo-controlled, etc.). HSC reviews the study design to ensure that the design adequately minimizes risk and that risks are reasonable in relation to potential benefits.

What are the primary outcome measures in your study?

List the primary aims of the research.

What prior studies or other preliminary evidence provide justification for conducting the proposed study?

Investigators should provide information that justifies the need for the study. The HSC uses this information to determine the appropriateness of exposing human subjects to risk for the scientific purpose.

What is standard care for the condition under study?

For clinical studies, please provide a description of the current standard of care for the health issue pertaining to your research.

Will subjects be withdrawn from standard care? If so, provide rationale.

For clinical studies, explain the circumstances for withdrawal of subjects from standard care and explain whether or not withdrawal from standard care will place subjects at a greater risk.

SECTION VII: SUBJECT SELECTION AND RECRUITMENT

(a) State the number of subjects to be pre-screened and enrolled at KUMC. “Pre-screened” subjects are those who are evaluated for study participation. “Enrolled” means those persons who meet study criteria, consent to participation and are included in the study. For multi-center studies, note the total number of planned participants.

(b) Check all categories that apply to the target population. If any vulnerable populations will be targeted, additional safeguards will apply as described below in item (c).

NOTE: Special requirements will apply if KUMC employees, students, residents, or fellows are *specifically targeted* for the research. In those cases, investigators must clearly inform these subjects that research participation is voluntary and will have no impact on employment or academic decisions.

(c) Describe special protections for any vulnerable populations. Federal regulations require that additional safeguards protect subjects who are likely to be vulnerable to coercion or undue influence, such as children, pregnant women, cognitively impaired persons, and economically or educationally disadvantaged persons. Ethical standards require that the study use the least vulnerable population to answer the research question, for example: adults before children, competent individuals before incompetent individuals, and non-institutionalized persons before including institutionalized persons. The HSC will consider the extent to which a proposed subject population is already burdened by poverty, illness, poor education, or chronic disabilities in deciding whether they are a suitable subject population.

Special protections may include mechanisms such as child assent, surrogate consent, or use of a consent monitor or patient advocate. Protections for pregnant women, fetuses, neonates and prisoners include additional regulatory requirements.

(d) Describe the plan to ensure equitable subject selection. Access to the study should be open to all persons, as appropriate to the scientific purpose. In evaluating this section, the HSC will take into account the purposes of the research, the setting in which the research will be conducted, and any special issues for research involving vulnerable populations, such as

children, prisoners, pregnant women, mentally disable persons, or economically or educationally disadvantaged persons.

(e) Investigators are asked to describe their ability to recruit the required number of subjects in a timely manner. The information assists the HSC in determining whether the investigator has sufficient resources to successfully complete the trial. Sufficient resources contribute to the protection of subjects. An incomplete trial would expose subjects to risk without the benefit of knowledge being gained, and low accrual in clinical trials might prevent the detection of important safety information.

(f) Indicate whether recruitment materials are included in the submission. If they are included, their approval will be noted in the approval letter.

Section VIII: Drugs, Biologics, Devices

Check all categories that apply to this study. Studies that use drugs, biologics, and/or devices must comply with both human subjects regulations and FDA regulations. Information about determining the need for an Investigational New Drug (IND) number is at:

http://www.fda.gov/cder/regulatory/applications/ind_page_1.htm. Investigational Device Exemptions are described at: <http://www.fda.gov/cdrh/devadvice/>

Pharmacy information must be provided for all clinical trials involving drugs or biologics. Investigators must use the services of the KU Hospital's Investigational Pharmacy if the study is an inpatient study. Use of the Investigational Pharmacy is also required if it is an outpatient study involving IV mixtures and conducted in a hospital owned area. Outpatient studies that are not managed by the Investigational Pharmacy must meet professional standards for dispensing, handling, storage, labeling, and accountability.

Section IX: Study Procedures

Check all appropriate boxes on the list of study procedures. The HSC uses this list to evaluate the level of physical, psychological, social, legal, and economic risks. This section also aims to identify early any additional compliance requirements that could cause delay. For example, HIV testing requires a disclosure of state reporting requirements in the informed consent document; use of a placebo requires disclosure of placebo risks in the consent document; drug testing and genetic testing indicate the need for additional confidentiality protections. *When the research involves radiation exposure or radioisotopes that are not considered standard care, investigators should contact the University's Radiation Safety Officer (RSO) as early as possible in the development of the protocol and consent form to get assistance on the Radiation Risk language (RSO's Phone Number 588-6132).*

Section X: Benefit/Risk Information

Provide sufficient information in this section so that the HSC can determine whether the study presents an acceptable risk/benefit ratio.

(a) and (b) Determination that the Risks are Minimized:

Provide a summary of how the risks to participants will be minimized. Risks, even when unavoidable, can be reduced or managed. The investigator is responsible for assuring that risks are reduced to those necessary to achieve the research objective.

Examples of minimizing risks include the following:

- Designing the study with adequate sample sizes to yield generalizable results
- Limiting the study population to the fewest people necessary to answer the research question
- Presenting the study design to an internal committee for review of scientific merit
- Ensuring the appropriate professional and ethical training of the study team
- Frequent monitoring by trained personnel who can identify and report unanticipated problems
- Providing formal monitoring by a Data and Safety Monitoring Board, Data Monitoring Committee or other central monitoring entity
- Coding the data and specimens to protect confidentiality
- Limiting inclusion criteria to those subjects who are most likely to benefit
- Appropriately excluding individuals or classes of subjects (*e.g.*, pregnant women, diabetics, people with high blood pressure) who may be more likely to experience study risks
- For double-blind trials, providing a mechanism for an external individual to break the code so that appropriate treatment can be provided in an emergency
- Providing the subject with a card or bracelet identifying them as an individual who is participating in a study with an investigational drug or device
- When feasible, using information from procedures that are already being done for diagnostic or treatment purposes so as not to place subjects at additional risk

(c) **Determination That the Risks Are Reasonable in Relation to Anticipated Benefits:**

Discuss why risks are reasonable in relation to benefits and in relation to the importance of the knowledge that may reasonably be expected to result. The HSC's assessment of risks and benefits takes into account the proposed subjects of the research (*e.g.*, children, pregnant women, terminally ill). The HSC considers whether or not there are other alternatives besides participating in this study (this may include standard therapy, palliative care, other research protocols, etc.). Finally, risk/benefit assessments will depend on whether the research: (1) involves anticipated benefits to individual participants; or (2) offers no benefits to participants but may result in important knowledge for society.

Section XI: Safety Monitoring

The application form should summarize the data monitoring plan to allow review by full committee.

- (1) Preparations for recognizing and responding to anticipated and unanticipated risks;
- (2) The type of data or events that are to be evaluated;
- (3) The roles of individuals who will be involved in the monitoring process (*e.g.*, the investigators, the research sponsor, a coordinating or statistical center, an independent medical monitor, a DSMB/DMC, and/or some other entity).
- (4) The time frames for reporting adverse events and unanticipated problems to the monitoring entity and the time frames for reporting unanticipated problems to the HSC.

- (5) The frequency of analysis of the events (e.g., monitoring may occur at specific points in time, after a specific number of participants have been enrolled, or upon recognition of harm).
- (6) Definition of specific triggers or stopping rules that will dictate when some action is required.
- (7) As applicable, procedures for communicating to the HSC on the outcome of reviews by the monitoring entity.

The HSC will determine the adequacy of the monitoring plan based on study-specific factors including: the phase of the study, level of risk, duration of the study, the number of sites, anticipated adverse events, disease state of the study population, vulnerability of the population and the nature of the study endpoints.

Depending on study-specific factors, monitoring may be conducted by the investigator and other study team members, an independent statistician, representatives of the sponsor (e.g., medical monitor, safety monitoring committee), or by an independent monitoring board

At its discretion, the HSC may require a data and safety monitoring board (DSMB) if one is not already in place. A DSMB is most often required for high risk studies or when the investigator and/or the institution have a potential conflict of interest.

Section XII: Informed Consent Process

(a) Check all boxes that apply to the study, to indicate the type of consent process being proposed. Investigators must ensure that the potential subject has all pertinent information and ample time to consider participation at the start of the study. The standard of informed consent also means that subjects remain fully informed of new information as the study progresses.

WRITTEN CONSENT: The HSC will require the investigator to develop an Informed Consent document that includes the following elements:

Informed Consent Checklist - Basic and Additional Elements To avoid delays in the review process, please include the following in the consent document:

Basic Elements

- _____ A statement that the study involves research
- _____ An explanation of the purpose of the research
- _____ The expected duration of the subject's participation
- _____ A description of the procedures to be followed
- _____ Identification of any procedures which are experimental
- _____ A description of any reasonably foreseeable risks or discomforts to the subject. *Note that potential risks may be physical, psychological, social, legal, or economic. **Any risks that may be irreversible should be clearly labeled as such.***
- _____ A description of any potential benefits to the subject or to others. *Benefits may pertain to the individual subject as well as to society. Benefits may take the form of increased knowledge, improved safety, technological advances, and better health.*
- _____ A disclosure of appropriate alternative procedures or courses of treatment, if any, that

might be advantageous to the subject

- _____ A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained
- _____ 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
- _____ An explanation of whom to contact for answers regarding the following:
 - a) questions about the research and research subjects' rights
 - b) questions about subjects' rights
 - c) whom to contact in the event of a research-related injury to the subject
- _____ A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits, to which the subject is otherwise entitled.

As applicable, the consent also must provide the following additional elements:

- _____ A description of standard care for the condition under study and how the proposed investigational treatment or procedure differs from standard care
- _____ A statement that the particular treatment or procedure may involve risks to the subject
- _____ Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent
- _____ Additional costs to the subject that may result from participation in the research
- _____ Consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject
- _____ 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
- _____ The approximate number of subjects involved in the study
- _____ Notification that the sponsor, oversight agencies and FDA (as applicable) may inspect identifiable records to verify the accuracy of the information collected

ORAL CONSENT: When an investigator requests to use an oral consent procedure, the HSC must review a copy of the oral consent script to be used. If HIPAA applies to the project, investigators should consult with the HIPAA Compliance Office about the need for an alteration of privacy authorization.

WAIVER OF CONSENT PROCEDURE: The HSC may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waive the requirements to obtain informed consent provided the HSC finds and documents that:

- (1) the research involves no more than minimal risk to the subjects; AND
- (2) the waiver or alteration will not adversely affect the rights and welfare of the subjects;
AND
- (3) the research could not practicably be carried out without the waiver or alteration;
AND
- (4) whenever appropriate, the subjects will be provided with additional pertinent information after participation.

NOTE: If investigators are requesting a waiver of consent for a study that involves individually-identifiable health information, the submission packet should include a request for a waiver of privacy authorization.

(b) This section obtains information about the process that will be used to obtain “legally effective informed consent.” Legally effective informed consent is a process that enables persons to voluntarily decide whether or not to participate as a research subject. An appropriate consent process implements the ethical principle of autonomy or “respect for persons” while it educates the potential subject in terms that he/she can understand.

Section XIII. Privacy and Confidentiality

In order to approve the project, the HSC must determine that there are adequate provisions to protect the privacy of subjects and maintain the confidentiality of data. For certain studies, an invasion of privacy or breach of confidentiality may present a significant risk of serious harm to subjects (*e.g.*, as when the researcher obtains information about subjects that would, if disclosed by the researcher, jeopardize their jobs or lead to their prosecution for criminal behavior). Privacy and confidentiality are distinct concepts, and the protections should be described separately.

(a) Describe privacy protections as potential subjects are identified and approached for study participation. If identifiable records are used to identify subjects prior to informed consent, then investigators must comply with HIPAA privacy standards about access to records. In biomedical studies, privacy is further respected by ensuring that the first recruitment contact comes from someone who has a treatment relationship with the patient. Finally, privacy is respected by conducting the consent interview in a non-public setting, to protect the conversation from being overheard.

(b) Describe how you will protect privacy during the conduct of the study. Privacy is protected by using personal information only in the manner described in the consent form and by sharing study information only with those who have been authorized to receive it.

(c) Describe confidentiality protections. Confidentiality of data is ensured by good data practices. These include locked file cabinets, storage of electronic data on the campus network that has firewall protection, strong passwords on computer files, and data access only for those involved in the study. Confidentiality also concerns persons and groups who will receive data. Data recipients should be those who have a legitimate role in the study, and potential data recipients should be disclosed in the consent form.

(d) When the study involves the use of sensitive information, investigators should consider the need for a federal Certificate of Confidentiality. Information about obtaining such a certificate is found at: <http://grants2.nih.gov/grants/policy/coc/>

(e) Describe how subjects will be identified. This information will be evaluated for standards related to research ethics and HIPAA. If subject selection involves a chart review by persons not involved in the individual’s care, the application packet should include a request for a waiver of privacy authorization, found at:

http://www.kumc.edu/hipaa/forms/KUMC_Research_Waiver_Application.doc

Section XIV: Pediatric Studies Only

Indicate the investigator's judgment about the level of risk to child subjects. The HSC's review of research involving children as subjects must consider the benefits, risks, and discomforts inherent in the proposed research and assess their justification in light of the expected benefits to the child-subject or to society as a whole. In calculating the degree of risk and benefit, the HSC weighs the circumstances of the subjects, the magnitude of risks from the research procedures, and the potential benefits the research may provide.

The federal regulations require the HSC to classify research involving children into one of four categories and to document their discussions of the risks and benefits of the research study. The four categories of research involving children that may be approved by the HSC, based on degree of risk and benefit to individual subjects, are as follows:

1. Research not involving greater than minimal risk [45 CFR 46.404].
2. Research involving greater than minimal risk, but presenting the prospect of direct benefit to an individual subject. Research in this category is approvable provided: (a) the risk is justified by the anticipated benefit to the subject; and (b) the relationship of risk to benefit is at least as favorable as any available alternative approach [45 CFR 46.405].
3. Research involving greater than minimal risk with no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition. Research in this category is approvable provided: (a) the risk represents a minor increase over minimal risk; (b) the intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational settings; and (c) the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition that is of vital importance for the understanding or amelioration of the subject's disorder or condition [45 CFR 46.406].
4. Research that is not otherwise approvable, but which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. Research that is not approvable under 45 CFR 46.404, 46.405, or 46.406 may be conducted or funded by DHHS provided that the IRB, and the Secretary, after consultation with a panel of experts, finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a significant problem affecting the health and welfare of children. The panel of experts must also find that the research will be conducted in accordance with sound ethical principles [45 CFR 46.407].

In all cases, the HSC must determine that adequate provisions have been made for soliciting the assent of children and the permission of their parents or guardians. When appropriate for the age of the children, the HSC requires both a parental consent form and a separate child assent form.

Section XV: Cancer and Cancer-related studies

Please indicate whether the protocol relates to cancer or cancer prevention. All cancer-related studies must obtain prior approval from the Kansas Masonic Cancer Research Institute's Protocol Review and Monitoring Committee. Cancer or cancer related studies may include the following:

Therapeutic/Treatment: Studies that evaluate new treatments or new ways to use a current or new treatment such as drugs or combinations, therapies, surgical or radiation techniques, or methods of treatment for cancer.

Prevention: Studies that look at cancer prevention, high-risk characteristics, and recurrence.

Ancillary or Companion: Studies that are in addition to or related to another study in order to get additional information on a group of subjects or to look at a different set of variables collected, or a cancer-related study that involves management of disease, quality of life, or follow-up on survival.

Correlative: Laboratory based cancer research involving human participants, human tissue or related by-products.

Section XVI: Certifications

Please obtain the appropriate signatures on your application prior to submission. Applications submitted without signatures will be returned. Department Chairs should sign applications for faculty members. If the principal investigator is the department chair, administrative certification should be obtained from the appropriate associate dean, dean, or other executive administrator.