Guide for Human Subjects Research at the University of Iowa
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Scope: This document provides information on human subjects research policies and is intended for use by investigators, researchers, Institutional Review Board members, members of other UI committees, other UI administrators or others who are involved with research that involves human participants.

Chapter 1 -- Introduction to the IRB and Human Subjects Office

The University of Iowa operates a centralized program to review and approve all research involving human subjects through the Office of the Vice President for Research. Before a research project involving human subjects is initiated, it must be reviewed and approved by an Institutional Review Board (IRB). While the principal investigator has primary responsibility for the conduct of the study, the University of Iowa IRBs are responsible for protecting the rights and welfare of study participants. Through its Federalwide Assurance, the University is held accountable to federal agencies that have established guidelines for the use of human subjects in research.

The University of Iowa Human Subjects Office (HSO), located at 105 HLHS, has several functions:
- To provide administrative support for three Institutional Review Boards
- To provide assistance to investigators who are preparing IRB applications
- To process applications as efficiently as possible
- To maintain records of IRB reviews and approvals
- To coordinate submissions to the Western Institutional Review Board (WIRB)

Other Administrative Offices for Researchers with External Support

In addition to the IRB review process, all human research with external support (funds, drugs, or devices) must be processed through the one of two areas within the Division of Sponsored Programs located in 100 Gilmore Hall. There are two primary types of support sources:

(1) For projects with government, foundation, or voluntary health agency support:
    Contact: dsp@uiowa.edu
    Note: Funding is not released until IRB approval has been obtained for the project.

or

(2) For projects with corporate support:
    Contact: dsp-contracts@uiowa.edu
    Note: IRB approval is not released to investigators until the contract has been finalized.

The Division of Sponsored Programs review and provide institutional sign-off for all research projects, including negotiation of contracts if applicable. Also, these offices notify the Grant Accounting Office to establish research accounts.
Chapter 2 — Foundation of Human Subjects Protection

The National Research Act of 1974 established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Commission was charged with identifying the basic ethical principles that should underlie research with human subjects. Members of the Commission were from diverse disciplines, including medicine, law, religion, and bioethics. In 1979 the Commission published its report, Ethical Principles and Guidelines for the Protection of Human Subjects of Research, commonly called the Belmont Report. Today's federal regulations for the protection of human subjects are based on the ethical principles of the Belmont Report. The Belmont Report identifies three basic principles as particularly relevant to the ethics of research involving human subjects.

A. Respect for Persons

The principle of respect for persons means respecting an individual's autonomy (his/her right to make decisions for him/herself). This means that individuals should participate in research voluntarily and be given enough information to make an informed decision about whether or not to participate.

"To respect autonomy is to give weight to autonomous persons' considered opinions and choices... To show lack of respect for an autonomous agent is to repudiate that person's considered judgments, to deny an individual the freedom to act on those considered judgments, or to withhold information ... when there are no compelling reasons to do so."

The Belmont Report further specifies that persons with diminished autonomy (e.g., children, cognitively impaired persons) are entitled to protection.

The principle of respect for persons is embodied in the informed consent process. Three elements crucial to the informed consent process are information, comprehension, and voluntariness. While there is no standard for the amount of information to be provided to potential volunteers, the Belmont Report suggests that "the extent and nature of information should be such that persons, knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether they wish to participate in the furthering of knowledge."

The investigator should adapt the presentation of information to the subject's level of understanding. When a subject's comprehension is limited due to immaturity or mental disability, respect still requires that the person be given the opportunity to choose whether or not to participate to the extent they are able. Permission from a third party who understands the subject's situation and can act in the subject's best interest further protects the subject from harm.

Finally, in order to be voluntary, consent must be given under conditions that are free of coercion and undue influence. "Unjustifiable pressures usually occur when persons in positions of authority or commanding influence ... urge a course of action for a subject." Consent is valid only if the agreement to participate in the research is given voluntarily.
B. Beneficence

The principle of beneficence requires that the investigator not only protect individuals from harm, but make efforts to secure their well-being.

"Two general rules have been formulated as complementary expressions of beneficent actions in this sense: (1) do not harm and (2) maximize possible benefits and minimize possible harms... The problem posed by these imperatives is to decide when it is justifiable to seek certain benefits despite the risks involved, and when the benefits should be foregone because of the risks."

Risks to subjects may be balanced against the benefits to subjects directly or to society as a whole.

When the investigator and the IRB perform a systematic risk/benefit assessment, they are applying the principle of beneficence. Risk is evaluated by considering both the chance or probability of harm and the severity or magnitude of the possible harm. Risk may include consideration of psychological, physical, legal, social, and economic harm. Benefit, on the other hand, is the anticipated positive value of the research to either the subject directly or to society in terms of knowledge to be gained.

"...the risks and benefits affecting the immediate research subject will normally carry special weight. On the other hand, interests other than those of the subject may on some occasions be sufficient by themselves to justify the risks involved in the research, so long as the subjects' rights have been protected. Beneficence thus requires that we protect against risk of harm to subjects and also that we be concerned about the loss of the substantial benefits that might be gained from research."

C. Justice

The principle of justice means that the benefits and burdens of the research are fairly distributed.

"For example, during the 19th and early 20th centuries the burdens of serving as research subjects fell largely upon poor ward patients, while the benefits of improved medical care flowed primarily to private patients... In this country, in the 1940's, the Tuskegee syphilis study used disadvantaged, rural black men to study the untreated course of a disease that is by no means confined to that population."

It is a violation of the principle of justice to select a class of subjects (e.g., welfare patients, an ethnic minority, institutionalized persons) simply because of easy availability rather than for reasons directly related to the problem being studied. The principle of justice requires that there be fair procedures and outcomes in the selection of research subjects.

"Justice is relevant to the selection of subjects of research at two levels: the social and the individual. Individual justice in the selection of subjects would require that researchers exhibit fairness: thus, they should not offer potentially beneficial research only to some patients who are in their favor or select only 'undesirable' persons for risky research. Social justice requires that distinction be drawn between classes of subjects that ought, and ought not, to participate in any
particular kind of research, based on the ability of members of that class to bear burdens and on the appropriateness of placing further burdens on already burdened persons."

Chapter 3  -- Scope and Purpose of Institutional Review Boards

A.  Federal Regulatory Authority

The federal regulations require the establishment of an Institutional Review Board (IRB) to review and approve human subjects research prior to its initiation. These regulations also require that specific points of information be included in the informed consent process, and that, in most cases, the consent process itself be documented in writing.

The University of Iowa has filed an assurance of compliance, called a Federalwide Assurance (FWA), with the Office for Human Research Protections (OHRP) in the Department of Health and Human Services (DHHS). The University is required to enter into this agreement because it receives federal funding for research involving human subjects. An FWA is a binding written agreement between the University of Iowa and DHHS. It states that the University is guided by the ethical principles of the Belmont Report, and will comply with federal regulations (45 Code of Federal Regulations Part 46, or simply 45 CFR 46) for all federally-funded human subjects research. The Food and Drug Administration (FDA) regulations under which the IRB operate are found at 21 CFR 56.

The Federalwide Assurance describes the responsibilities of the institution, the Office of the Vice President for Research, the IRBs, and the investigator. All investigators at the University of Iowa are expected to conduct research in accordance with the provisions of the Federalwide Assurance, regardless of the funding source for their research.

The Iowa City Veterans Affairs Medical Center (VAHCS) has its own FWA. The University of Iowa provides IRB review for human subjects research conducted at the Iowa City VAHCS under a Memorandum of Understanding.

Primary responsibility for assuring that the rights and welfare of the individuals involved are protected rests with principal investigator conducting the research. Faculty members who assign or supervise research conducted by students have an obligation to consider carefully whether those students are qualified to safeguard adequately the rights and welfare of subjects.

B.  What Needs Review by the IRB

Before a research project involving human subjects is initiated, it must be reviewed and approved by a University of Iowa Institutional Review Board (IRB).

All research involving human subjects must be reviewed by the IRB if

- the research is sponsored by the institution, OR
- the research is conducted by or under the direction of any employee or agent of this institution (including students) in connection with his or her institutional responsibilities, OR
- the research is conducted by or under the direction of any employee or agent of this institution using any property or facility of this institution, OR
an employee or agent of this institution (including students) meet the criteria for “engaged in research” as defined in OHRP guidance of October 16, 2008 (www.hhs.gov/ohrp/humansubjects/assurance/engage.htm) OR

the research involves the use of this institution's non-public information to identify or contact human subjects.

At the University of Iowa, “Human Subjects Research” is defined as an activity that either:

- Meets the DHHS definition of “research” and involves “human subjects” as defined by the DHHS regulations; OR
- Meets the FDA definition of “research” and involves “human subjects” as defined by FDA regulations.

1. What is Research?

**DHHS Definition of Research**

DHHS regulations define research as a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research even if they are a component of a larger non-research activity (e.g., instruction, demonstration).

**FDA Definition of Research**

FDA defines research as any experiment that involves a test article and one or more human subjects and that is one of the following:

- subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or
- is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.
- The term does not include experiments that are subject to the provision of 21CFR58, regarding nonclinical laboratory studies. (From 21 CFR 50.3(c); 21 CFR 56.102(c))

Under FDA regulations, the terms “research” and “clinical investigation” are synonymous.

*What is a test article?*

A test article means any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the Federal Food, Drug & Cosmetic Act. [21CFR50.3(j)].

For drug studies, FDA defines a clinical investigation as any experiment in which a drug is administered or dispensed to, or used involving one or more human subjects. For the purposes of this part, an experiment is any use of a drug except for the use of a marketed drug in the course of
medical practice. [21 CFR 312.3(b)]
(http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.3)

For device studies FDA defines an investigation as a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device. [21 CFR 812.3(h)]
(http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.3)

2. Who is a Human Subject?

DHHS Definition of a Human Subject

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

(a) data through intervention or interaction with the individual, OR
(b) identifiable private information.

What characterizes an intervention with an individual?

Intervention includes both physical procedures by which data are gathered (e.g., drawing blood) and manipulations of the subject or the subject's environment that are performed for research purposes.

An example of such an intervention would be an educational intervention such as randomly providing pamphlets to some patient-subjects that provide tips for sticking to medication regimens while not providing that information to a set of other patient-subjects with the intent of testing the effectiveness of such a program on increasing compliance with medication schedules. This type of project involves human subjects because there is an intervention (handing out educational pamphlets) with living individuals.

What characterizes an interaction with an individual?

Interactions include communication or interpersonal contact between investigator and subject.

An example of an interaction with a human subject could be a blood draw or finger stick for research purposes. In this case, there is an interaction with a living individual that is being done outside of the realm of regular patient care.

What is private information?

Private information includes 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 (e.g., medical record information).

Private information must be individually identifiable (i.e. the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.
Obtaining identifiable private information means receiving or accessing identifiable private information or identifiable specimens for research purposes. “Obtain” includes an investigator’s use, study, or analysis for research purposes of identifiable private information or identifiable specimens already in the possession of the investigator. In general, private information or specimens are individually identifiable when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

“Coded” in this sense means that:

a) identifying information (such as name or social security number) that would enable the investigators to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, and/or combination thereof (i.e., the code); AND

b) a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

What defines a “living” individual?
Since the definition of a human subject is a "living" individual, research which only involves only autopsy materials, cadavers or death records is not considered human subjects research and is not reviewed by the IRB.

*FDA Definition of Human Subject*
FDAs regulations define human subject as an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient. For research involving medical devices, a human subject is also an individual on whose specimen an investigational device is used.

3. **How do I know if my project is research involving human subjects?**

The University of Iowa IRB Chairs or HSO staff provides guidance and determination with regard to when an activity meets either the DHHS definitions for human subjects research or FDA definitions for clinical investigation with human subjects. Requests for determinations may be submitted via the HawkIRB application by completing a Human Subjects Research Determination form (HSRD). This short form is reviewed primarily within 48 hours of submission by the IRB Chair or their designee. A formal memo will be provided for those submissions that are not considered to meet the regulatory definition of Human Subjects Research. For those studies that do meet the regulatory definition of Human Subjects Research, a new project application is automatically initiated on the Principal Investigator’s behalf based on responses provided in the HSRD form. The remaining application will need to be completed and submitted for IRB review and approval prior to initiation of the research. Additional information on the Human Subjects Research Determination process can be found [here](#).

4. **Are researchers required to complete Human Subjects Protections Certification prior to submitting a research study to the IRB for review?**

Yes. All investigators conducting human subjects research at the University of Iowa or the VAHCS are required to complete an education program and become "certified" in human subject protections.
Who is required to obtain this education under this policy?

- All members of the research team, including the principal investigator and all other individuals (faculty, staff, or student) who have contact or interactions with research subjects or with their private, identifiable information;
- Faculty supervisors of student research projects;
- Investigators who are not affiliated with the UI, who are engaged in a UI research study and whose IRB of record will be IRB-01, IRB-02, or IRB-03 as designated by a formal, written agreement.

How do I become certified under this policy?

The option available for becoming certified is by completing the UI or VAHCS modules of the online tutorial called CITI. Instructions can be found on the HSO Website or here on how to complete this Human Subjects Protections Certification. For IRB-03 VAHCS researchers, completion of all applicable human subjects certification(s) and credentialing are required. If VA credentialing has not been completed, individuals cannot be added as research team members to the research project. If you are a VAHCS researcher and need to be assigned a HawkID for research purposes, please contact the VA research office to make this request.

C. University of Iowa Institutional Review Boards

There are three Institutional Review Boards at the University of Iowa. IRB-01, IRB-02, and IRB-03 review and approve research in accordance with Department of Health and Human Services (DHHS) regulations at 45 CFR 46 (e.g. biomedical, social science, or business). In addition, for studies involving products regulated by the Food and Drug Administration (FDA) regulations, the University of Iowa IRB-01 and IRB-02 complies with the requirements set forth in 21 CFR 11, 21 CFR 50, 21 CFR 56, 21 CFR 312, and 21 CFR 812 and 21 CFR 814, Subpart H. When research involving products regulated by the FDA is funded, supported, or conducted by FDA and/or DHHS, both the DHHS and FDA regulations apply. IRB-03 also reviews and approves research in accordance with 38 CFR 16 and 17 as well as applicable VA policies regarding human studies performed at the VAHCS or by VAHCS investigators as set forth in VHA 1200.05.

1. IRB-01 (Biomedical)

Any research project involving human participants, regardless of its source of funding, is reviewed by IRB-01 if:

- the Principal Investigator (PI) is from the College of Dentistry, Medicine, Pharmacy, or the Department of Communication Sciences and Disorders in the College of Liberal Arts.
- the PI is from the College of Nursing or the College of Public Health and the study involves a physical or physiological intervention that is greater than minimal risk, OR
- the study involves access to or creation of any protected health information about the subject that is maintained in a health care provider's records.

The chair may, at his/her discretion, refer the review of a research project to IRB-02 if he/she determines

(a) there is a conflict of interest among the investigator(s) and board member(s), OR
(b) there is more appropriate expertise on the other board.
Exceptions: Research projects involving the VAHCS, FDA-regulated research or that include physical or physiologic interventions involving more than minimal risk may not be referred to IRB-02 for review. For these projects, when there is a conflict of interest, the IRB-01 or IRB-03 chair can assign the project to a non-conflicted member of the IRB or, in the case of a potential conflict with more than one member of an assembled full board, the chair can re-schedule the project to a future meeting where there are no conflicts of interest. For these projects, when the IRB-01 or IRB-03 chair determines the need for more appropriate expertise, the chair can invite a consultant with more appropriate expertise to review and present the project to the IRB-01 or IRB-03 membership.

IRB-01 meets every Thursday (primarily for new project reviews and modifications) and every other Monday (continuing reviews). More information about IRB-01, including the current chairs and roster (list of members) request, is available by clicking on the following link, IRB-01.

IRB-01 is also convened on an “as-needed” basis for the specific purpose of reviewing reports of noncompliance, to make policy determinations, or to conduct additional project reviews. These convened full-board meetings are scheduled so that the majority of those in attendance are the rostered primary members of the board. When IRB-01 is convened in this manner, it is referred to as the IRB-01 Executive Committee.

2. IRB-02 (Behavioral/Social Science)

Any research project involving human participants, regardless of funding, is reviewed by IRB-02 if the Principal Investigator is from the College of Business, Education, Engineering, Law, Liberal Arts (except for those from the Department of Communication Sciences and Disorders), College of Public Health or Nursing.

EXCEPTIONS: Even if the PI is from one of the preceding colleges, IRB-01 would review the project if:
- the PI is from the College of Nursing or Public Health and the study involves a physical or physiologic intervention that is greater than minimal risk, OR
- the study involves access to or creation of any protected health information about the subject that is maintained in a health care provider's records.

The chair may, at his/her discretion, refer the review of a research project to IRB-01 if he/she determines
(a) there is a conflict of interest among the investigator(s) and board member(s), or
(b) there is more appropriate expertise on the other board.

IRB-02 meets as needed on fourth Wednesday of each month. More information about IRB-02, including the current chairs and roster (list of members) request, is available by clicking on the following link, IRB-02.

Policy issues and reports of noncompliance are reviewed during regularly scheduled IRB-02 full board meetings.
3. **IRB-03 (VAHCS)**

Any research project involving the Iowa City VAHCS, which includes VA patients, records, or occurs on VAHCS premises, is under the purview of IRB-03. Any research projects that occur at both the Iowa City VAHCS and the University of Iowa locations are reviewed under IRB-03. Any research project that has a research team member with a VA appointment will be required to be reviewed under IRB-03. The IRB-03 Full Board committee meets as needed typically once a month. Policy issues and reports of noncompliance are reviewed during regularly scheduled IRB-03 full board meetings.

D. **Non-UI Institutional Review Boards**

**Western IRB (WIRB)**

New protocols that are both industry-sponsored AND industry-initiated have the option to be sent to a commercial IRB for review. The University of Iowa has contracted with the Western Institutional Review Board (WIRB) for the review and oversight of these projects conducted at the UI. No other commercial IRB review will be allowed for these projects. Projects previously approved by IRB-01 will NOT be transferred to WIRB. For studies that have both an industry sponsor and are industry initiated remaining with the UI IRB for review, a one-time fee of $2000 is assessed.

WIRB provides IRB review and oversight for any research that meets the first condition:

- The study has funding from DOD Navy and requires the institution to sign a DOD addendum to the UI FWA.

The researcher has the option to submit to WIRB for research that meet all of the following conditions:

- The project is a study that involves human subjects and is designed to evaluate prospectively the safety and/or effectiveness of new drugs or devices or behavioral interventions.
- The protocol for the project was designed and written by the sponsor.
- The sponsor holds all INDs/IDEs for the protocol.
- The only sponsor of the research is a for-profit entity/company.
- The UI investigator has not previously submitted the study to another UI IRB.

The project does NOT involve any of the following:

1. Xenotransplantation
2. Embryonic stem cells
3. Review and approval by the **UI Institutional Biosafety Committee** (e.g. studies that involve recombinant DNA)
4. Any research funds from a federal or other not-for-profit funding source.

Studies that are eligible for WIRB review and oversight may not be conducted at the VAHCS. The VAHCS does not, at this time, allow the use of commercial IRBs for review of human subjects research at VAHCS facilities.
The UI IRB has the right to decide to keep any new research protocol at the UI for review by IRB-01. This will be decided on a case-by-case basis by an IRB-01 Chair or the HSO Director. The UI may decide to retain a protocol for IRB-01 review if the protocol has significant local context issues such as a unique vulnerable population, involves an investigative team that has had previous serious and/or continuing noncompliance issues, or if the research design or intervention adds unusual risk for the subjects. If you have questions about whether or not your protocol should be processed with the UI/WIRB procedures, please call the HSO.

If your project is designated to go to WIRB for review, there are some requirements of the UI prior to submission. First, the Division of Sponsored Programs must have a copy of the contract and protocol for the project. Second, if the project requires review by any UI committees, you will need to have the approvals of the applicable committee prior to WIRB review. Finally, you will need to send all of your WIRB submission materials to the UI HSO so that the UI/WIRB coordinator can check for your other committee approvals and the required UI consent language. At this point, the UI HSO will provide you with an approval memo for submitting your new project materials to WIRB for review. The HSO does charge a $1000 one-time fee for this administrative review. The following link will provide you a detailed description of the UI process for submission to WIRB and any required forms: UI/WIRB Procedures.

Once your new project has been sent to WIRB for review, WIRB is then the IRB of record for the project. At that point, all correspondence regarding the project will be with WIRB. In addition, after WIRB approval of the project, you will submit all modifications, continuing reviews, serious and/or unexpected adverse experiences, major protocol violations that result in additional risks to subjects, and project closure notice to WIRB using WIRB procedures. The UI HSO will not coordinate any of these submissions after the approval of the new project by WIRB. For more information on WIRB procedures, check out their website at www.wirb.com.

Chapter 4 – Categories of Review
Research projects are reviewed at a full board meeting unless the project qualifies for exempt status (see Section A of this chapter) or can be classified as minimal risk and meets the criteria for expedited review (see Section B of this chapter). The type of review depends on the risks posed to potential subjects.

What is minimal risk?

The federal regulations provide two definitions of minimal risk – one for prisoners, and another for non-prisoners (general population).

For the general population, the federal regulations define minimal risk to mean 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) & 21 CFR 56.102(i)]

For prisoners, the federal regulations define minimal risk as the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons. [45 CFR 46.303(d)]

The definition of minimal risk serves as a starting point for the IRB chair's determination
of the category of review. Risk includes not only physical risk, but also psychological, emotional, legal, social, and financial or the risk of loss of privacy or breach of confidentiality. If a project falls into an exempt category or meets the definition of minimal risk and falls into an expedited category as described below, the IRB chairs (or his/her IRB member designee) may review and approve the project. The categories of exempt and expedited are mutually exclusive. If the research does not fall into one of the exempt categories, then the expedited review categories are considered.

A. Exempt Human Subjects Research

The University of Iowa policy requires that all human subjects research proposals be submitted for review. However, certain types of human subjects research may be classified as exempt from the federal regulations [45 CFR 46.101(b) (DHHS) and 21 CFR 56.104 (FDA)]. The IRB chair (or his/her IRB member designee) is the sole authority for determining whether the research meets the exempt criteria, based on review and approval of the investigator's New Project application to the IRB. In making this determination the IRB chair (or his/her IRB member designee) considers any ethical issues including coercion. Exempt research projects have no requirement for continuing review.

Exemptions under the DHHS regulations are limited to research activities in which the only involvement of human subjects will be in one or more of the following categories.

1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of 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, interview procedures, or observation of public behavior, unless:
   (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
   (ii) disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability, loss of insurability 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 not otherwise exempt under category 2 above, if:
   (i) the human subjects are elected or appointed public officials or candidates for public office; OR
   (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

4) Research involving the collection or study of existing data, documents, records, pathological specimens, 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.

NOTE: Existing data, documents, records, pathological or diagnostic specimens means the
items must be “on the shelf” or in existence at the time the project is submitted to the IRB for review.

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: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payments for benefits or services under those programs.

NOTE: For exempt research and demonstration projects, the IRB chair (or his/her IRB member designee) determines that the project:

- Be conducted pursuant to specific federal statutory authority,
- Has no statutory requirements for IRB review,
- Does not involve significant physical invasions or intrusions upon the privacy interests of the subject,
- Has authorization or concurrence by the funding agency.

6) Taste and food quality evaluation and consumer acceptance studies (i) if wholesome foods without additives are consumed; or (ii) if 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 FDA or approved by the EPA or the Food Safety and Inspection Service of the US Department of Agriculture.

The exemption criteria above do not apply to research involving prisoners. (Subpart C of 45 CFR 46).

In addition, the exemption criteria listed as #2 above, does not apply to research involving children (Subpart D of 45 CFR 46) except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.

Unless at least one of the following criteria is true, clinical investigations involving human participants are subject to IRB review under FDA regulations

Exempt research under the FDA regulations:
1) Any investigation which commenced before July 27, 1981 and was subject to requirements for IRB review under FDA regulations before that date, provided that the investigation remains subject to review of an IRB which meets the FDA requirements in effect before July 27, 1981.

2) Any investigation commenced before July 27, 1981 and was not otherwise subject to requirements for IRB review under Food and Drug Administration regulations before that date.

3) Emergency use of a test article (see definition in Chapter 3, Section B1), provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test
article at the institution is subject to IRB review. See Chapter 9, Section “Emergency Use of a Drug or Device”

4) Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if 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 Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

When both DHHS and FDA regulations apply to research involving human subjects, the UI IRB applies the most restrictive regulations from each to the research being conducted to ensure the protections of the rights and welfare of the human participants.

B. Expedited Review

Federal regulations recognize certain kinds of research that may be reviewed by an IRB through an expedited review procedure [45 CFR 46.110 (DHHS) and 21 CFR 56.110 (FDA)]. Expedited review means that the IRB chairs (or his/her IRB member designee) are responsible for the review and approval. *Expedited review does not mean that the review occurs quickly.*

The IRB chair (or his/her IRB member designee) is the sole authority for determining whether the research meets the expedited criteria, based on review and approval of the investigator's application to the IRB. The chair (or his/her IRB member designee) retains the discretionary right to require full board review, even when the project appears to meet the criteria for expedited review. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless the investigator has documented that reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

The IRB Chair designates an experienced IRB member to conduct expedited review(s) consistent with the member’s expertise. When an application is submitted to the IRB, the application undergoes an initial administrative pre-screening process to ensure that the application is complete. Once the application is complete, the staff member who conducts administrative pre-screen sends the application to the appropriate person based on a pre-defined path of review and list of reviewers that includes IRB Chairs and Chair-designees for expedited review and application analysts to prepare for full board review.

The expedited review process may be used for the initial review of projects involving a) no more than minimal risk, and b) only those procedures listed in one or more of the following categories. The activities listed are not deemed to be of minimal risk simply because they are included on the list. Inclusion on the list merely means that the activity is eligible for expedited review when the specific circumstances of the proposed research involve no more than minimal risk to human subjects. If the research project as a whole involves more than minimal risk, it must be reviewed by the full board even if the activities are limited to those listed.
1) Research on drugs for which an investigational new drug application is not required or research on medical devices for which a) an investigational device exemption application is not required or b) 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, amounts drawn may not exceed 550 ml in an 8 weeks period and no more than 2 times per week; OR

   (b) from other adults and children, considering age, weight, and health, 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/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. Examples:
   (a) hair and nail clippings, in a nondisfiguring manner;
   (b) deciduous teeth at the time of exfoliation or if routine patient care indicates a need for extraction;
   (c) permanent teeth if patient care indicates a need for extraction;
   (d) excreta and external secretions (including sweat);
   (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or applying a dilute citric solution to the tongue;
   (f) placenta removed at delivery;
   (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
   (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;
   (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
   (j) sputum collected after saline mist nebulization.

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:
   (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 nonresearch purposes (such as medical treatment or diagnosis).

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.

Modifications to previously approved research projects may be expedited if the modification involves only a minor modification to the approved project during the (one year or less) period of approval. See Chapter 7, Section A below for a definition of minor modification.

The continuing review of research may be reviewed using the expedited procedures in the following instances:

- If the project was previously reviewed and approved using the expedited procedure and conditions have not changed such that the research would no longer be eligible for expedited review (e.g. protocol change or experience shows the research to be of greater than minimal risk).

- if continuing review of the research was previously approved by the convened IRB and conditions have changed to make the research eligible for expedited review under criteria 1 through 7 above (e.g. research is within those categories and experience confirms the research to be of no greater than minimal risk)

- if continuing review of the research was previously approved by the convened IRB and (a) the research is permanently closed to the enrollment of new subjects, and all subjects have completed all research-related interventions, and the research remains active only for long-term follow-up of subjects; or (b) no subjects have been enrolled and no additional risks have been identified; or (c) the remaining research activities are limited to data analysis.

- if continuing review of the research was previously approved by the convened IRB and a) the research is not conducted under an investigational new drug application or an investigational device exemption, and b) the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk, and c) no additional risks have been identified since IRB review at a convened meeting.
The expedited review procedure is not used for the continuing review of research where the research involves more than minimal risk (except for when no subjects have been enrolled and no additional risks have been identified) or where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections are implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal (except for when no subjects have been enrolled and no additional risks have been identified). The expedited review procedure is not used for classified research.

No studies involving prisoners may be reviewed under expedited procedures regardless of whether or not they meet the criteria above EXCEPT for new studies limited in scope to retrospective review of prisoners’ records and minor modifications to already approved research. In the case of these exceptions, approval of the research can only be granted after review of and comment on the protocol by the prisoner advocate member of the IRB.

C. Full Board Review

Human subjects research that is not classified as exempt or expedited requires review by the full IRB at a convened meeting.

How often does the full board meet to review applications?

IRB-01 meets once or twice each week, and IRB-02 is scheduled to meet twice a month. IRB-03 is scheduled to meet once a month, as needed.

How far in advance should I submit my application if it requires full board review?

Due to the volume for IRB-01, and the bi-monthly meetings for IRB-02, investigators are advised to allow a minimum of three to four weeks for an application to be scheduled for review at a convened meeting. IRB-03 investigators are advised to allow a minimum of four weeks for an application to be scheduled for review based on the IRB-03 meeting monthly schedule.

A full board meeting may be canceled by the chair due to:

a) insufficient number of applications requiring full board review,
b) University or VA holiday,
c) inability to secure a quorum for attendance, or
d) other reasons as may arise that make a scheduled meeting unnecessary or otherwise inappropriate.

How are projects reviewed by the full board?

The University of Iowa IRBs use a primary reviewer system for full board reviews. Application materials are normally sent to the IRB members scheduled to attend a meeting at least one week in advance of the meeting. All members attending the meeting receive the application itself, the Informed Consent Document, and other materials such as advertisements or recruitment letters. One member who is designated by the chair as the primary reviewer for a project, also receives the complete grant application or protocol, any sample consent documents (DHHS or other sponsor sample consent, if available) and for investigational drug/device studies, the Investigator's Brochure. At the discretion of the chair and/or primary reviewer, the investigator
may be invited to attend the meeting for the purpose of additional clarification or discussion. The investigator will be asked to leave the meeting for subsequent discussion and voting. The primary reviewer leads the discussion of each project at the full board meeting.

The board determines whether the project meets the criteria for approval or whether revisions to the study design are required. The Informed Consent Document is reviewed for accuracy, clarity, and inclusion of required and optional elements of consent. The primary reviewer makes a recommendation to the convened IRB to:

1) approve as submitted;
2) approve pending receipt and review of required minor revisions to study procedures, Informed Consent Document(s), or other written materials;
3) table pending review at a subsequent full board meeting after receipt of significant additional information or revisions, or
4) disapprove.

At the discretion of the chair, voting by a show of hands. The members vote to abstain, agree or disagree with the recommendation and, by a majority of those present at the meeting (when a quorum is constituted), the recommendation is either approved or disapproved.

Written minutes of each full board meeting include:
- which IRB (IRB-01, IRB-02, or IRB-03) reviewed the project,
- attendance (those recused or not present are named),
- actions taken by the board
- the number of votes to agree, disagree, and the number abstaining (without individual identification),
- protocol-specific regulatory determinations,
- justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample informed consent document (if there is one),
- Whenever a significant risk/non-significant risk determination is made, the rationale for the significant risk/non-significant risk device determination.
- the basis for requiring changes in or disapproving the research,
- the length of time until the next review (not to exceed one year),
- a summary of the discussion of controverted issues and their resolution,
- specific comments relevant to inclusion of certain populations in the research, and
- where appropriate, information regarding expedited approvals, modifications, terminations, emergency/single patient use, unanticipated problems involving risks to subjects or others, and any other business appropriate for board meetings.

D. Special Types of Approval – These only apply to specific, funded projects.

1. Overall Approval

Overall approval is limited to an IRB application for a training grant, center grant, or program project grant that involves human subjects. This type of approval allows the Principal Investigator and Sponsored Programs to provide a single IRB approval date to the funding agency for the overall award itself. Overall approval is therefore an administrative tool. It does not indicate approval for any of the specific projects described in the grant.

Human subjects may not be enrolled in any of the specific projects described in the grant under an overall approval alone. Overall approval is given via the expedited review procedure.
To obtain approval for the individual projects described in the training grant, center grant, or program project grant, the principal investigator of each individual project should submit a New Project Application through HawkIRB for each project that involves human subjects. When completing the application form for each individual project in HawkIRB, the investigator should indicate the funding source as the funding agency that provided the overall award.

2. Concept Approval

Concept approval is limited to an IRB application for a funded project where the funding agency has approved an initial period of time for development of the final protocol, questionnaires, data forms, or similar activities. Since the IRB may not approve "draft" protocols or Informed Consent Documents, concept approval shows that the IRB has approved the study in concept only, so that Sponsored Programs can award the funds for the preliminary work. Concept approval is therefore an administrative tool. It does not indicate approval for the enrollment of human subjects.

Human subjects may not be enrolled in a project given concept approval. Concept approval is given via the expedited review procedure. To obtain approval for enrolling human subjects, the investigator should submit a Modification/Update Form in HawkIRB for the study that received concept approval. In the Modification/Update Form, you should change Question IV.1 to indicate that you want the Regular review. This will open up additional questions for you to answer in order to complete the application. An Informed Consent Document and any other materials, such as interview scripts or questionnaires, should be attached to the Modification/Update Form.

Chapter 5 -- The Informed Consent Process

A. The Process of Consent and Assent

1. Consent & Assent

Obtaining informed consent is a basic ethical obligation for researchers. The process of consent should ensure that potential subjects are provided with information about the research project that is understandable and permits the subject to make an informed and voluntary decision about whether or not to participate. The amount of information and the manner of presentation is generally related to the complexity and risk involved in the research study. While the initial process is prospective and takes place prior to any research activity, consent should also be an ongoing educational interaction between the investigator and the research subject that continues throughout the study.

The informed consent process is not an exercise in persuasion. If an investigator has a relationship with potential subjects (physician-patient, instructor-student, employer-employee), care should be taken to avoid recruitment methods that may be seen as coercive due to the special relationship between parties.

Except in certain minimal risk studies, the Informed Consent Document:
- is typically signed after the investigator has verbally explained the purpose and procedures involved in the study, answered questions, and otherwise provided information that permits the subject to make a prospective, informed decision.
- must be signed and dated before any study data collection procedures begin.
- must be obtained using only the methods described and IRB approved within the HawkIRB application.
serves as a written source of information for the subject and documents the fact that the process of consent occurred.

Consent is a legal concept. Only legally competent adults can give legally effective informed consent. Children and those individuals who are not competent to provide consent should be given the opportunity to assent to participate in the research project. Assent is a knowledgeable agreement to participate in the project. Adequate provisions should be made for soliciting the independent, non-coerced assent from children or cognitively impaired persons who are capable of a knowledgeable agreement. In general, the IRB recommends that children age seven and older, and most cognitively impaired adults, be given the opportunity to assent.

If the person from whom assent is sought refuses, the person should not be enrolled, even if the parent or legally authorized representative gives permission. (The IRB may waive assent of children with life-threatening illnesses who are eligible for research treatment protocols.) Alternatively, if the person from whom assent is sought agrees to participate, the person may not be enrolled if the parent or legally authorized representative does not give permission. In rare circumstances, depending on the nature of the study and the age and circumstances of the child, the IRB may waive the requirement for parental or legally authorized representative permission.

The subject must affirmatively agree to participate in a research study. The UI does not recognize a “passive” consent (i.e. the assumption of agreement to participation in the absence of any response). For example, sending a letter home to parents telling them that the research is taking place in a school and giving them the opportunity to object if they do not want their child to participate is NOT recognized as a valid consent process by the UI IRBs.

An enrolled subject is anyone who has signed an Informed Consent Document, whether or not that individual actually completes the study. Thus, someone who signs a consent document but is determined during screening to be ineligible, or chooses not to continue, must still be counted as an enrolled subject.

In cases where assent is obtained from a child or cognitively impaired subject, permission must also be obtained from a legally authorized representative. [NOTE: See Chapter 8, Section D, Vulnerable Populations, for more information about enrolling cognitively impaired subjects in research studies.]

A child by DHHS definition is a person who has not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. By FDA definition, a child is a person who has not attained the legal age for consent to treatments or procedures involved in clinical investigations, under the applicable law of the jurisdiction in which the clinical investigation will be conducted. For purposes of research conducted in the state of Iowa, the term “child” as used in both the DHHS and FDA definitions is analogous to “minor” under Iowa Code and is viewed as “an unmarried person under the age of eighteen years.” (Iowa Code 600A.2(12))

In cases of human subjects research under the authority of the UI IRB(s) but conducted outside of the state of Iowa, the UI IRB confers with the UI Office of General Counsel regarding the applicability of other state, national, or international laws to the particular project. These cases are identified in the pre-review process of an application to the IRB and the advice of counsel is sought.
prior to the approval of the study. In general, the UI IRB will apply the law of the state in which the research is being conducted. For example, if a project involves children and one of the recruitment sites is in a bordering state, the laws of the bordering state will be evaluated to which individuals meet the DHHS and FDA definition of “children” at that site.

2. Legally Authorized Representative

In studies involving children in the state of Iowa, the legally authorized representative is:

- the parent, OR
- the court-appointed guardian

A legal guardian in the state of Iowa is defined as a person who is not the parent of a child, but who has been appointed by a court or juvenile court having jurisdiction over the child, to have a permanent self-sustaining relationship with the child and to make important decisions which have a permanent effect on the life and development of that child and to promote the general welfare of that child. A guardian may be a court or a juvenile court.

Unless otherwise enlarged or circumscribed by a court or juvenile court having jurisdiction over the child or by operation of law, the rights and duties of a guardian with respect to a child shall be as follows:

a. To consent to marriage, enlistment in the armed forces of the United States, or medical, psychiatric, or surgical treatment.

b. To serve as a guardian ad litem, unless the interests of the guardian conflict with the interests of the child or unless another person has been appointed guardian ad litem.

c. To serve as custodian, unless another person has been appointed custodian.

d. To make periodic visitations if the guardian does not have physical possession or custody of the child.

e. To consent to adoption and to make any other decision that the parents could have made when the parent-child relationship existed.

f. To make other decisions involving protection, education, and care and control of the child.

In studies conducted in the state of Iowa involving cognitively impaired adults, the legally authorized representative is:

- the designated proxy (such as a Durable Power of Attorney for Health Care)
- court-appointed guardian
- spouse [This does NOT include “common law” spouses]
- adult child
- parent
- adult sibling.

In studies involving cognitively impaired adults, permission must be sought from the first existing person in the above list, even if another relative is more conveniently available.

Examples:

- If a married person does not have a designated proxy or court-appointed guardian, the investigator must obtain permission from the spouse, even if an adult child or parent is present and available.
- If a divorced person has adult children and does not have a designated proxy or court-appointed guardian, then the investigator must obtain permission from an adult child, even
if a parent is present and available.

- If the potential subject is unconscious but there is an individual who claims to be the “common-law” spouse of the subject, unless you have documentation that the person is the designated proxy or court-appointed guardian of the potential subject, then you would have to obtain the permission of the next eligible LAR (i.e. adult child, parent, adult sibling).
- If the potential subject is being recruited from a site that is not in the state of Iowa (but the project is under the oversight of the UI IRB), laws governing the other site defining the legal ability of a person to consent on behalf of a subject to the subject’s participation in the procedures being conducted as part of the research will define the legally authorized representative of the subject being recruited at that site.

B. Standard Informed Consent Document

The purpose of an Informed Consent Document is to provide subjects with a written source of information for future reference and to document the fact that the process of informed consent occurred prior to the subject's participation. The form generally serves as a basis for the initial presentation of the study to the potential subject. Typically, informed consent is documented by using the written Informed Consent Document approved by the IRB and signed and dated by the subject or the subject's legally authorized representative at the time of consent. The subject or the representative must always be provided adequate opportunity to read the consent document, consider their participation, and ask questions before the consent document is signed. A copy of the Informed Consent Document should be given to the subject. Unless the investigator has requested and been granted a waiver of documentation of consent, the subject's signature on an Informed Consent Document is required prior to beginning any study procedures.

Although the research study and Consent Document must be reviewed and approved by the IRB at least once per year, subjects enrolled in the study generally sign the Informed Consent Document only once, when initially enrolled. The exception to this is when the IRB or study sponsor requires subjects to sign a revised Consent Document due to a modification in the protocol or adding new information that may affect the subject's willingness to participate further in the study. This illustrates one example of how the consent process is an ongoing interaction between the investigator and the research subject.

**Consent Template and HawkIRB**

The Informed Consent Document template is available via HawkIRB and contains the required text for preparing an Informed Consent Document. At the end of the template, there is an Appendix containing suggested language for special situations. By following the template, the investigator ensures that the basic and additional elements of consent as required by the federal regulations are included.

For all New Project applications, you must begin with the consent template that is available at the end of the HawkIRB application. In HawkIRB, the consent document is populated with template language based on your responses to various questions within the application. Thus, when you download the consent form from HawkIRB for editing prior to final submission, many of the pertinent sections of the consent template are already included.

The IRB expects the PI of the study and a contact person who is a member of the research team be listed at the top of the Informed Consent Document. The PI may be listed as both the PI and the
contact person for the study. All other members of the research team may be listed at the discretion of the PI, or may be provided in a separate listing to subjects. If a separate listing of research team members is provided, it does not need to be reviewed by the IRB unless other study information is also included on the document. **All members of the research team must continue to be listed in the HawkIRB application and IRB approved, even if they are not listed on the consent document. It is the PI’s responsibility to keep the listing of research team members in HawkIRB current (and on the consent as applicable.) Only members of the research team which are indicated as involved in the informed consent process in the HawkIRB application can review the informed consent document with a potential subject. This individual will also sign as the person who obtained consent in the appropriate section of the informed consent document.**

**NOTE:** The Informed Consent Document should not be used as a data collection tool. For example, collection of address, e-mail, screening information, phone numbers, SSN, hospital number, appointment scheduling, or other study data must not be collected on this document. Such information should be collected on a separate document. The use, storage and disposal (as applicable) of this information must be described in the HawkIRB application for review and approval by the IRB.

**Basic Elements of Informed Consent**

The basic elements of informed consent, as described in 45 CFR 46.116 (DHHS) and 21 CFR 50.25 (FDA), are as follows:

- 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.
- A description of any reasonably foreseeable risks or discomforts to the subject.
- A description of any benefits to the subject or to others which may reasonably be expected from the research.
- 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 studies regulated by the FDA, note the possibility that the Food and Drug Administration may inspect the records. [21 CFR 50.25(a)(5)]
- 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 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.
- 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.
Additional Elements of Informed Consent

The federal regulations stipulate that additional elements of informed consent should be provided when appropriate. The additional elements include:

- 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.
- Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
- Any additional costs to the subject that may result from participation in the research.
- The 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.

Common Problems with the Written Informed Consent Document

Some common problems with the Informed Consent Document include the use of jargon, technical, or scientific terms that a lay person would not understand, and units of measure given in metric rather than the lay equivalents. Ordinary language should replace technical terms (e.g., upper extremities are better referred to as arms, hematoma as a bruise, venipuncture as taking blood from your arm with a needle, and so forth.) A website that is helpful for converting medical terminology to lay language can be found by clicking on the following link, Medical Terminology in Lay Language.

But perhaps the most common problem with Informed Consent Documents is that they are written at a reading level several grades higher than the average subject would understand. Informed Consent Documents should be written at a reading level that potential subjects would understand. For most projects, an eighth grade reading level is suggested. Most word processing programs can determine a document's reading level.

Tips for writing a "user-friendly" Informed Consent Document:

- Write the Consent as though you were speaking to the person who will read it, using “you” and “your,” “we” and “our,” rather than third person.
- Use language that could be understood by a junior high student.
- Put technical jargon into lay terms (e.g., describe the amount of a blood draw in teaspoons rather than milliliters; use “cancer” rather than “carcinoma”).
- Clearly define complicated terms (e.g., randomization means the study treatment you’ll receive will be decided by chance, like flipping a coin).
- Don’t give a lot of technical information that participants don’t need to know (e.g., complicated methods of determining drug doses, exhaustive lists of specific lab tests).
Teenage Subjects and How to Handle Wording on the Consent Document

If you plan to recruit teenage subjects (in this instance, teenage means a child older than 12 but less than 18 years of age), and the Informed Consent Document is written at an appropriate reading level, both the teenager and the parent/guardian should sign the Informed Consent. The teenager’s signature on the Informed Consent Document indicates knowledgeable agreement to participate (assent), and the parent/guardian’s signature indicates legal consent.

In this situation, rather than using “you/your child,” use the word “you” throughout, and insert the following statements at the very beginning of the Consent:

- If you are the parent/guardian of a child who is being invited to be in this study, the word “you” in this document refers to your child. You will be asked to read and sign this document to give permission for your child to participate.
- If you are a teenager reading this document because you are being invited to be in this study, the word “you” in this document refers to you. You will be asked to read and sign this document to indicate your willingness to participate.

Signature Lines

In general, the Informed Consent Document must include signature lines for:

1. the subject AND [See Exception #1]
2. the person who obtained consent AND [See Exception #2]
3. for studies involving children, a parent or legal guardian; for studies involving cognitively impaired individuals, a legally authorized representative.

Exceptions:

1. In some types of studies (e.g., mail-out surveys), the investigator may request a waiver of the subject’s signature (see waiver of documentation of consent in Chapter 5 below) when submitting the New Project Application. In such cases, the conclusion of the Informed Consent Document (which could be formatted as a letter to the subject) should inform the subject that returning the survey will be considered evidence of consent.

Note: the HIPAA Privacy Rule does not permit a waiver of documentation of authorization if the study data include protected health information. Thus, studies which utilize mailed surveys and wish to also obtain HIPAA authorization to access medical record information must include a process for obtaining a signed combined consent and HIPAA authorization.

2. When there is no verbal communication with potential subjects (e.g., mail-out surveys), the signature of the person who obtained consent may also be deleted.
NOTE: An auditor/witness signature line is needed only if specifically required by the IRB or the funding agency/company. However, if this line is included on the consent, the consent must always be witnessed and this line signed.

C. Special Consenting Circumstances & Documents

1. VAHCS Consent Process
   The Veterans Affairs Medical Center requires that the standard Informed Consent Document be copied onto its own special form. The instructions for its use are on the Forms page of the Human Subjects Office website and the form is a template choice on the Consent/Assent attachments page of HawkIRB.

   If your project involves the VAHCS and tissue/sample storage for future use, you should check with the VAHCS Research Office (158-7645) to determine if this is allowable PRIOR to adding the other site to the tissue storage section of the consent document. Include a written statement from the VAHCS research office acknowledging permission to store tissue/samples for future use as an attachment to the HawkIRB application.

2. Record of Consent or UIHC Consent Process
   When a research project involves any physical interaction or specimen collection at the University of Iowa Health Care (UIHC), it is UIHC policy found under the Information Management – Medical Record Policy and Procedure manual that a signed copy of the Record of Informed Consent (RIC) be placed in the subject’s medical record chart. All content added within the Record of Consent must be approved by the IRB prior to use. The Informed Consent Document signed by the subject (or a copy) is NOT placed in the medical record. The RIC provides a link between the UIHC patient and the study in which they participate, however, it protects the privacy and confidentiality by providing limited information about the research study. The RIC is signed by the research team member who obtained consent from the subject and documents that consent has been obtained.

   A template Record of Informed Consent is available as a choice on the Consent/Assent attachments page of HawkIRB. The VAHCS does not recognize the Record of Informed Consent. Any research studies that occur under IRB-03 or at the VAHCS will be required to place the informed consent document in the medical record. The Record of Informed Consent will not be used at the VAHCS.

3. Assent Process
   An Assent Document is used when the investigator recruits subjects who, by age or circumstance, are not able to give legally effective informed consent. When legally effective informed consent cannot be obtained, the investigator should obtain the "assent" of the child or cognitively impaired subject. This form documents the child’s or cognitively impaired subject's knowledgeable agreement, or assent, to participate in a research project. The investigator should respect the decision of a child or cognitively impaired subject not to participate, even when the parent or legally authorized representative gives permission, unless specifically instructed otherwise by the IRB.

   For studies involving children, the IRB may recommend that this form be used with children who are in the 7-12 age range, but it may also be used when teenagers (as defined in Chapter 5,
Section B above) are being recruited to enhance their comprehension if the study involves complicated procedures.

When using an Assent form, the child or cognitively impaired adult should sign the Assent to indicate knowledgeable agreement (assent) to participate. In addition, the parent/guardian or legally authorized representative should sign the full Informed Consent Document to document his/her permission for the child or cognitively impaired adult to participate.

A template Assent Document is available as a choice on the Consent/Assent attachments page of HawkIRB.

4. Non-English Speaking Subjects & Consent
See the Revised Short Form Consent policy outlined on the HSO Website found here.

5. Waivers & Consent
Waiver of Documentation of Consent
In some situations, the IRB may waive the requirement for obtaining a signed Informed Consent Document. The DHHS regulations (45 CFR 46.117(c)) state that a signed consent form may be waived if the IRB determines that:

- 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;

  Example 1: Some types of studies that fall into this category are survey or interview studies that contain highly sensitive (e.g., criminal behavior, sexual behavior) questions.

  OR

- 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.

  Example 2: Studies that may meet these criteria include mail out surveys about topics that could not reasonably damage a participant's reputation or employability or be otherwise stigmatizing.

The FDA regulations (21 CFR 56.109(c)) state that a signed consent form may be waived if the IRB determines that:

- the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context; OR

- the requirements in 21 CFR 50.24 for an exception from informed consent for emergency research are met.

Waiver of documentation of consent may mean that no written document is provided to the subject at all:

Example 3: Random-dial telephone survey study. In this type of study, the telephone interview would begin with a script that includes all of the required elements of consent, but the
study subjects would receive no written information about the study, either before or after the interview. The telephone script containing the elements of consent must be included in the New Project Application to be reviewed and approved by the IRB.

The waiver of documentation of consent may also mean only that the subject's signature does not have to be obtained. The regulations stipulate that the IRB may still require that the investigator provide the subject with a written statement about the research when granting a waiver of documentation.

Example 4: In a mailed-out survey study, the IRB may determine that it is reasonable for the investigator to provide the subjects with a cover letter containing all of the basic elements of consent. The letter would simply conclude with a statement that returning the survey or questionnaire would be considered agreement to participate.

A template of an Informed Consent as a Letter to the Subject is available as a choice on the Consent/Assent attachments page of HawkIRB.

Waiver of Elements of Consent (Not available under FDA regulations)

Some research projects would not be possible if informed consent from participants were required. The IRB may consider waiving the requirement for some or all of the elements of informed consent (45 CFR 46.116(d)) only if the study is not under the authority of the FDA. The regulations state that informed consent may be waived in full or in part if the IRB determines that:

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

Example 1: Studies in which all of the elements of consent have been waived. These may be retrospective chart review studies, or studies of existing pathology specimens (all specimens to be studied have already been collected and are "on the shelf" at the time of the IRB application).

In the types of situations given in the preceding example, presuming that the study can be classified as minimal risk and that adequate provisions for protecting the confidentiality of the data are in place, the IRB chairs generally find that obtaining consent is impracticable (not possible).

There are certain types of studies in which some of the elements of consent can be waived. These include, but are not limited to, certain types of ethnographic research, and studies that require deception.

Example 2: In a minimal risk study involving playing a computer game to test subjects' responses to differential pay-offs or reinforcements, the investigator might indicate in the Informed Consent Document that the purpose of the study is to test reaction time. This deception may be necessary because the study would be compromised if subjects were told the true purpose. In this scenario, one of the basic elements of consent -- the purpose of the study -- could be waived by the IRB chair, and not included in the Informed Consent Document.

If the investigator seeks a waiver of any or all of the elements of consent, the New Project
Application should describe the reasons for the request, paying particular attention to why the research project would be "impracticable." The term "impracticable" means more than simple inconvenience - it means that the research could not be conducted without the waiver.

**Exception from Informed Consent and Waiver of Informed Consent Requirements in Certain Emergency Research**

Both the FDA regulations and the DHHS regulations allow for some types of emergency research to be conducted without prior consent of the subject or their legally authorized representative. The FDA “exception from Informed Consent” regulations are found at 21 CFR 50.24. On October 2, 1996, the Secretary of DHHS announced under 45 CFR 46.101(i), a waiver of the applicability of the 45 CFR 46 requirement for obtaining and documenting informed consent for a strictly limited class of research, involving research activities that may be carried out in human subjects who are in need of emergency therapy and for whom, because of the subjects’ medical condition and the unavailability of legally authorized representatives of the subjects, no legally effective informed consent can be obtained. See the Special Topics section on Emergency Research for additional information.

**D. Privacy and Confidentiality**

An issue of primary importance is the protection of both the privacy of research subjects and maintaining the confidentiality of data. Federal regulations [45 CFR 46.111(a)(7) (DHHS) and 21 CFR 56.111(a)(7) (FDA)] require that the IRB only approve research where there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. Although related, the concepts of privacy and confidentiality are distinct from one another. Confidentiality means the ethical or legal right that information is considered private and will be held secret unless consent is provided permitting disclosure.

Privacy is the freedom from unauthorized intrusion or the state of being let alone and able to keep certain personal information to oneself. By its nature, research may invade the privacy of individual subjects in that it may require the collection, use, or access to identifiable information that would otherwise not be shared with others. When this is required for the purposes of the research, the private information involved should be the minimum necessary to accomplish the goals of the research.

The investigator must have sound plans to protect the subject's identity, must collect only the necessary identified information to conduct the study, and must have procedures in place to maintain the confidentiality of the research records. Care should be taken to explain the mechanisms that have been devised, for example, the use of numbering or code systems or safely locked files in private offices. Furthermore, the investigator should describe who has access to the data and under what circumstances a code system may be broken. Without appropriate safeguards, problems may arise from long-term retention of records.

**Special Circumstances for Added Protections:**

1. **Video/Audio tapes and/or Photographs.** 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 after explicitly mentioning these practices.

2. **HIPAA.** If a research study involves protected health information and involves consent from subjects, the consent document signed by the subject must contain a section entitled
“Will My Health Information be Used During this Study?” This section of the consent serves as “authorization” from the subject for researchers to access or create health information about the subject. For more information about HIPAA and protected health information, click on the link on the title of this paragraph.

3. Social Security Numbers (SSNs): If a SSN is being obtained and used in the course of a research study, several actions on the part of the investigator will need to be completed as required by UI Policy. This policy would apply to all IRB-01 and IRB-02 studies as applicable. A copy of the UI policy can be viewed here and should be reviewed in its entirety for specific information relating to research studies. Section X of the HawkIRB application under question X.2 will need to be answered Yes. Section X under question X.3 will need to include ALL intended uses of the Social Security Number. Completion of this section will also trigger notification to the UI ITS department and may result in additional reporting requirements as mandated by UI ITS.

Collection of the SSN can be required only where it is legally required (for example, where IRS regulations require collection of the SSN if the subject is to be paid) or where there is a business necessity for its collection. Where neither of these situations exist, a subject may voluntarily provide his or her SSN. Whether collection is required or voluntary, the researcher is obligated to inform the subject of ALL intended SSN use(s). If collection of the SSN is not legally required or if there is no business necessity for collection of the SSN, the subject must approve all uses of the SSN by initialing his/her choice. Unless there collection of the SSN is legally required or there exists a business necessity for collection, collection of the SSN is strictly optional on the subject’s part and is not required for participation on the study. The only exception to this policy is for research projects that occur at the VAHCS. The VAHCS requires the collection of the SSN for any payment. This action can be completed by adding the new social security template section immediately following the “What Will Happen” section of the consent to inform the subject of the following information:

- The SSN is being retained for use by the research team, PI, etc.
- ALL uses/reasons why the SSN is being retained.
- Who will be provided with or use the SSN? (ie is the SSN being sent to a sponsor or coordinating center?)
- A statement informing subjects that providing the SSN for the outlined use is strictly optional and not required for participation in the study. The subject is required to initial their choice.

NIH Certificate of Confidentiality and other Safeguards to prevent potential criminal prosecution of the participating human subject.

(from NIH Office of External Research web site)

What is an NIH Certificate of Confidentiality?

Certificates of Confidentiality are issued by the National Institutes of Health (NIH) to protect the privacy of research subjects by protecting investigators and institutions from being compelled to release information that could be used to identify subjects with a research project. Certificates of Confidentiality are issued to institutions or universities where the research is conducted. They allow the investigator and others who have access to research records to refuse to disclose identifying information in any civil, criminal, administrative, legislative, or other proceedings, whether at the federal, state, or local level.
Identifying information in this context is broadly defined as any item or combination of items in the research data that could lead directly or indirectly to the identification of a research subject. By protecting researchers and institutions from being compelled to disclose information that would identify research participants, Certificates of Confidentiality help achieve the research objectives and promote participation in studies by assuring privacy to subjects.

For what types of research might I obtain a Certificate of Confidentiality?
Certificates can be used for biomedical, behavioral, clinical or other types of research that is sensitive. Sensitive means that disclosure of identifying information could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation.

Examples of sensitive research activities include but are not limited to the following:
- Collecting genetic information;
- Collecting information on psychological well-being of subjects;
- Collecting information on subjects' sexual attitudes, preferences or practices;
- Collecting data on substance abuse or other illegal risk behaviors;
- Studies where subjects may be involved in litigation related to exposures under study (e.g., breast implants, environmental or occupational exposures).

How long is the protection afforded by the Certificate in effect?
A Certificate of Confidentiality protects personally identifiable information about subjects in the research project while the Certificate is in effect. Generally, Certificates are effective on the date of issuance or upon commencement of the research project if that occurs after the date of issuance. The expiration date should correspond to the completion of the study. The Certificate will state the date upon which it becomes effective and the date upon which it expires. A Certificate of Confidentiality protects all information identifiable to any individual who participates as a research subject (i.e., about whom the investigator maintains identifying information) during any time the Certificate is in effect. An extension of coverage must be requested if the research extends beyond the expiration date of the original Certificate. However, the protection afforded by the Certificate is permanent. All personally identifiable information maintained about participants in the project while the Certificate is in effect is protected in perpetuity.

Are there circumstances when I am allowed to disclose subject research information?
While Certificates protect against involuntary disclosure, investigators should note that research subjects might voluntarily disclose their research data or information. Subjects may disclose information to physicians or other third parties. They may also authorize in writing the investigator to release the information to insurers, employers, or other third parties. In such cases, researchers may not use the Certificate to refuse disclosure. Moreover, researchers are not prevented from the voluntary disclosure of matters such as child abuse, reportable communicable diseases, or subject's threatened violence to self or others. However, if the researcher intends to make any voluntary disclosures, the consent form must specify such disclosure.

How do I let subjects know that a Certificate of Confidentiality is in effect for the study?
In the Informed Consent Document, investigators should tell research subjects that a Certificate is in effect. Subjects should be given a fair and clear explanation of the protection that it affords, including the limitations and exceptions noted above. The University of Iowa Informed Consent Document template contains suggested language to describe the protection afforded by a Certificate of Confidentiality.
How do I apply for and obtain a Certificate of Confidentiality?

The investigator may choose to apply for a Certificate of Confidentiality on his or her own, or the IRB may require that an investigator obtain a Certificate prior to conducting the research. Investigators who intend to apply for a Certificate of Confidentiality should contact the Human Subjects Office regarding procedural steps for IRB approval and communicating with NIH. Complete information regarding the NIH Certificate of Confidentiality is available on the NIH Office of Extramural Research web site.

What are the procedures at the UI?

Because NIH requires that the investigator submit an IRB-approved Consent Document that includes a description of the Certificate of Confidentiality, the investigator must wait until after receiving IRB approval before applying for the Certificate. This means that the investigator will have in hand a stamped, approved Informed Consent Document that describes the special protections of a Certificate, but will not yet have the Certificate itself. Therefore, in order to ensure that the Consent is not used before obtaining the Certificate, the HSO places a "watermark" across each page of the stamped Consent that indicates it may not to be used to enroll human subjects.

If I already have received a Certificate of Confidentiality will it cover my research if I add a substudy or make substantial changes to my protocol?

NIH reviews the informed consent document and the study protocol when determining whether or not a Certificate of Confidentiality can be granted. If there are substantial changes or substudies added to an initial protocol, the Certificate of Confidentiality will need to be amended. The investigator will be required to submit correspondence between the Principal Investigator and NIH reflecting review and approval of the additional substudy information and the most current informed consent document attached to the application. In cases where a substudy or other substantial changes have been added to the protocol, in order to ensure that the Consent is not used before obtaining an amended Certificate, the IRB will not review and approve any changes until all applicable documentation regarding the Certificate of Confidentiality is included for review.

The PI should apply for a Certificate following the instructions on the NIH web site (http://grants.nih.gov/grants/policy/coc/appl_extramural.htm). The application letter must be signed by a University of Iowa institutional official so the PI should bring the application letter to the Human Subjects Office and the HSO will obtain the institutional official's signature and return the signed letter to the PI.

UI Procedures Summarized:
1. Submit research project application to the HSO. Include an Informed Consent Document with the Certificate of Confidentiality Language inserted.
2. After project approval by the IRB, you will receive an IRB stamped, approved consent document with a “watermark” across each page. YOU MAY NOT USE THIS CONSENT DOCUMENT TO ENROLL SUBJECTS AT THIS TIME.
3. Apply for the Certificate following the instructions of the NIH web site (http://grants.nih.gov/grants/policy/coc/appl_extramural.htm). This involves crafting an application letter to the NIH.
4. After finalizing the application letter, bring it to the Human Subjects Office. HSO staff will obtain the UI institutional official’s signature and will return the signed letter to you.
5. Send application to NIH and await Certificate.
6. When you receive the Certificate from the NIH, you will need to submit a
modification application via HawkIRB. Attach a copy of the certificate.

7. The IRB chair will review the application and upon approval the “watermark” will be removed from the approved consent document and it will be released to the PI through HawkIRB.

Note: If the IRB requires you to obtain a Certificate of Confidentiality as a condition of approval, you will need to revise your consent document and send it back to our office for the “watermark.”

E. Recruitment and Subject Compensation Issues

1. Recruitment

Recruitment strategies in any form must be reviewed by the IRB PRIOR to their implementation. There are some recruitment strategies that are either not allowed or allowed in very limited circumstances at the UI. They include the use of finder’s fees or recruitment incentives and the use of “cold calling” potential research subjects.

Finders Fees/Recruitment Incentives:

UI policy strictly prohibits the acceptance or use of finders fees, recruitment incentives, or bonuses of any type to enroll study subjects. A finder’s fee or recruitment incentive may include bonuses given by sponsors to investigators or research team members (coordinators) to boost enrollment or referral fees given to physicians for referring his/her patients to another investigator’s study. Payments to investigators, research team members, or subjects for recruitment that are provided to the individual outside of the UI system are NOT allowed.

Cold Calling:

UI policy generally restricts the use of “cold calls” to recruit subjects to research studies. The VAHCS prohibits the use of cold calls to recruit subjects to research studies. An introductory letter or other informational material must first be sent or given directly to subjects prior to telephone contact. Exceptions may be made on a case-by-case basis, for example, if the potential subjects have previously agreed to be listed on a research registry for future research studies, are currently participating in a study conducted by the same investigator, or are frequently seen by or are well known to the investigator.

Acceptable strategies for recruitment of subjects for research can be varied and may include:

- Advertising to promote the study
- Direct communication with identified groups (patients, students, personnel)
- Referrals from other sources such as other physicians or disease registries
- Accessing listings such as listservs, mailing lists (with permission) and in some cases, medical records (see Partial HIPAA waiver below.)

Partial HIPAA waiver for Recruitment

What is a waiver of HIPAA authorization?

A waiver of HIPAA authorization is a regulatory determination that is made by the board. Under 45 CFR 164.512(i)(1)(i), an IRB of a covered entity can waive in full or in part the individual authorization required by HIPAA for use and disclosure of protected health information for research purposes.

In order for a research study to qualify for a waiver, the board must document that the use and
disclosure of protected health information involves no more than minimal risk to the privacy of individuals based on evidence that the study has:

- An adequate plan to protect identifiers from improper use and disclosure
- An adequate plan to destroy the identifiers at the earliest opportunity
- Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity

In order to grant a waiver, the board must also determine and document that:

- the research could not practicably be conducted without a waiver
- the research could not practicably be conducted without access to protected health information

**What types of waivers of HIPAA authorization can be granted by the IRB?**

The board or IRB Chair can determine that a study qualifies for a partial waiver or a full waiver. The IRB can grant a partial waiver to allow for limited information to be collected from the medical record. For example, a partial waiver must be granted in order to collect eligibility information about potential subjects from the medical record such as whether a person or persons have a specific disease. One situation in which the IRB might grant a full waiver is for a medical record review study that has a waiver of consent.

**Wasn’t the board already waiving authorization by declaring that the use of protected health information was ‘preparatory to research’?**

Not exactly. Although the regulations allow for use of protected health information in reviews preparatory to research [45 CFR 164.512(i)(1)(ii)], the board did not have to document that determination as a ‘waiver’ or consider the waiver criteria.

**Why is the board granting the partial waiver and documenting the waiver criteria now?**

The board is granting the partial waiver more often now for a variety of reasons:

1) The institution (UI) decided that in order to collect protected health information a partial waiver must be obtained by a research team. Although this decision is enforced by the IRB, it was not made by the IRB
2) The VA does not recognize the ‘preparatory to research’ clause in the regulations; the waiver is the only option available to VA researchers who want to access PHI prior to consent.
3) There has been increased confusion and scrutiny in the human subjects protections world about which activities can be considered ‘preparatory to research’; the only activity that the regulations name specifically as ‘preparatory to research’ is to ‘prepare a research protocol’.
4) The new HawkIRB application questions allow the board to clearly and easily view justification for waiver requests.

**Which studies should request a partial waiver of HIPAA authorization?**

Any study for which the Principal Investigator or research team plans to access or use protected health information about persons prior to their consent to participate in the research study should request the partial waiver. The access to protected health information can come from electronic or paper file medical record access or by way of the healthcare provider’s personal knowledge of the patients’ health information.

**How is the partial waiver of HIPAA authorization requested in the HawkIRB application?**
The request for a partial waiver of HIPAA authorization opens up in the application based on the PI’s response to Section VII, Question D.1, “Check all materials/methods that will be used in recruiting subjects (you will need to attach copies of all materials at the end of the application)”. In order for the waiver justification questions to open up, the PI must select the option, “Use of any information available to the researchers or their colleagues because this person is a patient OR use of any information considered to be Protected Health Information (PHI) OR review of patient/clinic records, Describe source of records”. Selecting this option opens up questions VII.D.2-VII.D.7 which address the waiver criteria listed above. However, it may be necessary to ‘read between the lines’. Researchers often describe access to PHI in the “describe” comment boxes for the options “Existing Registry/database”, “Referral from colleague”, and “Other”. The waiver justification questions will not open up if the use of PHI is described under any of these options.

What is PHI?
Protected health information (PHI) is health information that:
1) is transmitted or maintained in any form (electronic, oral, paper) by a covered entity; and
2) identifies the individual or could reasonably be used to identify the individual; and
3) 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 healthcare to an individual.

What is a ‘covered entity’?
A covered entity is:
1) a health plan
2) a health care clearinghouse (billing service)
3) a health care provider that transmits health information electronically

Is the University of Iowa a ‘covered entity’?
Yes, The University of Iowa including UIHC is a ‘hybrid entity’ which is a single legal entity with covered (e.g., UI Health Care, student health, College of Dentistry) and non-covered functions.

Is the VAHCS a ‘covered entity’?
Yes, the VAHCS is a covered entity.
Advertising Materials

IRB approval of design and content: All recruitment strategies, which include but are not limited to; the mode, method, means, and content of all such recruitment strategies must be reviewed and approved by the IRB prior to their use. Recruitment letters, posters and brochures reviewed by the IRB must contain all information, text, and graphic design elements for the final product. IRB approval would be required prior to implementation of any changes in content or graphic design of recruitment materials. Color and graphic design may make the document more attractive and appealing to potential subjects. However, design of recruitment materials must not include graphics, text, fonts, or design effects that emphasize compensation or could be coercive to potential subjects. Certain recruitment strategies (such as Noon News, press releases, mass e-mail) have guidelines for format, content and documentation of IRB approval. For example, an IRB approval stamp is required on Noon News announcements, Cambus posters and press releases distributed through UI channels. It is important to consult the guidelines for each office or department prior to the IRB-submission of the advertisement, poster or message.

Example 1: You have a study that involves comparing an investigational drug to a placebo. The advertisement for this study should therefore not mention the study drug only. Rather, it should indicate that some subjects in the study will receive a placebo, or describe the purpose of the study as comparing the investigational drug to a placebo.

Any material aimed at recruiting potential subjects into a study (including the final copy of the printed advertisement, audio or video tapes or websites) must be reviewed and approved by the IRB prior to being used. Recruitment messages in any form should not be coercive or perceived as “marketing” of the study. Suggested guidelines for an advertisement or recruitment letter or webpage appear below:

DO NOT:

- emphasize (for example, in large or bold type) the payment amount.
- include the name of commercial sponsors or products.
- use phrases such as "help needed" or "subjects wanted." Instead use "you are invited" or "participants invited."
- state or imply a certainty of a favorable outcome or other benefits beyond what is outlined in the consent document and protocol.
- Emphasize how “important” the study is or include exculpatory language
- Make flashy marketing claims or sales pitches
- make claims that the drug, biologic or device is safe or effective for the purposes under investigation.
- make claims either explicitly or implicitly that the drug, biologic or device is known to be equal or superior to any other drug, biologic, or device or inconsistent with FDA labeling.
- use terms such as “new treatment,” “new medication,” or “new drug” without explaining that it is investigational.
- promise “free medical treatment,” when the intent is only to say subjects will not be charged for taking part in the investigation.
- allow compensation for participation in a trial offered by a sponsor to include a coupon good for a discount on the purchase price of the product once it has been approved for marketing.
DO:

- include the purpose of the project and/or briefly state what is expected of the subject.
- include the time commitment required of the subject.
- include the investigator's University department affiliation and where the research will take place.
- list a contact name and phone number.
- If participants will be paid for their time/effort, it is recommended that the wording "You will be paid for your time and effort" be used, rather than specifying a specific amount. Compensation should not be excessive to the nature of the project.
- Include in summary form, the criteria that will be used to determine eligibility for the study.
- Include a brief list of benefits, if any

The following are suggestions for creating effective recruitment messages for IRB review and approval:

**Invite subjects to participate:** The title or invitation to participate should be brief and informative for potential subjects. The title should state that this is a research study. Avoid phrases such as “help needed” or “research subjects wanted.” The recommended wording is “you are invited” or “participants invited.”

**Identify who is conducting study:** State that the research study is a University of Iowa study and give the name of the department or college in which the study is conducted.

**State the purpose of the study:** Use lay terms to briefly address why the study is being done.

**Describe what subjects will be asked to do:** Provide a brief description of the study procedures subjects will be asked to do for participation in the study.

**Describe the primary inclusion / exclusion criteria:** Potential subjects need to know whether or not they would be eligible to participate. Only include the criteria that subjects would know about themselves. Limit the exclusion criteria to the most common reasons a person would be ineligible to participate. If there are a lot of inclusion/exclusion criteria, it is not necessary to list all of them.

**Include the time commitment:** Provide a general statement about the overall time commitment for the subject.

**Describe the primary study procedures:** Provide a brief overview of the main study procedures. If the study protocol includes many study activities for the subject, it is not necessary to list them all in the recruitment poster or brochure.

**State whether subjects will be paid for participation:** Do not emphasize (large font or bold type) that payment is offered. See the policy here for additional information on Inclusion of compensation amounts in recruitment materials.

**Provide contact information:** Provide the name and/or contact information for a member of the research team that the potential subject can call to find out more information about the study or to volunteer to participate. The contact information does not have to be the name and contact information for the Principal Investigator.
Example #1 (print ad):

Knee Osteoporosis Research Study
<graphic of knee here>

The University of Iowa, Department of Orthopaedics is conducting a research study on the development and progression of knee osteoporosis. Participants must be 50-79 years of age and have knee pain and/or a history of knee injury. Persons who have had both knees replaced are not eligible to participate.

Research study participants will be asked to attend 3 study visits lasting approximately 2 hours each. The study will include blood tests, questionnaires and bone density testing. You will be paid for your time and effort.

For more information contact
Amy Smith at 319-335-XXXX or 1-800-XXX-XXXX.

Example #2 (Noon News):

The Department of Ophthalmology invites teens (age 14-17) to participate in a research study about eyesight of new drivers. Subjects must have a learner’s permit or driver’s license. Parental consent required to participate. Study involves 3 visits for eye exams, interviews and behind-the-wheel testing. Compensation provided. Call 356-XXXX.

OR

ALLERGY STUDY: Interested persons are invited to participate in an allergy study being conducted by Dr. Mary Brown at the University of Iowa, Department of Internal Medicine. Study involves 6 visits over 3 months, and having blood drawn. Compensation available. If you are at least 18, have seasonal allergies, and would like more information, contact Sam Smith at 335-1111.

Example #3 (poster):

<graphic across the top: outline of 3 women with hearts in red>

Heart Disease Prevention

Women age 50-79 who are past menopause are invited to participate in a 5-year research study conducted by the University of Iowa, Department of Cardiology. This study is testing an investigational medication for the prevention of heart attacks. Some subjects will receive a placebo (inactive pill) and others will receive the investigational medication. This is a blinded study so study subjects and investigators will not know which pill subjects are receiving.

To qualify you must not have had any of the following:

- A heart attack
- Balloon angioplasty
- Heart surgery
Subjects will attend weekly visits for the first 2 weeks to determine eligibility. Random assignment to the study medication or placebo will occur at the third study visit. Follow-up visits will be scheduled at 1, 3 and 6 months and then visits will be semi-annually after that for the remainder of the 5 years.

For more information please call 1-319-384-XXXX or 1-800-XXX-XXXX

NOTE: Additional templated materials are made available on the Attachments page in HawkIRB after you have completed section VII of the application.

Use of UI staff, students or faculty as research subjects

UI Students as Research Subjects

Consistent with an overall concern that no research subject should be coerced, researchers should take particular precautions to avoid the unintentional or subliminal coercion that may occur when a potential research subject is also a student. For this reason, researchers should avoid using their own students as research subjects. Researchers who wish to use their own students should be able to provide a good scientific reason, rather than convenience, for selecting those students as research subjects. The research project should be relevant to the topic of the class, and participation should be part of the learning experience for the students.

In instances where investigators can provide a good reason for using their own students in their research, the IRB generally requires that someone other than the investigator (instructor) obtain informed consent and collect the data. When this is not possible, the IRB will consider other methods for obtaining consent and collecting data that would not reveal to the instructor whether or not a student participated in the research project until after final grades have been determined. The students should be informed of what these procedures are in the Informed Consent Document. Below are a few situations specific to the recruitment of students for research projects.

Extra Credit

The IRB may approve projects that give extra credit to students who participate in a research project only when alternative means of obtaining equivalent extra credit with equivalent effort is made available to students who do not wish to volunteer as research subjects. The IRB carefully reviews the alternatives to ensure that students are not being coerced into participating. For example, if volunteering for a survey project takes 30 minutes and the student's output is not evaluated for its quality to determine whether extra credit is given, the alternative should involve 30 minutes of effort and the output should not be evaluated (beyond assurance that a good faith effort was made).

The Informed Consent Document should make clear the consequences of withdrawing from a project prior to completion (e.g., will extra credit be given despite withdrawal?). As a general matter, the IRB favors giving credit even if the subject withdraws, unless the student withdraws immediately or there is clear evidence of bad faith on the part of the student.

Faculty Use of Class Assignments as Research Data

There may be circumstances when an investigator wishes to use required class assignments (e.g., journal entries in a communications study course) in his or her research. The course syllabus should clearly state that the assignments are required for the course, but that at the end of the semester, the instructor will ask the student to give permission to use the assignments for research purposes. It should be clear that participation will not affect a student's grade. The syllabus should
describe the procedure to be used to ensure that the instructor does not know who has consented until after final grades have been determined (e.g., Informed Consent Document could be included with ACE forms and kept in a secretary's office until after grades have been determined).

Departmental Subject Pools

Some departments or colleges employ "subject pools" where students enrolled in introductory courses are recruited by investigators from both within and outside of the department for participation in research projects. Departments or colleges may impose their own standards for the type of research that may be conducted in this setting, and for who may have access to such subjects. Investigators who recruit from "subject pools" are still required to submit their projects to the IRB for review and approval. Beyond the considerations outlined above, academic units may impose their own additional constraints on using students as research subjects.

UI staff or Research Team members as Research Subjects

The recruitment of UI staff as research subjects should be undertaken with caution and is generally not allowed. It is important that supervisors in research settings refrain from recruiting or enrolling their own employees and staff to participate in their research. There can be inherent coercion in these situations and so should be avoided. However, the recruitment of UI staff who are unaffiliated with the research is acceptable.

Referrals from other sources

Referrals from other sources can include the sending of information about ongoing research to other local sources asking that they either pass the information on to potential subjects, or obtain written permission to refer the subject to the study investigator. It can also include distributing study information to appropriate advocacy groups or student groups perhaps by giving lectures or presentations to these groups. As stated previously, this type of recruitment strategy would require review and approval by the IRB prior to implementation but is otherwise not discouraged as long as you follow the strategies as outlined in the “Advertising Materials” section above.

2. Subject Compensation

Payment for participation in research may not be offered to the subject as a means of coercive persuasion or undue influence. Rather, it should be a form of recognition for the investment of the subject's time, loss of wages, or other inconvenience incurred. Payments should be based on the research subject’s time and/or reimbursement for reasonable expenses incurred during his/her participation in the research study. This could include payment for parking, lodging or transportation. Payment should not be excessive to the nature of the project. Another example of subjects compensation involves blood donation for participation in a research study. The compensation amount should not be reflective of the amount of blood donated but rather one set amount that will be compensated to subjects regardless of the amount of blood donated.

Accordingly, compensation may not be withheld contingent on the subject's completion of the study. In most cases involving continued participation, compensation should be given on a reasonable prorated basis to avoid the impression that the investigator is coercing the subject to continue in a study or is punishing the subject for non-compliance. If compensation is pro-rated when a subject withdraws prior to completing the study, explain in your consent process how it is pro-rated. Documentation of all amounts of compensation and the complete schedule of the
payment plan will be required within the research application reviewed by the IRB and the informed consent document reviewed by the subject.

The policy covering inclusion of compensation amounts in recruitment materials can be found [here](#).

Information on the UI procedures for how to process payment for research subjects can be found [here](#).

**Chapter 6 -- New Project Applications and IRB Review and Approval.**

Investigators are required to submit an application for IRB review PRIOR to initiating a research project. In September 2004, the Human Subjects Office began requiring all new project applications be submitted using a new electronic database system, HawkIRB. HawkIRB is an online application submission tool that uses “smart form” technology to guide investigators through the application process. Instructions for completing the new project application are contained within each section of the HawkIRB system. Many [educational sessions](#) are held when new aspects of the system are introduced. HSO staff are available for consultation and help using the system. Please refer to the list on our [HawkIRB FAQ](#) page.

**A. Signatures**

The principal investigator must sign the assurance document and attach it to the HawkIRB new project application. This page must be printed following completion of the New Project application in HawkIRB. If the Principal Investigator changes over the course of an IRB approved research protocol, a new signed assurance document with all applicable signatures will be required via a modification form. This signed page should be attached to the HawkIRB application in the Assurance section on the attachments page of the HawkIRB application prior to initial submission. This page assures that the PI is in compliance with all federal, state, and University policies as they apply to the study. In signing the final page of the application form, the investigator assures that:

- s/he is ultimately responsible for the conduct of the study.
- s/he agrees to comply with all applicable UI policies and procedures, and applicable federal, state and local laws.
- the application is consistent with proposal(s) submitted to external funding agencies.
- the research will only be performed by qualified personnel.
- all persons assisting with the research are adequately informed about the protocol and their research-related duties and functions.
- s/he will not implement any changes in the approved IRB application, study protocol, or informed consent process without prior IRB approval (except in an emergency, if necessary to safeguard the well-being of a human participant).
- If unavailable to conduct this research personally, as when on sabbatical leave, or permanently leaves the institution s/he will arrange for another investigator to assume direct responsibility for the study. Either this person is named as another investigator in this application, or s/he will notify the IRB of such arrangements.
- s/he will obtain Continuing Review approval prior to 12:01 a.m on the date the approval for the study expires. S/he understands if s/he fails to apply for continuing review, approval for the study will automatically expire, and all study activity must cease until IRB approval is granted.
- If protected health information is used or created as part of this research project, the
research team agrees NOT to reuse or disclose the information to any other person or entity (beyond the named research team) except as required by law, for authorized oversight of the research project, or unless subsequent IRB approval is obtained for such reuse or disclosure.

- If members of the research team access protected health information from a covered component in order to seek consent/authorization for research, such access is necessary for the research, is solely for that purpose, and the information will not be removed from the covered component.
- Neither the principal investigator nor any member of the research team have entered into a financial arrangement with a sponsor of this study whereby the value of the compensation to the principal investigator or any member of the research team for conducting the study could be influenced by the outcome of the study.
- s/he further assures that the proposed research is not currently being conducted and will not begin until IRB approval has been obtained.

The investigator is expected to be familiar with the policies contained in the University of Iowa Federalwide Assurance. Additional information on Principal Investigator oversight and responsibilities can be found here.

The signature of the departmental executive officer (department chair) also is required on the signature page of the New Project Application. If the departmental executive officer is the principal investigator, s/he may sign as both the investigator and the DEO. This signature of the DEO is an assurance that the PI:

- Is qualified to conduct the research as described in the application.
- Has adequate resources, facilities, and numbers of qualified staff to conduct the research as described in this application.
- Has used sound study design consistent with the standards of the investigator’s area of research.
- Has available time to oversee and conduct the project.

A student researcher may be listed as the principal investigator on the application forms, but a faculty or staff member must be a member of the research team and sign the application as the supervisor. The faculty signature assures that:

- s/he will meet with the student investigator on a regular basis and monitor study progress.
- The student is knowledgeable about the regulations and policies governing research with human subjects and has sufficient training and experience to conduct this particular study in accord with the approved protocol.
- If s/he will be unavailable to supervise this research personally, as when on sabbatical leave, s/he will arrange for an alternate Faculty Supervisor to assume direct responsibility in her/his absence and s/he will advise the IRB by letter in advance of such arrangements.

Additional information on Principal Investigator oversight and responsibilities can be found here.

**B. General Guidance**

The HawkIRB system requires the investigator to respond to all applicable items on the New Project Application in order to submit the project to the HSO. Still, the most common problem with New Project applications is that not enough detail is provided for the IRB chair or members to evaluate the study's purpose and/or procedures.
In particular, investigators are required to provide detailed information regarding how potential subjects are initially identified, and how consent is obtained. The Principal Investigator must accurately and completely describe the study procedures in the HawkIRB application. The more complete the initial description is, the less likely that time will be spent with correspondence back and forth between the investigator and Human Subjects Office staff and/or IRB chairs to fill in the details. The New Project application in HawkIRB will guide you through what is required with regard to supporting documentation. In general, a complete submission for IRB review includes the following items as applicable:

- HawkIRB application
- Written protocol
- Reports of prior investigations that provide relevant information to the review
- Informed Consent Document(s) or other consenting materials
- Sample Informed Consent Document(s) (for example, the DHHS or other sponsor sample consent, if available).
- Recruitment materials
- Survey instruments
- Grant application
- Investigator’s Brochure
- Other materials specific to the proposed study (e.g. sponsor correspondence with a regulatory agency such as the FDA regarding test article risk, etc.)

There are detailed instructions regarding how to attach your supporting documentation to the electronic application. Staff in the Human Subjects Office are available to respond to questions by e-mail or phone. We are also available to consult individually with you on how to use the HawkIRB system. Investigators with unique situations are encouraged to contact the Human Subjects Office.

C. Research Team

As part of the New Project Application, you will be asked to list all members of your research team for the project. You should include all individuals who have contact or interactions with research subjects or their private, identifiable information as research team members on your application. As a reminder, only the research team members listed appropriately in the HawkIRB application can be involved in the informed consent process.

Members of the research team also need to be designated as key personnel. The Principal Investigator is always considered key personnel. Research team members are automatically considered key personnel if they have a University of Iowa Faculty designation. Non faculty team members are considered key personnel if:

- They have the authority to make independent decisions about the direction of the research and the subsequent conclusions about the results.
- They could include individuals who are likely to be authors on manuscripts or to present research findings at national conferences.
- It does not include administrative personnel or individuals who perform routine, pre-defined, or incidental tasks related to the project.
For UI team members, you will be asked to provide the person’s name, e-mail address, department, the date the person complete human subjects protections training, and whether or not the individual will be a contact person for the project. If the person has completed human subjects protections training and is entered into our database, his/her certification date will show up automatically in HawkIRB. You will not be able to submit your application until all members of the research team have met this requirement. Information about how to obtain the required training can be found on the HSO website. All team members must have an active faculty, staff, or student appointment at the University of Iowa to be considered UI research team members. The HawkIRB system will reflect a deactivated status if no formal appointment with the University is in place.

If there are personnel not affiliated with the University of Iowa (that is, they are not actively appointed faculty, staff, or students of the UI) who will be conducting or are engaged in your research, they also need to have their activity reviewed by an IRB. This includes any individual that may be working or volunteering with the research team, even on a short-term basis such as students during summer months or students participating in clinical or educational rotations or classes. If these individuals are not affiliated with an entity that has an IRB, you may be able to list them as a non-UI member of your research team. However there are additional procedural steps and documentation that need to be provided in your application in order for you to add non-UI personnel to the research team list on your application. Please refer to Chapter 9, Special Topics on Collaborative Research. Before adding non-UI personnel to your research team, you should first contact the HSO to discuss your situation.

D. Supporting Documentation

The New Project Application must be accompanied by some basic materials, when appropriate. HawkIRB will prompt you to attach materials based on your responses to questions in the application. You are required to attach any required materials electronically. If you only have a hard copy of your supporting documentation, you will need to use some means (for example, scanning the document) to convert the document to a single electronic file, so that it can be attached to the HawkIRB application. There are detailed instructions within HawkIRB that will guide you through attaching those materials. There are also some instructions regarding attachments on our HawkIRB FAQ page. Some of the materials that you may need to attach include:

- Informed Consent Documentation. Depending on your study, this may include: the standard ICD, the VAHCS ICD, Record of Consent, Assent documents, Spanish short form documents, or the consent as a letter document. To create any of these documents, you will need to start with the template provided in HawkIRB, download them to your computer, make edits, and re-attach them to your HawkIRB application.

- Recruitment materials. These may include brochures, flyers, newsletters (if they include recruitment announcements or are provided to potential subjects prior to signing the consent), advertisements, audio-tapes, video-tapes, websites, or other materials used to inform people about the study.

- The complete grant proposal. This should include the budget pages and appendices.

- The study protocol & sample consent, if available. If the study involves a clinical or therapeutic intervention, this may include a pharmaceutical company protocol or investigator-initiated study protocol. If available, the DHHS-sponsored or other sponsor
sample consent should be included.

- Data collection materials. This would include questionnaires, surveys, stimuli, etc., that will be used in the study.

- Phone script(s). You will need to include these for situations that will involve screening or providing consenting information to participants via telephone.

For collaborations with non-UI entities:
- Letter(s) of agreement. If you are collaborating with an outside agency, company or clinic and that non-UI entity is giving you access to its clients, files, or premises, you will need to attach a letter of agreement from that agency that confirms knowledge of the project's purpose and permission for the investigator to conduct the study there.
- Individual Investigator’s Agreement. See the section in Special Topics on Collaborative Research.

For studies that require review by the Pharmacy & Therapeutics Committee or involve investigational drug interventions:
- Investigator’s Brochure. You will need to attach a copy of the Investigator’s Brochure for the investigational drug under study.

- Investigational New Drug (IND) number documentation. If the study involves an investigational drug, you will need to attach documentation of the IND number from the sponsor (if this is not indicated on the Investigator’s Brochure or protocol). In the case of investigator-held INDs, a copy of the FDA letter that informed the PI of the IND number.

- G-12 form. If the study involves an investigational drug, or if FDA-approved drugs are being used off-label, you will need to fill out and attach a G-12 form.

For studies that require review by the Medical Radiation Protection Committee (MRPC):
- The appropriate Radiation Protection Committee Research Application Form (either the regular or short form of this application).

E. Application Processing/Workflow

Once you have submitted your project through HawkIRB, it is automatically assigned an IRB Identification number. The IRB ID number remains with the study and is never reused. The IRB ID number appears on all correspondence, and on the approval stamp of the Informed Consent Document. A description of how you can track the progress of your application through HawkIRB is included on our HawkIRB FAQ page. Click on “Workflow: Tracking your Submitted Application.”

1. Admin Pre-Screening/Staff Review

All applications are screened by Human Subjects Office staff. At the pre-screening step, the application is being reviewed to ensure that the correct form has been used, all questions have been answered on the application, all attachments are present, etc. You may receive questions from the HSO staff at this step of the process requesting additional information or attachments. The application is not considered “accepted” into our review process until the project moves out of this step and into the HSO Staff Screen.
2. HSO Sr. Staff Screen
At this step, the application is being given a more in-depth screening by HSO Sr. staff prior to being sent to the Chair or their designee for review or before being prepared for a full board meeting.

3. IRB Review

Exempt or Expedited Review (IRB-Chair Review):
The IRB chairs (or his/her IRB member designee) determine whether the project is eligible for exempt status, expedited review, or requires full board review. If exempt or expedited review is appropriate, the chair or designated HSO staff may correspond with the investigator via HawkIRB with requests for additional clarification or materials prior to final approval. If the project is sent back to the PI, it is returned to the PI inbox and is noted in workflow as being under “PI review.” This means that it requires information/edits from the PI and that the PI has to send it back through HawkIRB after the changes/additions have been made.

Full Board Review: (Pre-Meeting Prep, Scheduled, Post-Meeting Prep):
If the project requires full board review, the date of the full board review will be listed under the heading “Agenda Date” on the Project Summary page in HawkIRB. The HSO will notify the investigator if s/he is requested to attend the meeting. The HSO distributes copies of the Application Form, Informed Consent Document, and other supporting materials to members attending the meeting about a week in advance. The IRBs use a primary reviewer system, in which one IRB member is assigned the role of reviewing and presenting the study to the members at the full board meeting. If the study is potentially funded, the primary reviewer also reviews the grant application itself (or the pharmaceutical protocol and Investigator's Brochure). The primary reviewer IRB member may contact the investigator for clarification prior to the meeting date. Any requests for revisions will come from the full board itself after the meeting.

The Principal Investigator should review the workflow in HawkIRB to track the project progress. Email notifications are not sent for the stages of meeting preparation. In HawkIRB, when the project is ready to be scheduled to a full board meeting, it shows in workflow as “Pre-Meeting Prep.” At this stage, the application and materials are being prepared for a full board meeting.

When the application moves in workflow to “Scheduled,” it has been scheduled to a meeting. You can check the date of the meeting by using the Project Summary page and looking under “Agenda Date.”

When the application moves to “Post-Meeting Prep,” the project has been reviewed by the full board and is now waiting for minutes from the meeting to be written and approved by an IRB chair. After the minutes are finalized by the IRB chair, they are sent to the Investigator and arrive in the PI’s inbox.

F. Criteria for Approval
In order for the IRB (or IRB chair or his/her IRB member designee in the case of expedited projects) to approve a project, the following requirements must be satisfied [45 CFR 46.111 (DHHS) and 21 CFR 56.111 (FDA)]:

- 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.

- **Risk/Benefit Ratio.** 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. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

- **Selection of subjects is equitable.** In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

- **Informed consent sought.** Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by [45 CFR 46.116 (DHHS) or 21 CFR 50 (FDA)].

- **Informed consent documented.** Informed consent will be appropriately documented, in accordance with, and to the extent required by [45 CFR 46.117 (DHHS) or 21 CFR 50.27 (FDA)].

- **Data safety monitoring.** When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

- **Protect privacy & maintain confidentiality.** When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

- **Vulnerable Populations.** When subjects are likely to be members of a vulnerable population, there are appropriate additional safeguards in place to protect the rights and welfare of these subjects.

**G. Revisions Prior to Final Approval**

For studies that are classified as exempt or expedited, the investigator must satisfactorily respond to all requests from the chair or his/her IRB member designee for revisions and/or clarification or additional information. The chair or his/her IRB member designee may approve projects as submitted or require modifications prior to approval. Chairs or their IRB member designee are not empowered to disapprove projects; in such cases, the application is submitted for full board review. When the chair or his/her IRB member designee determines all revisions have been made and that the study meets all criteria for approval, s/he approves the project and for expedited studies determines the interval for the next continuing review (not to exceed one year.)

For studies that require full board review, the investigator receives the meeting minutes electronically through HawkIRB. These minutes document the IRB's determinations. If the IRB requires minor revisions prior to final approval, the minutes will indicate that the study has been approved pending receipt of the required revisions with a designated timeframe of 14 days for receipt of the revisions. Minor revisions include revisions to the protocol and/or application that are made by the IRB and require only a simple concurrence by the investigator(s). If the investigator(s) provide concurrence with the revisions, the IRB chair alone may review and approve the submitted revisions. If the investigator does not respond within the allotted time...
period, the application may be withdrawn from further consideration. If the investigator wishes to pursue the project at a future date, s/he would then need to submit another New Project application, incorporating comments from the prior IRB review.

If the IRB requires revisions that require more than simple concurrence of the investigator(s), the minutes will indicate that the study has been tabled. The investigator must respond in full to all issues raised by the IRB prior to the project being returned to the full board for further review.

In the HawkIRB workflow, you may see the following categories in regard to your project after it has been reviewed by the full board:

- **Approved Pending.** This means that the application is approved pending revisions and response by the PI as indicated in the minutes. The PI/delegate(s)/contact persons on the research team receive an e-mail notification by HawkIRB of this status. The application is routed to the PI and requires a response within 14 days from the PI prior to final approval.
- **Tabled.** This means that the application was tabled at the meeting pending revisions and clarifications by the PI. The PI/delegate(s)/contact persons on the research team receive an e-mail notification by HawkIRB of this status. The application is routed to the PI and requires a response from the PI within 21 days prior to being scheduled to a future full board meeting.
- **Disapproved.** This means the application was disapproved after review by the full board. The PI/delegate(s)/contact persons on the research team receive an email notification by HawkIRB of this determination.
- **Withdrawn.** For all applications EXCEPT for Reportable Event Forms (REFs), this means the application has been withdrawn, either at the request of the PI, or by the IRB if the PI failed to respond in a timely manner to requests for more information. The PI/delegate(s)/contact persons on the research team receive an email notification by HawkIRB of this status.
- **Withdrawn. (REFs only).** This means that the reported event submitted on the REF did not meet the criteria for reporting to the IRB. To review these criteria, refer to Chapter 7, Section C.
- **Approved.** This means the application has been approved and is waiting for final processing in the HSO before being released to the PI. When the project is released, the PI/delegate(s)/contact persons on the research team will receive an email notification.

**H. Notification of Approval**

Upon receipt of final approval by the IRB chairs, HawkIRB automatically stamps approved Informed Consent Document(s) and other materials (e.g. letters to subjects, ads) with the IRB ID number, the date of approval, and the date of expiration. This stamp is typically in the upper right corner of the document. Questionnaires and data collection forms are generally not stamped. The HawkIRB system notifies the PI and designated members of the research team of the approval and allows access to currently approved documents.

Ultimately, it is the Principal Investigator's responsibility to maintain accurate files of IRB correspondence, approvals, and research records during the life of the study and after completion of the research. The Principal Investigator is required to retain records for three years for studies that do not involve the use of protected health information, indefinitely for VA studies, or six years for studies that involve the use of protected health information. IRB records are retained in accordance with VHA Records Control Schedule (RCS 10-1). All correspondence and IRB documentation
related to the project is available electronically through the HawkIRB application.

The investigator has access to the electronic IRB-approval memo in HawkIRB. The approval memo includes the type of review (full board, expedited, or exempt), date of next continuing review, and a summary of investigator responsibilities. This memo reminds investigators that changes in research activity may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to subjects.

There is also a statement within HawkIRB that the approved project was electronically signed by the IRB chair. This statement includes the name of the chair and the date and time of the electronic signature.

Please Note!
The PI and research staff is required to use the currently approved, stamped consent document when enrolling research subjects unless a documented exception has been granted by the IRB.

Final release of the approval for projects that have external funding.

If your study is funded by a government or non-profit agency, you will also receive an "Assurance Identification/IRB Certification/Declaration of Exemption" (NIH 310) form for new project, continuing review, and modifications adding new funding sources. This form will be sent to either your sponsor directly or to you in a separate campus mailing from Sponsored Programs. It will contain the same date as the IRB approval memo, and will be signed by the Institutional Official. It indicates the IRB ID number, PI Name, Project Title, sponsoring agency or organization, and other information about the type of IRB review.

If the project is industry sponsored, the IRB approval is not released to the investigator until the contract has been finalized by the Division of Sponsored Programs.

I. Limitations on IRB-Approved Projects – Rules to understand before you begin

IRB approval is limited to the specified procedures in the HawkIRB New Project Application

An approved project is limited in its conduct to the recruitment activities and study procedures that were described in the initial New Project application. In other words, the investigator may perform only those activities that s/he described. If the investigator wishes to change the study recruitment activities or procedures from what was initially described, s/he should submit a Modification/Update application for IRB review and approval prior to implementation (see next chapter for more information on Modification/Update applications).

IRB approval is for a limited time period

Each project is approved for a specified period of time, and human subjects research activity may not continue beyond that date without approval of a Continuing Review application (see next chapter for more information on Continuing Review applications). The electronic approval memo indicates the due date for the next continuing review. The date by which the continuing review must be approved is also available on the project’s Summary page on HawkIRB.

The IRB may require that review occur more frequently than annually; for example, in studies that carry a greater degree of risk, the board may decide to review the study after the first several
The study is approved to enroll a limited number of subjects

All projects are approved to enroll only the number of subjects indicated in the New Project application. If the investigator finds that actual enrollment is approaching that limit, a Modification application should be submitted requesting an increase in the number of subjects to be enrolled in the study. The application must be approved before additional subjects may be enrolled beyond the originally approved number.

When is a subject considered enrolled?

An enrolled subject is anyone who has signed an Informed Consent Document, whether or not that individual actually completes the study. Thus, someone who signs a consent document but is determined during screening to be ineligible, or chooses not to continue, must still be counted as an enrolled subject.

Only currently-approved consenting and recruiting materials may be used

Finally, only the current, approved Consent Document may be used for documenting informed consent. Documenting consent on a Consent Document on or after the expiration date stamped on that document is not permitted and may not constitute valid consent. With each Continuing Review, the investigator receives newly-stamped versions with the approval notification. Even if the content is identical, you are expected to use the current, stamped version of all stamped materials.

In addition, only the currently approved recruitment materials and methods should be used to recruit subjects. No changes can be made to the approved materials without IRB approval via a Modification application.

J. Appeal of IRB Decisions

Investigators may appeal the IRB requirement for specific changes in the protocol and/or consent documents(s). If the application is being reviewed under expedited procedures, the Chair works directly with the investigator to resolve outstanding issues. Such appeals are documented as responses in the HawkIRB system or via e-mail to the Chair. If the Chair and investigator cannot resolve the issue(s), the project is referred to full board for review.

If the full board IRB decides to require specific changes or to disapprove a research activity, the minutes from the meeting provide the reasons for its decision. The investigator may appeal any of the requested changes or the disapproval. Such appeals should be submitted in writing via HawkIRB as a response to the meeting minutes. Such appeals must be reviewed at a full board meeting. The basis for appeals must include new information that was not previously submitted to or considered by the IRB. The investigator should provide a rationale for the appeal and any other relevant supporting documentation. If the appeal requires discussion or explanation beyond what is provided to the board in written format, the investigator may be invited by the Chair to attend the full board meeting at which the appeal is presented. The investigator is invited for the purpose of answering questions and participating in discourse with board members. The investigator will leave prior to IRB discussion and vote on the issues. The IRB will notify the investigator in writing via
the meeting minutes of the discussion and vote on the appealed issue(s).

In the case of a decision by the IRB to disapprove, suspend, or terminate a project, the decision may not be reversed by any other person or entity including the Associate Vice President for Research, or any other officer/agency of the University of Iowa, state government, or federal government.

K. Other University Committees Reviewing Human Subjects Research

The University of Iowa Institutional Review Boards coordinate reviews with other institutional committees as described on the Human Subjects Office web page. None of these committees are a formal part of the University of Iowa IRB structure, but there is communication between the committees regarding status of review and/or conditions of approval.

Other committees that review human subjects research applications include:
- Conflict of Interest in Research Committee (CIRC)
- Institute for Clinical and Translational Science – Clinical Research Protocol Review Committee (formerly GAC)
- Holden Comprehensive Cancer Center Protocol Review & Monitoring Committee (PRMC)
- Institutional Biosafety Committee (IBC)
- Medical Radiation Protection Committee (MRPC)
- Nursing Research Committee (NRC)
- Pharmacy and Therapeutics Committee (P&T)
- VAHCS Research and Development Committee (VAHCS)
- Joint Office for Compliance Research Billing

IRB review does not occur until after determinations of the IBC, the PRMC, JOC Research Billing, and the CIRC. Final IRB approval (but not review) is held for the review and determinations of the MRPC, P&T, and NRC Committees. For IRB-03, final IRB approval (but not review) is held for the review and determinations of the VAHCS Privacy Officer and Information Security Officer. Neither IRB review nor approval is held for the determinations of the VAHCS R&D Committee, the GAC.

Information regarding these committees, and a contact person for each, is available by clicking on the above links.

Chapter 7 – After Initial IRB approval.

Investigators have a variety of IRB communication and record-keeping responsibilities after the research project is initiated. Major responsibilities are described below. There may also be additional responsibilities from your funding agency or other regulatory agencies.

A. Modifications

Any change in the conduct of a study must be reviewed and approved by the IRB prior to implementing the change. The exception to this is when the change is necessary to eliminate apparent immediate hazards to subjects. The investigator is required to promptly notify the IRB of any changes made without IRB approval to eliminate apparent immediate hazards to subjects using the Modification Form as described below. The convened IRB will review these modification forms to determine that any changes made by the investigator to eliminate apparent immediate
hazards to the subjects were consistent with ensuring the subjects’ continued welfare. The approval memo notifies the investigator of this responsibility.

Modifications include, but are not limited to:

- procedural changes to a protocol,
- adding or removing investigators or research team members,
  - NOTE: If a PI is leaving the institution, a new PI must be submitted and approved prior to the current PI’s departure. A signed assurance document is required of a newly named PI of a research study. If a PI is on extended leave from the institution, contact the HSO to discuss continued oversight of any open studies.
- Changes to the title of the project,
- requests for additional subjects beyond the original approved number,
- change in funding sources,
- changes in how subjects are being recruited or followed-up
- new or revised advertisements,
- changes to Informed Consent Documents, surveys, questionnaires, correspondence with potential or current subjects, or additional new items,
- protocol changes.

Modifications to an approved project should be submitted on a Modification/Update Form. A modification may be submitted at the same time as a continuing review. Instructions for the completion of these applications are contained within the HawkIRB system.

Minor modifications are modifications to a research project and/or consent documents that pose no additional risk to subjects (e.g. changes in title, co-investigator(s), funding sources). If the modification is an addition or modification of procedures, it must fall into one of the categories eligible for expedited review. To be considered a minor modification, it must also maintain similar or increased safeguards to protect the subject. These minor modifications may be approved by the chair or his/her IRB member designee alone using the expedited review procedure. More extensive modifications may require full board review. In either case, revisions or clarifications may be required. **All modifications must be approved by the IRB prior to implementation.**

Once a PI has received a protocol amendment from a study sponsor, it is the PI's responsibility to submit the amendment in a timely manner for IRB review and approval. Based on guidance from the FDA, potential subjects who meet eligibility criteria under a pending amendment to the protocol **may not be enrolled** until after the amendment is approved by the IRB. Further, the FDA will hold the PI responsible for compliance with this requirement. The sponsor does not have the authority to override this FDA regulation, and therefore, it is inappropriate for the PI to request "special permission" from the sponsor to implement any aspect of the amendment before IRB approval. Rather, the PI should move as quickly as possible towards submitting the amendment for IRB approval.

On occasion the IRB receives questions about whether or not "protocol violations" or "protocol deviations" need to be reported to the IRB. Please refer to Section C of this chapter for more information on reporting requirements.

**B. Continuing Review**

The IRB is required to review and approve all non-exempt research projects at intervals appropriate to the degree of risk, but not less than once a year [45 CFR 46.109(e) (DHHS) and 21
This is called "continuing review." Continuing review for non-exempt research is required to occur as long as the research remains active for long-term follow-up of the research subject, even when the research is permanently closed to the enrollment of new subjects and all subjects have completed all research-related interventions and to occur when the remaining research activities are limited to collection of private identifiable information.

As described above, the Informed Consent Document(s) indicate the project's expiration date. If a project initially received expedited review and risks to subjects remain minimal, the continuing review may be expedited (reviewed by the chair alone). If a project initially received full board review, the project generally requires full board continuing review. The calculation of the approval period for research is based on the date and length of time at which the IRB approved the protocol by either a convened Full Board meeting or through the expedite review process. Investigators are encouraged to allow three to four weeks from date of submission for full board review and approval. A schedule for full board continuing review of IRB-01 projects is available on the HSO web site.

Due date for submitting an application for continuing review

It is the Principal Investigator's responsibility to submit an application for continuing review in sufficient time to permit the IRB chair or full board to review and approve the application prior to its expiration date. The date by which the continuing review must be approved is also available on the project’s Summary page on HawkIRB. As a service to investigators, the HawkIRB system sends the reminders to the Principal Investigator, and all contact persons listed for a given application. The reminder schedule is based on the Last Possible Submission Date (LPSD) of the project. The LPSD is the date that you need to have your project submitted to the Human Subjects Office to ensure that you can obtain review and approval PRIOR to the project expiration date. The Principal Investigator, his or her delegates, and contact persons will receive automated reminders on the following schedule:

- A reminder memo is sent via email 30, 14, 7 and 1 day before the LPSD of the project.
- On the day of the LPSD (if a continuing review application has not yet been received by the HSO) you will receive notice by email that there will not be sufficient time prior to the expiration of the project for review and approval. This notice will state that IRB approval will lapse as of 12:01 a.m. on the expiration date and no further research activity may occur on or after that date. The Principal Investigator will be asked to submit your continuing review application or close the project.

- NO HUMAN SUBJECTS ACTIVITY (which includes the enrollment and follow-up of subjects and the collection and/or use of research data) MAY TAKE PLACE ON OR AFTER THE EXPIRATION DATE unless there is an over-riding safety concern (as determined by an IRB Chair) and until the continuing review application is approved by the IRB and released by the HSO.

- On the day prior to the date of expiration, the Principal Investigator, his or her delegates, and contact persons will receive notice that the project will lapse and that no human subjects activity may take place after 12:01 a.m. on the expiration date. The Principal Investigator will have 10 working days from the date of this notice to obtain review and approval of the continuing review for the project or it will be administratively closed by the IRB through the Human Subjects Office.
If the HSO closes the study due to no response, the HSO sends the Principal Investigator a notification via email of study closure. The investigator's departmental executive officer (DEO) may also receive notification of closure. In cases of on-going externally funded projects, the Division of Sponsored Programs also receives a copy of the closure notice and make an independent determination regarding the need to notify the sponsor. Once the HSO closes a project, the only way for the project to resume is for the investigator to submit a New Project Application (via the HawkIRB system) for IRB review and approval.

How to submit a continuing review application

The continuing review information is required to be submitted via HawkIRB. You should log onto the HawkIRB system and choose your open project from your inbox. From there, you can choose to open either of the following forms:

- Continuing review form [Use this form if you are not submitting a modification/update in conjunction with your continuing review]
- Modification/Update + Continuing Review Form.

Instructions for completing and submitting the forms are within each HawkIRB application.

Review and Approval Process for Continuing Reviews

Procedures for expedited or full board review, criteria for approval, and revision prior to approval, are identical to those described above for New Projects. Notification of approval of a Continuing Review form is identical to that described for New Projects. The system notifies the PI and designated members of the research team of the approval and allows access to currently approved documents.

C. Other Reporting Requirements for Investigators

The following list are events that are reportable by investigators to the UI IRB:

1) Any unanticipated problems involving risks to subjects or others which occur at the UI/VAHCS or that impacts subjects or conduct of the study.
2) A serious adverse drug event (either expected or unexpected) occurring in a UI/VAHCS subject.
3) A serious adverse device effect (either anticipated or unanticipated) occurring in a UI/VAHCS subject.
4) An unanticipated serious adverse device effect occurring in a non-UI/VAHCS subject.
5) Receipt of new information (including risk or benefit) that may impact the willingness of subjects to participate or continue participation in the research study.
6) Any incidents of noncompliance with the federal regulations or the requirements or determinations of the IRB.

Investigators are required to report to the appropriate UI IRB if any of the above items #1-6 occur in a study where IRB-01, IRB-02, IRB-03 is the IRB of record. (For WIRB studies, items #1-6 are reportable directly to WIRB.).
What are unanticipated problems involving risk to subjects or others?

An unanticipated problem involving risks to subjects or others is any event or problem that:

- was unexpected (in terms of nature, severity or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied AND
- suggests that the research places subjects or others (those not directly involved in the research such as research staff or family members) at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized AND
- is related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience or outcome may have been caused by the procedures involved in the research).

What is a serious adverse drug event?

A serious adverse drug event is any adverse drug experience (associated with the use of the drug) occurring at any dose that results in any of the following outcomes:

- death,
- life-threatening adverse drug experience
- inpatient hospitalization or prolongation of existing hospitalization
- a persistent or significant disability/incapacity
- a congenital anomaly/birth defect
- important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug event when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed above.

What is an unexpected adverse drug event?

An unexpected adverse drug event is any adverse drug experience (associated with the use of the drug), the frequency, specificity, or severity of which is not consistent with the current investigator brochure; or, if an investigator brochure is not required or available, the specificity or severity of which is not consistent with the risk information provided to the subjects and the IRB.

What is an unanticipated adverse device effect?

Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death the frequency, specificity, or severity of which has not previously been identified in the investigational plan or application, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

What is noncompliance?

Noncompliance is a failure to follow the federal regulations with respect to protection of human subjects in research or failure to follow the determinations of the IRB with respect to conduct of the research as approved by the IRB.

1. Unanticipated Problems Involving Risks to Subjects or Others Which Occur at UI/VAHCS or That Impact Subjects or Conduct of the study.

An unanticipated problem involving risks to subjects or others has been defined above.
Examples of unanticipated problems involving risks to subjects or others include, but are not limited to:
- a breach of confidentiality
- a subject complaint when the complaint indicates unexpected risks or cannot be resolved by the investigators,
- a research team member experiences harm in the conduct of the study,
- a new risk of the study drug, device, or study procedure is identified by an outside source (sponsor, federal regulatory agency, outside site, etc.)

When a research study includes investigational drugs or devices, some unanticipated problems may also meet the definition of an unexpected adverse drug experience (serious or otherwise), or an unanticipated adverse device effect.

Investigators must report any unanticipated problem involving risk to subjects or others using the Reportable Event Form (REF) in the HawkIRB system. This form includes a description of the event, the date of occurrence, whether it is a local or outside report, how the event affected the rights, safety or welfare of the subject or others, current status of subjects, and any planned changes or modifications to the project as a result of the event. Reports from the investigator to the IRB must be submitted via HawkIRB within ten working days of the event or notification to the investigator of the event.

The IRB chair compares the content of the REF with the previously approved project materials such as applications, informed consent document(s), protocols, investigator brochures, or other supporting documents to determine whether this event meets the definition of an unanticipated problem involving risk to subjects or others. If the chair agrees the event meets the definition of an unanticipated problem involving risks to subjects or others, the chair determines whether the event represents minimal risk of harm or more than minimal risk of harm to subjects enrolled under the UI study. If the event represents minimal risk of harm, the chair reviews and signs the report through the HawkIRB system. If the event represents more than minimal risk of harm to subjects enrolled under the UI study, the report is referred to the convened IRB for review.

All reports of unanticipated problems involving risks to subjects or others are electronically filed with the appropriate research study. These reports are also reviewed by the IRB at the time of continuing review. Reports of all such problems for all projects reviewed by the Chair or convened IRB are provided by e-mail to all IRB-01, IRB-02, or IRB-03 members as appropriate on a monthly basis.

2. Serious adverse drug event (either expected or unexpected) occurring in a UI\VAHCS subject.

If a subject is enrolled by U/VAHCS investigators, the investigator must report to the UI IRB either serious adverse drug events or unexpected adverse drug events. By definition, these events must be associated with the use of the drug.

Investigators must report any serious adverse drug event using the Reportable Event Form (REF). This form includes a description of the event, the date of occurrence, the type of risk, whether the event was unexpected, the outcome, and an assessment of degree of relatedness to the research. The form also includes the proposed actions to be taken by the investigator with regard to
modifying approved study materials (including change in consent documents or other notification procedures) and notifying current subjects. Reports from the investigator to the IRB must be submitted via HawkIRB within ten working days of the event or notification to the investigator of the event.

Reports of serious and expected adverse drug events occurring in a UI/VAHCS subject are reviewed by an IRB Chair to verify that the event would be considered “expected” based on the information previously reviewed and approved by the IRB. If the Chair verifies that this information is correct, the Chair signs the report through the HawkIRB system.

All reports of serious and unexpected adverse drug events occurring in a UI/VAHCS subject are reviewed by the IRB Chair and/or the IRB in the following manner. The IRB chair compares the content of the REF with the previously approved project materials such as applications, informed consent document(s), protocols, investigator brochures, or other supporting documents to determine whether this event meets the definition of an unanticipated problem involving risk to subjects or others. If the chair agrees the event meets the definition of an unanticipated problem involving risks to subjects or others, the chair determines whether the event represents minimal risk of harm or more than minimal risk of harm to subjects enrolled under the UI study. If the event represents minimal risk of harm, the chair reviews and signs the report through the HawkIRB system. If the event represents more than minimal risk of harm to subjects enrolled under the UI/VAHCS study, the report is referred to the convened IRB for review. The full board determines whether subjects must be notified of the new information, and if so, the method of notification and whether any study materials (e.g. consents, protocol) must be updated to reflect the new information.

All reports of serious adverse drug events occurring in a UI/VAHCS subject are electronically filed with the appropriate research study. These reports are also reviewed by the IRB at the time of continuing review. In addition, reports of all serious adverse drug events for all projects reviewed by the Chair or full board IRB are provided by e-mail to all IRB-01 or IRB-03 members on a monthly basis.

In addition to the above requirements, investigators conducting human gene therapy research must submit a written report of serious adverse experiences that are unexpected and associated with the use of the gene transfer product to the NIH Office of Biotechnology Activities (NIH/OBA), the U of I Institutional Biosafety Committee, the IRB, and the FDA or study sponsor within specified timeframes as found in Appendix M-I-C-4 in the NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines). Gene therapy investigators must submit annual reports to OBA as set forth in Appendix M-I-C-3 of the NIH Guidelines.

3. Serious adverse device effects (either anticipated or unanticipated) occurring in a UI/VAHCS subject.

If a subject is enrolled by UI/VAHCS investigators, the investigator must report either serious adverse device effects or unanticipated adverse device effects. By definition, these effects must be associated with the use of the device.

Investigators must report any serious adverse device effect occurring in a UI/VAHCS subject to IRB-01 or IRB-03 using the Reportable Event Form (REF). This form includes a description of the
effect, the date of occurrence, the type of risk, whether the effect was unanticipated, the outcome, and an assessment of degree of relatedness to the research. The form also includes the proposed actions to be taken by the investigator with regard to modifying approved study materials (including change in consent documents or other notification procedures) and notifying current subjects. Reports from the investigator to the IRB must be submitted via HawkIRB within ten working days of the event or notification to the investigator of the event.

Reports of serious and anticipated adverse device effects occurring in a UI\VAHCS subject are reviewed by an IRB Chair to verify that the effect would be considered “anticipated” based on the information previously reviewed and approved by the IRB. If the Chair verifies that this information is correct, the Chair signs the report through the HawkIRB system.

Reports of serious and unanticipated adverse device effects occurring in a UI\VAHCS subject are reviewed by the UI\VAHCS IRB Chair and/or UI IRB in the following manner. The IRB chair compares the content of the REF with the previously approved project materials such as applications, informed consent document(s), protocols, investigator brochures, or other supporting documents to determine whether this event meets the definition of an unanticipated problem involving risk to subjects or others. If the chair agrees the event meets the definition of an unanticipated problem involving risks to subjects or others, the chair determines whether the event represents minimal risk of harm or more than minimal risk of harm to subjects enrolled under the UI\VAHCS study. If the event represents minimal risk of harm, the chair reviews and signs the report through the HawkIRB system. If the event represents more than minimal risk of harm to subjects enrolled under the UI\VAHCS study, the report is referred to the convened IRB for review. The full board determines whether subjects must be notified of the new information, and if so, the method of notification and whether any study materials (e.g. consents, protocol) must be updated to reflect the new information.

All reports of serious adverse device effects occurring in a UI\VAHCS subject are electronically filed with the appropriate research study. These reports are also reviewed by the IRB at the time of continuing review. In addition, reports of all serious adverse device effects for all projects reviewed by the Chair or full board IRB are provided by e-mail to all IRB-01 or IRB-03h members on a monthly basis.

4. **Unanticipated serious adverse device effects occurring in a non-UI\VAHCS subject.**

FDA regulations (21 CFR 150(b)(1)) require the sponsor to report the results of any evaluation of an unanticipated serious adverse device effect to all reviewing IRBs and participating investigators. Any such reports are initially received by the investigator who is in turn responsible for reporting this information to the IRB-01 or IRB-03. By definition, these effects must be associated with the use of the device.

Investigators must report any evaluation of unanticipated serious adverse device effects conducted by the sponsor occurring in a non-UI\VAHCS subject to IRB-01 or IRB-03 using the Reportable Event Form (REF). This form includes a description of the effect, the date of occurrence, the type of risk, the outcome, and an assessment of degree of relatedness to the research. The form also includes the proposed actions to be taken by the investigator with regard to modifying approved study materials (including change in consent documents or other notification procedures) and notifying current subjects. Reports from the investigator to the IRB must be
submitted via HawkIRB within ten working days of the event or notification to the investigator of the event.

All reports of unanticipated serious device effects occurring in a non-UI\VAHCS subject are reviewed in the following manner. The IRB chair compares the content of the REF with the previously approved project materials such as applications, informed consent document(s), protocols, investigator brochures, or other supporting documents to determine whether this event meets the definition of an unanticipated problem involving risk to subjects or others. If the chair agrees the event meets the definition of an unanticipated problem involving risks to subjects or others, the chair determines whether the event represents minimal risk of harm or more than minimal risk of harm to subjects enrolled under the UI\VAHCS study. If the event represents minimal risk of harm, the chair reviews and signs the report through the HawkIRB system. If the event represents more than minimal risk of harm to subjects enrolled under the UI\VAHCS study, the report is referred to the convened IRB for review. The full board determines whether subjects must be notified of the new information, and if so, the method of notification and whether any study materials (e.g. consents, protocol) must be updated to reflect the new information.

All reports of unanticipated serious adverse device effects occurring in a non-UI\VAHCS subject are electronically filed with the appropriate research study. These reports are also reviewed by the IRB at the time of continuing review. In addition, reports of all unanticipated serious adverse device effects for all projects reviewed by the full board are provided by e-mail to all IRB-01 or IRB-03 members on a monthly basis.
5. **Receipt of new information (including risk or benefit) that may impact the willingness of subjects to participate or continue participation in the research study.**

   During the course of a study, researchers may become aware of new information that would impact a subject’s decision to participate, or continue participating in the research study. For example, interim analyses of data may identify a trend which impacts the safety of subjects, or may identify early efficacy (benefit) of one of the interventions under study. In addition, results from other research studies or changes in standards of practice or care may affect conduct of a study and would need to be communicated to research subjects.

   Investigators must report any new information that may impact the willingness of subjects to participate to IRB-01, IRB-02, or IRB-03 using the Reportable Event Form (REF). This form includes a description of the new information and its potential impact on subjects. Reports from the investigator to the IRB must be submitted via HawkIRB within ten working days of the event or notification to the investigator of the event. In addition, a modification form must be submitted describing the investigator’s proposed method for providing this information to subjects.

   Reports and modifications related to new information are reviewed by an IRB Chair to determine if the method and information provided to subjects is appropriate. If the Chair verifies that this information is correct and notification is appropriate, the Chair signs the report and modification through the HawkIRB system. The Chair refers the review to the full board when s/he believes the information or notification method is not appropriate, or if the new information significantly impacts the safety of current or potential subjects. When protocol changes are immediately required to eliminate apparent immediate hazards to subjects, the Chair may approve notifications prior to full board review.

6. **Noncompliance with Federal Regulations or the Requirements or Determinations of the IRB**

   Investigators who are self-reporting noncompliance with federal regulations or the requirements or determinations of the IRB to IRB-01, IRB-02, and IRB-03 use the Reportable Event Form (REF). This form includes a description of the noncompliance and description of impact on the rights, safety, or welfare of subjects or others. Reports from the Investigator to the IRB must be submitted via HawkIRB within ten working days of the event or notification to the investigator of the event.

   Others may report noncompliance as described in Chapter 10 of this Guide. All reports of noncompliance, regardless of the source are reviewed by the IRB Chair and/or UI IRB according to the procedures described in Chapter 10 of this Guide.

D. **IRB Education and Compliance Program**

   The IRB Education and Compliance Specialists are full-time HSO staff members who conduct pre- and post-approval monitoring of human subjects research under the purview of the University of Iowa IRB and WIRB. The program also provides educational resources, training sessions, and other programming to University of Iowa faculty, staff and students.
The IRB Education and Compliance Program started in 2001. The main goals of this program are:

1) To make sure research is being conducted in accordance with federal regulations and University of Iowa Standard Operating Procedures.
2) To provide researchers an independent review of their research procedures, determining from a source other than the investigator’s continuing review that no material changes have occurred in the project since the previous IRB review.
3) To provide researchers one-on-one and group educational opportunities regarding human subjects research.
4) To facilitate communication between the IRB/HSO and researchers at the University of Iowa.

In addition to the monitoring staff, IRB members or other professional staff in the Human Subjects Office acting on behalf of the IRB may conduct monitoring activities.

1. Monitoring

The IRB Education and Compliance Specialists conduct monitoring of IRB-approved projects. Monitoring can also be conducted prior to IRB approval. All human subjects research projects are subject to review at any time.

Studies are selected for monitoring by:

a. Compliance Monitoring Visit Goals

- The annual goal is to conduct approximately 100 compliance monitoring visits for IRB-01 and IRB-02.
- The number of monitoring visits per month for each IRB is based on the percentage of studies reviewed by each board. This is approximately 80% IRB-01 and 20% for IRB-02.
- Compliance monitoring visits for IRB-03 are conducted by the VA Research Compliance Officer.
- The number of Monitoring visits may fluctuate due to IRB-Directed monitoring, IND/IDE Educational Sessions and other IRB/HSO projects.
- Fewer studies may be selected for Post-Approval Responsibilities Review (PARR) and Post-Approval Monitoring and Education (Pam & Ed) visits during the summer months and in December. IRB-directed monitoring visits will be conducted as needed throughout the year.

b. Study Selection

(1) Post-Approval Responsibilities Review (PARR)

- **Full-Board Review Studies** - Selected by the IRB Chair after review at a convened IRB meeting. The Chair is provided with a list of the monitoring history for all studies on the meeting agenda. The information provided about each study includes:
  - Whether or not an investigator has had previous monitoring
  - The type of monitoring
  - The date(s) of the Monitoring visit(s).
• **Expedited Review Studies** – Identified by the Education and Compliance Specialists from the HawkIRB reports of approved New Projects. After initial screening to remove studies that are approved for a waiver of consent, studies will be randomly selected for monitoring from among the remaining studies on the report.

• **Primary selection criteria:**
  - Studies involving unusual levels or types of risks to subjects
  - Studies involving vulnerable subject populations
  - Studies involving the collection and storage of sensitive information
  - Investigator and/or faculty advisor (for student Principal Investigator) who is new to the University of Iowa or who has not previously had monitoring of any research project
  - UI Investigator is the holder of the IND or IDE
  - Investigator who previously failed to comply with IRB determinations or the federal regulations

• The IRB Chair may select any study or investigator for education or compliance monitoring regardless of the investigator, study design or IRB review process.

• For studies selected from an IRB meeting agenda, a Senior Application Analyst attending the IRB meeting will collect the Monitoring List and provide it to the Education and Compliance Specialists.
  - If a study was selected, the Chair may provide the rationale for the selection in case any special preparation is needed for the compliance monitoring visit.
  - If a study was not selected, and the Chair doesn’t specify that no study was selected, the selection of a study for compliance monitoring will be added to the agenda for the next Chairs meeting.

• **IND/IDE Educational Sessions** - All Sponsor-Investigators under UI IRB oversight who are IND/IDE-holders (and the PI if s/he is not the IND/IDE-holder) must have an IND/IDE Educational Session to review record-keeping and reporting requirements. These studies will be identified on the meeting list after the New Project application is approved by the full board. If the Principal Investigator has not yet had a PARR visit, that will be conducted along with the IND/IDE Educational Session.

(2) **Post-Approval Monitoring and Education (Pam & Ed)**

• Studies will be selected for monitoring from the HawkIRB report of all open, not previously monitored, projects. After initial screening to remove studies that are only open for data analysis or approved for a waiver of consent, a study (or studies) for monitoring will be randomly selected from the remaining studies in the report.

• **Primary selection criteria:**
  - Studies involving unusual levels or types of risks to subjects
  - Studies involving vulnerable subject populations
  - Studies involving the collection and storage of sensitive information
  - Investigator and/or faculty advisor (for student Principal Investigator) who is new to the University of Iowa or who has not previously had monitoring of any research project
  - UI Investigator is the holder of the IND or IDE
  - Investigator who previously failed to comply with IRB determinations or the federal regulations
• **IND/IDE Educational Session** – A visit will be conducted with any researcher under UI IRB oversight who holds the IND/IDE but has not yet had an IND/IDE Educational Session. These studies will be flagged for review by the Senior Application Analyst after the Continuing Review or Modification application is approved by the full board.

(3) **IRB-Directed Monitoring (Directed)**

- An IRB Chair or the Board may direct a monitoring or educational session for a specific PI or study. The Chair or the Board may provide a specific, directed focus for the visit or they could request a general educational session.
- Directed visits may be as a result of a subject complaint, a complaint or information from a research team member, questions about description of study activity in Continuing Review applications or any other information that might raise a concern about the conduct of the study.

c. **Notification**

- Initial notification of selection for Monitoring is sent by e-mail to the Principal Investigator and any contact persons on the research team. The message will be sent from the Education and Compliance e-mail mailbox.
- Follow-up by e-mail and/or telephone if no response within 3 days.
- The e-mail will contain an overview and description of the visit.
- For PARR visits, the Education and Compliance Specialist will track the project through HawkIRB. Notification will be sent after the study has been approved and released by the IRB. Notice for Pam & Ed, IND/IDE Educational Sessions and IRB-Directed monitoring visits will be sent as soon as the study is selected for monitoring.

d. **Scheduling**

- The compliance monitoring visit typically lasts 2 hours.
- Additional time may be necessary to review research files, including signed Consent Documents. The research team does not need to be present for the Consent Document or research file review.
- If possible, review of research files and signed Consent Documents will be conducted prior to the visit with the Principal Investigator and research team.
- Visit scheduling will be conducted either electronically or over the telephone.
- Visit will be scheduled within 30 days of IRB approval of the New Project (PARR visits) or study selection for the ongoing studies (Pam & Ed and IND/IDE visits) unless other arrangements are requested by the Principal Investigator. IRB-Directed visits will be scheduled within one week or as quickly as possible.
- The Principal Investigator is required to attend. The Principal Investigator may decide which research team members, if any, would attend the visit. The Principal Investigator is encouraged to invite the person responsible for preparing HawkIRB applications for the study.
- For student Principal Investigators, the faculty advisor for the research project may attend the visit or schedule a separate visit to provide information about study oversight. The
faculty advisor component of the Monitoring visit may be conducted via telephone or e-mail.

- The Principal Investigator is responsible for arranging for meeting space with a computer with internet access. A projector hooked to a computer will be necessary for visits held in a conference room.

e. **Preparation for Compliance Monitoring Visits**

- Review the HawkIRB application, attachments, minutes, other committee review and workflow communication between the IRB/HSO and the Principal Investigator.
- Prepare the monitoring form to include any additional questions for the Principal Investigator regarding the content of the HawkIRB application and/or conduct of the study.

f. **Conduct of the Monitoring Visit**

- The Education and Compliance Specialist conducts a two-part review process.
  - One part is a two-hour interview with the Principal Investigator and members of the research team. The Principal Investigator is required to attend this interview. S/he may invite members of the research team to attend. The Principal Investigator is strongly encouraged to invite the person responsible for preparing HawkIRB applications for the study.
  - The other part is a review of signed Informed Consent Documents (if study enrollment has begun). This part may also include a tour of the research lab, review of sample storage, research records or subject files.
- Monitoring visits will be conducted using the standard monitoring form (See Appendix ____ of the *Guide for Human Subjects Research at the University of Iowa*). The visit covers the Assurances, HawkIRB system and planned or actual procedures for conducting the study.
- Principal Investigators and other attendees from the research team will receive a handout with educational points and links to additional educational resources that are discussed during the visit.
- The review of signed Consent Documents and any other study records will be conducted before the interview with the Principal Investigator and any research team members whenever possible.

g. **Reporting**

1. **Report to IRB Chair**

- A report is provided electronically via HawkIRB to the Chair for review and approval.
- The draft report contains an overview of the monitoring visit, including the questions asked, information gathered and any findings. Educational points provided during the visit are removed from the report to the Chair.
- The Chair makes the final determinations regarding required actions and findings that require referral to full-board. (See section regarding ‘Noncompliance Review’ in the *Guide for Human Subjects at the University of Iowa*).

2. **Report to Principal Investigator**

- After the Chair signs the report, a copy will be provided to the Principal Investigator and any team members who attended the compliance monitoring visit. The report will be sent via HawkIRB.
- The report consists of a table of any findings from the Monitoring visit and any
corrective actions required of the Principal Investigator and/or research team by the IRB. Sections of the Monitoring form with no findings will be removed from the final report to the PI.

h. Response to Monitoring Report

- The deadline for response to any required actions will be two weeks from the date the report is sent out. This deadline is provided in the table of Findings and Required Actions.
- A written record of Monitoring activities will be attached electronically to the monitoring section of the HawkIRB research application.
- If a response has not been received by a few days before the deadline, a ‘gentle reminder’ of the deadline may be sent to the PI and Research Team Members.
- The IRB Chair may extend the deadline as necessary either upfront or upon request from the PI prior to the deadline. For example, the deadline may be extended when it falls on a University holiday or when there are other extenuating circumstances for the Principal Investigator.
- If no response is received, the report may be sent to the full board for consideration of study suspension until the issue is resolved.

i. Findings of Potential Noncompliance

- Monitoring Reports with findings of potential noncompliance that require full-board review will be scheduled for discussion at the next available IRB Chairs meeting. The IRB Chairs will discuss agenda items for future Executive IRB Meetings that will be considered for possible noncompliance (serious and/or continuing).
- Follow procedures described in Chapter 10 of the *Guide for Human Subjects Research at the University of Iowa* for IRB review of incidents of noncompliance.

j. Response to Complaints by Subjects or Others

- The Education and Compliance program will field and investigate all complaints regarding the conduct of human subjects research that is overseen by the University of Iowa Institutional Review Board. All complaints received by HSO staff, IRB Chairs and/or IRB members will be forwarded to an Education and Compliance Specialist for inquiry.

  - **Investigation** - When a complaint is received, attempts will be made to obtain additional information from the complainant, if possible. The inquiry may also involve contact with the Principal Investigator and/or research team member(s) of the specific study addressed in the complaint. The information collected will be informally presented to an IRB Chair. If further information is required the IRB Chair may request an IRB-directed Monitoring visit. Response to any complaints involving noncompliance or unanticipated problems involving risks to subjects or others will follow the procedures described in Chapter 10 of the *Guide for Human Subjects Research at the University of Iowa*.

  - **Tracking** - Information gathered regarding complaints will be recorded in an Access database stored on the HSO shared drive (I:\HSO\Procedures\Complaints and...
Concerns). The entry will include any specific directives from an IRB Chair for additional follow up or monitoring. Due to the potential sensitive nature of these complaints, access to the database will be limited to HSO staff and IRB Chairs.

k. All IRB-03 studies that enroll VA subjects
Beginning FY2009, VHA research facilities must conduct complete audits of informed consent documents and tri-annual regulatory audits for all research studies that are active (open to enrollment or closed to enrollment but still with data collection or data analysis). Initial informed consent audits will include all informed consent documents signed in the previous 12 months, including re-consents of previously enrolled subjects. Subsequent informed consent audits will continue on an annual basis. Human Subjects research study audits may be conducted more frequently as deemed appropriate.

For protocols undergoing a regulatory audit, Principal Investigators will be notified in advance and provided a regulatory audit template.

The VA Research Compliance Officer (RCO) has tools available, such as a Principal Investigator Guide, an informed consent audit template and a sample subject enrollment log, that may assist in ensuring that all elements of informed consent documentation and conduct of research are met. These documents can be obtained by contacting the RCO directly or the VA IRB page of the HSO Website.

The VA Research Compliance Officer (RCO) under the Medical Center Director will conduct all informed consent and regulatory audits. All audit findings will be forwarded to UI IRB. Under the Office of Research Oversight (ORO) guidelines, the RCO must report all identified serious or continued noncompliance (as defined in the revised VA Handbook 1058.01) identified during an audit to the Medical Center Director, the Associate Chief of Staff for Research (ACOS/R) the Research and Development Committee and the Institutional Review Board (IRB) Chairperson. The Medical Center Director will then report the noncompliance to the ORO Regional Office, the Office of Research and Development (ORD) and VISN leadership.

2. Educational Sessions and Resources
The IRB Education and Compliance Program also offers training in the use of HawkIRB and presentations on a variety of topics related to human subjects research for faculty, staff, and students at the University of Iowa.

a) HawkIRB Training Sessions – These 1 ½ to 2 hour sessions offer an overview of the technical aspects of HawkIRB as well as guidance on the completion of HawkIRB forms. Principal Investigators, delegates, and research team members will learn about the HawkIRB system and how to submit various types of applications.

Separate training sessions are offered for (1) New Project Applications and (2) Continuing Review/Modifications/Reportable Event Forms and Project Closure. A schedule and description of HawkIRB training sessions is available on the Human Subjects Office web site.

b) Topical presentations – Presentations are offered on a variety of topics related to the conduct of human subjects research and the IRB review process. These presentations
may be given by HSO Staff, IRB Chairs, and other experts from the UI Campus or from outside the University of Iowa. A schedule and description of these topical presentations is available on the Human Subjects Office web site.

c) Study Initiation Educational Sessions – Approved projects are selected for a study initiation session at the time of IRB or Chair review of the HawkIRB New Project application. These sessions are scheduled within a month of IRB approval unless other arrangements are requested by the Principal Investigator. The session typically lasts two hours. Study enrollment may begin after the receipt of IRB approval. The educational session may be conducted either before or after the start of study enrollment.

Education is provided about the following topics:
- The HawkIRB system
- Roles and responsibilities of the Principal Investigator and members of the research team
- Recruitment procedures
- Screening procedures and the collection of screening data
- Consent process, proper documentation of consent, and tracking of optional agreements
- Enrollment tracking
- Study procedures
- Reportable events
- Storage of study documents, data, and specimens or samples
- Privacy and confidentiality protections
- Data analysis
- Drug/device accountability
- Subject payment

d) ‘By Request’ Educational Sessions – The Principal Investigator, research team members or departmental personnel may request a general session similar to a Study Initiation Educational Session. Or, the IRB Education and Compliance Program Specialists can conduct a session to meet the specific needs of a research group or members of a particular department.

e) ICON Presentations – Web-based education about issues related to human subjects research at the University of Iowa. More information on how to access ICON presentations can be found on the HSO Website.
**E. Project Closure**

**When should I close my project with the IRB?**

Projects should NOT be closed unless all of the following are completed:

- Protocol indicated research activities including interaction with subjects and collection of data or specimens
- Collection of data about subjects even when no subject contact is necessary
- “Cleaning” of data
- Analysis of identified or linked data for research purposes or during the publication process
- Any other research use of the data which involves access to identified or linked (coded) data or specimens collected during the conduct of research

When a study ends, is closed, canceled for any reason, or is prematurely completed you must complete a Project Closure Form. A Project Closure Form serves as notification to the Human Subjects Office that IRB continuing review of the study is no longer needed.

If no subjects have been enrolled in a study for a period of three or more years, the IRB may require that the project be closed, unless there are extenuating circumstances for keeping the project open (e.g., the study is about a rarely-seen condition). If a project is closed and no subjects have been enrolled, study records must be maintained for at least three years after the closure was submitted.

*Take care not to close the project too soon! Once a Project Closure Form is submitted, no more data may be collected about any of the subjects in the study and no more contact with subjects for research purposes is allowed. There is no mechanism to re-open a closed study.* Therefore, if an investigator is still collecting follow-up data about subjects (either directly from subjects or indirectly from existing records), the project should remain open until all data have been collected, even if new subjects are no longer being enrolled.

**How do I submit a project closure?**

If your project was started in the HawkIRB system or has been transferred to the HawkIRB system, you should use HawkIRB to close the project. Log-on to HawkIRB and choose the project you wish to close. Choose the “Project Close Form” and follow the directions to submit the project closure. *Take care not to close the project too soon! Once a Project Closure Form is submitted, no more data may be collected about any of the subjects in the study and no more contact with subjects for research purposes is allowed. There is no mechanism to re-open a closed study.*

In adherence with federal regulation once a research project is formally closed with the IRB via the HawkIRB electronic system, all research related activity must halt. Research activity includes contact with subjects, review of identifiable subject data, analysis of identifiable subject data, etc. If new information that may affect the safety or medical care of enrolled subjects is discovered or provided to the research team after a project has been closed, notification to the IRB must occur within ten working days of the event or notification to the investigator of the event. In order to inform subjects of the new information, IRB approval is required prior to subject notification of such information. In order to provide the appropriate IRB approval to notify subjects of the new information, a HawkIRB new project application submission will be required for a previously closed project. The project application will require an explanation including the new information.
that was discovered or provided to the research team and a plan for how the information will be disseminated to the enrolled subjects. All relevant materials in connection with the method of dissemination will need to be included in the HawkIRB application for IRB approval. In most cases, a waiver of informed consent can be obtained in order to provide the new information to the enrolled subjects.

F. Record Keeping

What (if any) IRB related documentation do I need to keep?

Every principal investigator is required by University/VAHCS and federal regulations to maintain records of all correspondence relating to the use of human subjects in research. Copies of the Human Subjects application forms, notices of approval, and signed Informed Consent Documents must be maintained in the investigator's records. All records of human subject research are subject to inspection by federal authorities and the University of Iowa IRB.

How long do I have to keep records pertaining to my research?

Copies of all research records for studies that do not involve protected health information must be kept for at least three years after the close of the study. Copies of all research records for studies that involve protected health information must be kept for at least six years after the close of the study. Copies of all research records for VAHCS studies must be kept indefinitely after the close of the study. Studies that involve drugs or devices seeking FDA approval must be kept for two years after the FDA has taken final action on the marketing application. Sponsors may require a longer retention rate.

Chapter 8 – Vulnerable Populations

Federal regulations involving human subjects in research include specific protections for children, pregnant women and fetuses, and prisoners. In addition, the IRB expects the investigator to provide additional information regarding cognitively impaired individuals in research as well as indicate in the application any other populations that the investigator might consider to be particularly vulnerable in a research setting. Examples of these additional types of vulnerable populations include those persons who are educationally or economically disadvantaged, students (see Chapter 5, Section E1 of this Guide for more information regarding students in research), or other groups that may require special consideration.

A. Pregnant Women, Human Fetuses and Neonates

Federal regulations direct that IRBs require additional safeguards before approving research involving fetuses, pregnant women, or neonates (45 CFR 46, Subpart B).

The IRB may approve research involving pregnant women or fetuses if all of the following conditions are met:

a) where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

b) the risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means;
c) any risk is the least possible for achieving the objectives of the research;

d) if the research holds out the prospect of direct benefit to the pregnant woman, the prospect of direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, the woman’s consent is obtained OR

e) if the research holds out the prospect of direct benefit solely to the fetus, then the consent of the pregnant woman and the father is obtained except that the father’s consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest;

f) each individual providing consent under (d) or (e) is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

g) for children who are pregnant, assent and permission are obtained in accord with the regulations for children in research;

h) no inducements, monetary or otherwise, will be offered to terminate a pregnancy;

i) individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

j) individuals engaged in the research will have no part in determining the viability of the neonate.

Neonates, neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

a) where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;

b) each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate;

c) individuals engaged in the research will have no part in determining the viability of the neonate;

d) the requirements regarding neonates of uncertain viability (see below) or nonviable neonates (see below) have been met as applicable.

**Neonates of uncertain viability.** Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research unless the following additional conditions have been met:

1. The IRB determines that:
   a) the research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective; or
   b) purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research.

   AND

2. The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent’s legally authorized representative is obtained (except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest).
Nonviable neonates. After delivery nonviable neonates may not be involved in research unless all of the following additional conditions are met:

1. Vital functions of the neonate will not be artificially maintained;
2. The research will not terminate the heartbeat or respiration of the neonate;
3. There will be no added risk to the neonate resulting from the research;
4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
5. The legally effective informed consent of both parents of the neonate is obtained (note: waiver or alteration of the consent does not apply here). If either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of the legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements.

Viable neonates. A neonate, after delivery, that has been determined to be viable may be included in the research only to the extent permitted by and in accord with the requirements for children involved in research (see Section C below).

Research not otherwise approvable will only be allowed in this vulnerable population if:
(a) the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates; AND
(b) the Secretary of DHHS, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following an opportunity for public review and comment, including a public meeting announced in the Federal Register has determined that the research may take place.

Research involving human fetal tissue (placenta, or tissue from a spontaneous or induced abortion or from a still birth) is evaluated as tissue specimen research, using the guidelines for research involving specimens. Studies using human fetal tissue for transplantation research and studies of human embryos involve very explicit regulations concerning consent and study procedures. Investigators wishing to conduct transplantation research with human fetal tissue should contact the Human Subjects Office well in advance of IRB application submission to discuss applicable regulations.

B. Prisoners
Because incarceration could affect a person's ability to make a truly voluntary and uncoerced decision whether or not to participate in a research project, the federal regulations provide additional safeguards for the protection of prisoners (45 CFR 46, Subpart C). A prisoner is defined as any individual involuntarily confined or detained in a penal institution. This definition includes 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.

At the University of Iowa, any project that recruits prisoners must be reviewed at a full IRB
meeting with a prisoner advocate present. If the project was not initially approved to recruit prisoners, then the investigator may not enroll a prisoner (e.g., a prisoner who is brought to UIHC for treatment who happens to be eligible for a research study may not be enrolled unless the HawkIRB application indicates the enrollment of prisoners.)

The prisoner rules also apply for a subject who at a later date becomes a prisoner, because it is unlikely that the IRB review of the research project contemplated the constraints imposed by incarceration. Therefore, if an investigator determines that a subject has become a prisoner at some later date after enrollment, and the study involves additional research interventions or interactions with that subject, the subject must either be dropped from follow-up, or a modification application must be submitted requesting review for inclusion of prisoners as subjects.

When a prisoner is a subject, in addition to the usual criteria for approval, the IRB must find that:

1) the research under review represents one of the categories of research permissible under 45 CFR 46.306(a)(2);

2) any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

3) the risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers;

4) procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;

5) the information is presented in language which is understandable to the subject population;

6) adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and

7) where the Board finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners’ sentences, and for informing participants of this fact.

Four categories of research involving prisoners are permitted under the federal regulations. They are:

1) studies of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

2) studies of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

3) research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere); and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults; or
4) research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject.

The Informed Consent Document must include additional information for potential subjects regarding the fact that participation or non-participation will have no effect on the duration of incarceration or terms of parole. Suggested language is in the Appendix of the Informed Consent Document template.

C. Children

Categories of Research Involving Children

Federal regulations permit IRBs to approve a research project involving children after determining which of the following categories applies, and only if the project satisfies all of the conditions in the applicable category [45 CFR 46, Subpart D (DHHS) and 21 CFR 50 Subpart D (FDA)]:

1) Research that does not involve greater than minimal risk may be approved if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians. The IRB may determine that permission of one parent or guardian is sufficient.

2) Research involving greater than minimal risk, but presenting the prospect of direct benefit to an individual subject, or a monitoring procedure that is likely to contribute to the subject's well-being, may be approved if the IRB finds that:
   - the risk is justified by the anticipated benefit to the subject;
   - the relationship of anticipated benefit to risk is at least as favorable as that presented by available alternative approaches; and
   - adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.

   The IRB may determine that permission of one parent or guardian is sufficient.

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, may be approved if the IRB finds that:
   - the risk represents a minor increase over minimal risk;
   - 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 situations;
   - the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the subject's disorder or condition; and
   - adequate provisions are made for soliciting assent of the children and permission of their parents or guardians.

   In compliance with federal regulations, the IRB must determine that permission of both parents is required, unless one parent is deceased, unknown, incompetent, or not reasonably available, or unless only one parent has legal responsibility for the care and custody of the child.

   The regulations also indicate that children who are wards of the state, or any other agency, institution, or entity can only be included in research in this category if the research is related to their status as wards or conducted in schools, camps, hospitals, institutions, or similar settings in
which the majority of children involved as subjects are not wards. If one of these criteria is met and
the research is approved, the IRB must require appointment of an advocate for each child who is a
ward in addition to the person acting as guardian or in loco parentis. One person may serve as the
advocate for multiple wards, however this advocate must have the background and experience to
act in, and agrees to act in, the best interests of the child for the duration of the child’s participation
in the research and cannot be associated in any way (except as advocate or member of the IRB)
with the research, the investigator(s), or the guardian organization.

4) Research that is not otherwise approvable which presents an opportunity to understand,
prevent, or alleviate a serious problem affecting the health or welfare of children may be approved
if the IRB and the Secretary of DHHS, after consultation with a panel of experts in pertinent
disciplines and following an opportunity for public review and comment, find that:

- the research in fact satisfies one of the above three conditions; or
- the research presents a reasonable opportunity to further the understanding, prevention, or
  alleviation of a serious problem affecting the health or welfare of children;
- the research will be conducted in accordance with sound ethical principles; and
- adequate provisions are made for soliciting the assent of children and the permission of
  their parents or guardians.

In compliance with federal regulations, the IRB must determine that permission of both parents
is required, unless one parent is deceased, unknown, incompetent, or not reasonably available, or
unless only one parent has legal responsibility for the care and custody of the child.

The regulations also indicate that children who are wards of the state, or any other agency,
institution, or entity can only be included in research in this category if the research is related to
their status as wards or conducted in schools, camps, hospitals, institutions, or similar settings in
which the majority of children involved as subjects are not wards. If one of these criteria is met and
the research is approved, the IRB must require appointment of an advocate for each child who is a
ward in addition to the person acting as guardian or in loco parentis. One person may serve as the
advocate for multiple wards, however this advocate must have the background and experience to
act in, and agrees to act in, the best interests of the child for the duration of the child’s participation
in the research and cannot be associated in any way (except as advocate or member of the IRB)
with the research, the investigator(s), or the guardian organization.

Assent

When children are involved in research, the IRB may require the assent (knowledgeable
agreement) of the child, in addition to the permission of the parent(s). (See also Chapter 5, Section
A, Informed Consent and Related Issues, for more information about assent.) Children should be
asked whether or not they wish to participate in the research. The IRB determines whether all or
some of the children are capable of assenting and determine how the assent is to be obtained and
documented.

The regulations do not specify a certain age at which assent must be sought, but for most studies,
the IRB suggests obtaining assent beginning at about age seven. In certain studies involving
treatment for an illness or condition that is available only in the context of research study, the IRB
may determine that the assent of the child is not necessary.

The IRB must determine and document whether assent is required of all children in the research,
some of the children in the research or that assent is not required of any of the children in the research.

D. Cognitively Impaired Persons

NOTES:
- See Chapter 5, Section A, Informed Consent and Related Issues, for more information about who may provide consent on behalf of an incompetent adult.
- A commonly used questionnaire, the Evaluation to Sign Consent, which is posted on the "Forms/Templates" pages of the HSO web site, may be used to assess an individual's capacity to provide consent -- see below for more details.

Individuals in a wide variety of situations may have impaired decision-making capacity. For example, impairment may occur at times of great stress. Impaired capacity is not limited to individuals with neurologic, psychiatric, or substance abuse problems; conversely, individuals with neurologic, psychiatric, or substance abuse problems should not be presumed to be decisionally impaired. Some research questions may be answered only by research that involves persons with impaired decision making capacity; precluding this research would contribute to needless suffering. The most severely impaired individuals have the greatest need for the benefits of research on etiology and treatment. While this area is controversial, limiting research to the least impaired individuals would hamper research on the underlying causes and potential therapies of many disorders. Not all research will directly benefit the individual participant but may offer future benefits to others who have or will develop the condition or disorder. For example, genetic studies, biochemical measures, or other non therapeutic approaches may benefit subsequent generations.

Unlike research involving children, prisoners, pregnant women, and fetuses, no additional Department of Health and Human Services (DHHS) regulations specifically govern research involving persons who are cognitively impaired. While limited decision-making capacity should not prevent participation in research, it is important to keep in mind that additional scrutiny is warranted for research involving this population.

The NIH offers the following Points to Consider to assist IRBs and clinical investigators in their effort to protect participants in research who are, or may be, or may become decisionally impaired:

**Conflicting Roles and Potential Conflicts of Interest**

Potential and actual research participants, especially those with permanent or transient cognitive impairments, may find it difficult to understand the difference between research and treatment, and to understand researchers' multiple roles, making "therapeutic misconceptions" particularly problematic, and possibly creating confusion among participants and their families. It is essential that the consent process (including consent documents) clearly indicate differences both between individualized treatment and research and between clinician and clinical investigator.

**Assessing Capacity to Consent**

Individual's capacities, impairments, and needs must be taken into account in order to develop practical and ethical approaches to enable them to participate in research. A clear understanding of the implications of various cognitive impairments, along with a careful consideration of proposed clinical research methodology, is required. Assessment is complex; simply answering a certain number of factual questions about a protocol may not be an adequate assessment. A key factor in participants' decision making is their appreciation of how the risks, benefits, and alternatives to
participation in the study apply to them personally.

Limited decision making capacity covers a broad spectrum. A healthy person in shock may be temporarily decisionally impaired. Another may have been severely mentally retarded since birth, while yet a third who has schizophrenia may have fluctuating capacity. Researchers should be sensitive to the differing levels of capacity and use assessment methods tailored to the specific situation. Further, researchers should carefully consider the timing of assessment to avoid periods of heightened vulnerability when individuals may not be able to provide valid informed consent.

Both IRBs and clinical investigators must keep in mind that decision making capacity may fluctuate, requiring ongoing assessment during the course of the research. The consent process should be ongoing. The IRB, at its discretion, may require an outside witness to observe the consent process.

Because no generally accepted criteria for determining competence to consent to research exists for persons whose mental status is uncertain or fluctuating, the role of the IRB in assessing the criteria proposed by the investigator is of major importance. The selection of an appropriate representative to consent on behalf of those unable to consent for themselves must be accomplished without clear guidance from statutes, case law, or regulations.

**Comprehension**

The determination of a subject's ability to understand the implications of the decision to participate in research is best made by the clinician/investigator. In most cases, it will be the clinician/investigator who is in the ideal position to evaluate the subject's ability to understand the implications of the research and whether the subject is making a rational decision to participate. Likewise, in most studies it is the clinician/investigator who can best make a judgment of the subject's ability to understand and follow the protocol.

In developing the consenting process, the investigator is obligated to incorporate any special accommodations necessary to assure that the subject population or their surrogates comprehend the nature and purpose of the study. Useful techniques may include simplified consent documents, supplemental summary sheets, formal Q&A sessions for the subject and family or friends, and waiting periods after the initial discussion before the prospective subject actually enrolls.

There is no universally accepted test or standard for making a determination of comprehension. This process should operate in research studies in much the same manner as the informed consent process in clinical treatment that does not involve research.


**Voluntary Agreement**

Closely related to the determination of the ability to comprehend the nature of the study is the importance of ensuring that subjects' participation is completely voluntary. Some knowledge and assessment of the subject's competence is relevant to a determination of whether voluntary participation is evidenced by a written consent, or in the case of persons lacking legal capacity to consent, their assent. Research should not be conducted against the wishes of the subject, and
making certain that the written documents are indeed a reflection of reality is the function of the
individual researcher and the IRB.

Second Signature on the Consent Document
There are many situations in which a subject should be encouraged to authorize the
involvement of family members. However, the permission of another party will be required only
when the subject is determined to lack the legal ability to provide an informed consent. This would
include children (when research is conducted in the state of Iowa, unmarried persons under the age
of 18) and persons adjudicated incompetent. This also includes persons who are not capable of
understanding the nature of their illness or the risks, benefits, and natural consequences of
participation. Also see Chapter 5, Section A, Informed Consent and Related Issues, for more
information about who may provide permission for an incompetent adult to participate in a research
study.

In conclusion, in all human research, varied degrees of research risk and decisional impairment
call for varied levels of scrutiny and safeguards; additional protections may be highly advisable in
certain circumstances. But treating all individuals who have cognitive deficits as incapable of
understanding research is inaccurate and disrespectful of their autonomy. Many individuals,
adequately informed, may be willing to undertake certain risks so that they, or others, may benefit
in the future. Researchers and IRBs must strive for a balance that maximizes potential benefits and
opportunities, recognizes and extends individual autonomy, and minimizes risks associated
with scientific inquiry.

Chapter 9 – Special Topics

Collaborative Research
UI IRBs may approve human subjects research activities at locations for which the IRB has an
understanding of the local research context or the University is assured that there is appropriate
oversight for the conduct of human subjects research. The UI IRBs approve collaborative projects
within the UI and have mechanisms in place to assure appropriate oversight of collaborative
research with non-UI entities.

1. With other UI Personnel
The UI encourages collaborative research projects across departments. Research team members
can be from any department on the UI campus. There are some projects that may develop into the
sharing of information with other researchers who are not members of the research team. Research
team members should not share data or specimens with investigators outside of the research team
for the project unless the subject is informed of this possibility in the informed consent document.
Refer to the section on Data and/or Specimens below for more information.

2. With non-UI entities
In the conduct of cooperative research projects, each institution (entity) is responsible for
safeguarding the rights and welfare of human subjects and for complying with any applicable
for cooperative research projects which involve more than one institution (or entity). To avoid
duplication of review efforts by IRBs, institutions can choose to conduct joint reviews, rely upon
the review of another qualified IRB, or make other arrangements to establish oversight
responsibilities.
Discussion of how to assure the rights and welfare of human subjects in research at each entity involved in the research usually begins with an evaluation of whether or not each entity is “engaged” in human subjects research. An entity becomes “engaged” in human subjects research when its employees or agents (agents include all individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility):

i) intervene or interact with living individuals for research purposes OR

ii) obtain individually identifiable private information for research purposes

An entity is automatically considered to be “engaged” in human subjects research whenever it receives a direct DHHS award to support such research. In these cases, the awardee institution bears ultimate responsibility for protecting human subjects under the award. OHRP has provided guidance (http://www.hhs.gov/ohrp/humansubjects/guidance/engage08.html) and examples for when institutions are considered to be “engaged” in research and examples of when institutions are NOT “engaged” in research. The UI IRB makes a determination about whether or not a cooperating outside institution is engaged in human subjects research. This determination is made by the appropriate UI IRB Chair based on the outside institution’s role and whether or not that role meets any of the criteria for “engaged in research” as defined in the guidance above. Any questions an IRB chair might have regarding making that determination are posed to OHRP by phone call or e-mail. Please call the HSO for more information if there is any question about the involvement of outside institutions in human subjects research.

Once the determination is made that the outside institution is engaged in human subjects research, the following are the UI IRB policies with regard to IRB oversight at those institutions.

1) When the outside institution is receiving federal funds through a subcontract with the UI, the UI Division of Sponsored Programs requires documentation that the outside institution holds an FWA through the subcontract process. If the outside institution does not hold its own FWA, the UI requires that they obtain one prior to finalization of the subcontract.

If this is the case, and the other institution obtains its own FWA, there are a few methods of IRB oversight that the UI IRB would consider acceptable based on the circumstances of the project and the role of the other institution. The UI IRB could either

- accept a concurrent review of the research project with the other institution’s own IRB, or
- be the IRB of record for the other institution. This agreement is formalized through the use of an IRB Authorization Agreement, or
- accept the other institution’s IRB as the IRB of record for the project. This would be in cases where the UI determines that the outside institution’s IRB review will provide more appropriate expertise, oversight, and/or knowledge of local context for the UI role in the study. This agreement is formalized using an IRB Authorization Agreement or other equivalent agreement. The outside IRB is then added to the UI FWA. Research projects utilizing the VAHCS are not eligible to receive this type of deferred judgement.

EXCEPTION: Under limited circumstances, when the UI is able to assure understanding of the local context in relation to the proposed research and has sufficient resources to provide appropriate oversight during the conduct of the research, the UI may choose to extend its FWA to cover the outside institution’s role in the individual project. This agreement is formalized using an Individual Investigator’s Agreement.
There are two instances whereby this mechanism will NOT be allowed:

a. If the non-assured institution is the primary awardee for an DHHS-funded project OR
b. If the non-assured institution routinely engages in the conduct of human subjects research.

If either of the above conditions applies to the cooperating institution or investigator, the non-assured institution will be required to obtain its own OHRP-approved FWA.

2) When the outside institution is not receiving federal funding for the study through a subcontract with the UI, the UI IRB requires that the research be conducted under either the other institution’s IRB oversight or the UI IRB takes on oversight of the research. In the former instance, the IRB will require documentation that the outside IRB will provide this oversight. In the latter instance, this agreement is documented through a formal IRB Authorization Agreement.

The UI IRB will oversee research for an outside institution only when the UI IRB is able to assure understanding of local context in relation to the proposed research and has sufficient resources to provide appropriate oversight during the conduct of the research.

For each of these mechanisms of collaborative research oversight, you must have the approval of the designated IRB(s) of record PRIOR to conducting any research that involves human subjects. Documentation of complete contact information at each applicable collaborative site will also be required prior to the start of any research activity. So, you must have the signed agreements and requirements finalized prior to the final approval of the project by the UI IRB and before you can conduct multi-institutional research projects that involve human subjects. The final determination to enter into any agreements described in this section is made by the UI Institutional Official.

For projects that involve international sites, please see the section below on International Research.

Conflict of Interest –

The University of Iowa revised its Conflict of Interest in Research policy in August 2012, in order to be in compliance with the federal regulation. The regulation places the responsibility for determining the existence of a financial conflict of interest in research on the institution rather than the investigator. Researchers must disclose all financial interests in outside entities in the eCOI Disclosure System, and then the Conflict of Interest in Research Office reviews the disclosures in the context of all routing forms and IRB applications.

Conflict of interest in research involves situations in which an investigator has a significant financial interest that may compromise, or have the appearance of compromising, professional judgment in the design, conduct, or reporting of research.

The policy applies to all individuals involved in research at the University, regardless of job title,
who contribute in a substantive way to the development, execution, and reporting of research, and who are granted a significant degree of freedom in exercising independent judgment. The terms “Investigator,” “Key Personnel” and “Significant financial interest” are defined below.

a. "Investigator" means the principal investigator or project director and any other person, whether faculty, staff, or student and regardless of title or position, who has the authority to make independent decisions related to the design, conduct, or reporting of University research. Also includes subgrantees, contractors, collaborators, or consultants of the University.

b. “Key personnel" means a PHS project director or principal investigator and any other individual who contributes to the scientific development or execution of a project in a substantive, measurable way, and who is included in the grant application, progress report, or any other report submitted by the institution, whether or not they receive salaries or compensation under the grant.

c. "Significant financial interest" means anything of monetary value or potential monetary value held by an investigator (and by the investigator's spouse and dependent children), and that reasonably appears to be related to the investigator's institutional responsibilities, as follows:

(1) With regard to any publicly traded entity, remuneration received from the entity in the twelve months preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds $5,000. [For purposes of the definition of "significant financial interest," remuneration includes salary and any payment for services not otherwise identified as salary (e.g., consulting fees, honoraria, paid authorship), equity interest includes any stock, stock option, or other ownership interest, as determined through reference to public prices or other reasonable measures of fair market value.]

(2) With regard to any non-publicly traded entity, the value of any remuneration received from the entity in the calendar year preceding the disclosure, when aggregated, exceeds $5,000, or any equity interest (e.g., stock, stock option, or other ownership interest);

(3) Intellectual property rights and interests (e.g., patents, copyrights), upon receipt of income related to such rights and interests; or

(4) A position giving rise to a fiduciary duty, such as director, officer, partner, trustee, employee, or any position of management.

(5) For investigators applying for or conducting research funded by the PHS, any reimbursed or sponsored travel related to the investigator's institutional responsibilities (i.e., travel is paid on behalf of the investigator and not reimbursed to the investigator so that the exact monetary value may not be readily available). Disclosure of this interest will include the purpose and duration of the trip, the identity of the sponsor/organizer, and the travel destination.
The HawkIRB research application has an interface with the eCOI disclosure system that automatically updates once a financial disclosure has been completed. Question II.6 in the HawkIRB application automatically designates the Principal Investigator and all faculty members listed on the research team as “key personnel.” The Principal Investigator, or their delegate, will be responsible for indicating whether or not all remaining research team members should be designated as “key personnel.” Any designated key personnel will be required to complete a COI training module and annual financial conflict of interest disclosures. HawkIRB will not allow any form type (new, modification, continuing review, or modification + continuing review) to be submitted until this annual financial disclosure requirement is met.

The Conflict of Interest in Research Office (COIR) reviews all financial interest disclosures and flags those interests considered significant. Those are disclosures meeting the threshold(s) outlined in the PHS regulation and UI policy. The COIR Office makes a determination on a project-by-project basis whether the disclosed financial interest is related or could impact the research. Review by Conflict of Interest in Research Committee (CIRC). Where the Conflict of Interest Officer has determined that a financial conflict of interest exists, the Conflict of Interest in Research Committee will develop and recommend a management plan that specifies the actions that have been and/or will be taken to manage the financial conflict of interest. In so doing, the CIRC will consider the nature of the research, the nature and size of the interest, the degree to which the conflict is related to the research, the extent to which the interest could be affected by the research, and any management strategies that would mitigate or eliminate the conflict.

Management strategies may include, but are not limited to:

i. Public disclosure of financial conflicts of interest (e.g., when presenting or publishing the research);
ii. For research projects involving human subjects research, disclosure of financial conflicts of interest directly to participants;
iii. Appointment of an independent monitor capable of taking measures to protect the design, conduct, and reporting of the research against bias, or the appearance of bias, resulting from the financial conflict of interest;
iv. Modification of the research plan;
v. Change of personnel or personnel responsibilities, or disqualification of personnel from participation in all or a portion of the research;
vi. Reduction or elimination of the financial interest (e.g., sale of an equity interest); and
vii. Severance of relationships that create actual or potential financial conflicts.

Specific provisions applicable to human subjects research. As a general policy, the University will not allow an investigator with a financial conflict of interest to conduct a clinical research project whose purpose is to evaluate the safety or effectiveness of a drug, medical device, or treatment. In such cases, disclosure or standard conflict management strategies may be inadequate and adequate monitoring plans may be difficult or impossible to implement. This prohibition applies not only to the principal investigator of a clinical research project, but also to any investigator involved in the design, conduct, or reporting of the research. A principal investigator would thus be prohibited not only from serving in that role, but in any investigator role on the study. While the review of a significant financial interest is being considered by COIR and CIRC, any existing research projects will be asked to halt subject recruitment and enrollment until a formal decision by CIRC has been reached.
The CIRC will determine if the researcher's significant financial interests could directly and significantly affect the design, conduct, or reporting of research. In making the determination, the CIRC considers the nature of the research, the nature and size of the financial interest, the degree the conflict is related to research, the extent the interest may be affected by the research and strategies proposed to reduce or eliminate the conflict. The CIRC will determine whether the COI can be managed, and if so, the committee will develop a written management plan outlining the obligations s/he must comply with in the conduct and reporting of the human subjects research project.

The management plan is provided to the Vice President for Research who has the authority to accept, reject or amend the plan. Once accepted, the plan is sent to the investigator, who agrees to the requirements by signing it and returning it to the Conflict of Interest in Research Office. A copy of the signed management plan is sent to the investigator's departmental executive officer and dean, the Human Subjects Office, Sponsored Programs, and to the principal investigator of the study, if different from the investigator who was found to have a COI. The notice to Sponsored Programs and the Human Subjects Office serves as notice that these offices may continue with their respective reviews.

A designated HSO staff member will attach the management plan to the CIRC section of HawkIRB. The HawkIRB application is then reviewed to ensure the content is consistent with the management plan, and any required changes to the Informed Consent Document (ICD) are made prior to review by the IRB. The IRB Chair or a convened full board will conduct the final review of the HawkIRB application and management plan.

**Course-Related Student Projects**

See the Revised Policy located on the Human Subjects Website found [here](#).

**Data and/or Specimens**

Most research involves the collection of data and/or specimens. This section outlines some issues with regards to data and/or specimen collection.

**Existing Data or Specimens**

**Case Reports**

Case reports (i.e. write-up of a single patient case) do not need prospective review by the IRB. Publishing a case report does not meet the federal regulatory definition of “human subjects research.” The IRB will review and provide approval for case reports when they are being submitted to a journal that requires IRB approval as a condition of publication – this is the journal’s requirement and not an IRB requirement.

**Chart/Record Reviews**

A human subject is defined, in part, as a living individual about whom an investigator conducting research obtains identifiable private information. Therefore, medical chart or other kinds of record review research (e.g., student records) require IRB review and approval. The IRB chair may authorize a waiver of informed consent for chart/record review research studies if the
study is minimal risk, the rights and welfare of the subjects are not adversely affected, the research could not practicably be carried out without the waiver, and, when appropriate, subjects are provided with pertinent information after participation.

Generally, a waiver of consent is granted when all of the chart/record information that will be used in the research study exists in the original records prior to the date of the IRB application -- such studies are considered retrospective chart/record reviews. However, if some or all of the information that will be used in the research will be taken from charts/records dated some time in the future (i.e., after the date of the IRB application), then consent from some or all subjects may be required.

In order to assist the IRB in making the determination for waiver of consent, the investigator should provide the inclusive dates of chart/record information that will be used in the study. In addition to describing the purpose or hypothesis being studied, and the types of analyses that will be done, the investigator should provide the IRB a list of specific variables that will be used from the original source. This can be provided within the HawkIRB application by including the data collection forms that will be used for compiling the chart/record data.

If the research study involves gathering data from the UIHC medical record, the UIHC Joint Office for Compliance requires that a "Request for Information" form be completed and signed. The IRB ID number and date of IRB approval for the project in which the data will be used must be included.

Existing Specimens

Research involving existing specimens (e.g., all specimens are "on the shelf" at the time the application for IRB review is submitted) may be classified as exempt only if there is no link, either in the investigator's records or elsewhere (e.g., pathology department), linking the specimen back to the identity of the subject. Even though it may be difficult or time-consuming to determine the subject's identity, if there is a link, the research cannot be classified as exempt, but may be eligible for a classification of expedited research.

Research involving specimens, all of which have already been obtained at the time of the IRB application, may be eligible for a waiver of consent. For further information regarding a waiver of consent, please see Chapter 5 of this Guide.

Secondary Analysis of Existing Data

Any research that involves secondary use of data where individual subject records that are used which would include private identifiable information, requires IRB review. For example, an investigator who plans to analyze an existing data set obtained from another source that includes private identifiable information should submit an application for IRB review if the data set contains records on individual human subjects. If the data set contains no identifiers (either direct or linked code numbers), and the results will not be submitted to the FDA, the project is not human subjects research. Otherwise, the project may be eligible for expedited review. If you have questions about whether or not your project requires IRB review, please contact the Human Subjects Office at (319) 335-6564 or by email at mailto:irb@uiowa.edu.

The IRB chair may waive informed consent if research is minimal risk, the rights and welfare of the subjects are not adversely affected, the research could not practicably be carried out without the waiver, and, when appropriate, subjects are provided with pertinent information after participation. Secondary analysis of already aggregated data sets (e.g., meta analysis) does not require IRB review, since the investigator does not obtain individual human subject information.
Prospectively Collected Data or Specimens

Specimens
If the study involves the collection of extra tissue or specimens beyond what is needed for a clinical procedure, IRB review and approval and an Informed Consent Document is required. In such cases, the subject should be informed as to the purpose for obtaining the specimen. If the specimen is going to be retained for future use beyond the purpose of the study for which it was obtained, the subject should be informed regarding who might have future access, for what purposes the specimen might be used, how to request destruction or removal of the specimen from future research use, whether there are plans to compensate the subject should a product be developed. The Informed Consent Document template contains suggested language addressing these issues.

Specimens (e.g., blood, tissue, other bodily fluids) collected as part of standard clinical procedures that are unused at the completion of the diagnostic or treatment process and are destined for disposal are often referred to as discarded specimens. The UIHC surgical consent form notifies patients that such materials may be discarded or used in research. However, the purpose of the UIHC surgical consent form is for a patient to consent to a surgical procedure. It is not intended for or adequate as an Informed Consent Document to participate in research. Therefore, studies involving discarded specimens obtained prospectively may require an Informed Consent Document. As a general rule, if the study requires obtaining other identifiable information about the patient (demographic, diagnostic) for use in the analysis, consent may be required. The chair may consider waiving informed consent only if the requirements for waiving informed consent are met.

Data Registry
A research registry is defined as the collection and maintenance of data in which:

1. the individuals in the registry have a common condition,
2. the individuals in the registry may be contacted for future studies, and
3. the names/data of the individuals may be used by investigators other than the original research team.

If a registry is being created, the investigator should include the name of the registry, the method of data storage, how subjects are informed of their inclusion in the registry, and how subject identity and information is protected in the New Project Application. The Informed Consent Document should inform a potential subject that if s/he decides to participate, his/her name will be stored in a registry and s/he may be contacted in the future by investigators other than the current research team.

Not all compilations of individuals' names and associated data constitute a research registry. A database is not necessarily a registry. The key element in a registry is that names and other identifying information are being stored so that people other than the original research team may access the registry information in the future to contact individuals for other studies. For further guidance, please contact the Human Subjects Office.

Specimen/Data Repositories
If a University of Iowa researcher stores human specimens for the specific purpose of providing
specimens and/or associated data to others who are not members of the original “specimen collection” research team, the IRB may require that the researcher provide additional information to the IRB for establishing a formal repository. The IRB has developed these special procedures based on guidance from the Office for Human Research Protections in the Department of Health and Human Services.

**Purpose for Establishing a Formal Repository:**
- to give the “collector investigator” authority and responsibility for distributing specimens or data from the repository if certain pre-determined guidelines are met
- to minimize the paperwork burden on “recipient investigators” (those individuals with whom the PI intends to share the specimens or data)

**Features of a Formalized Repository:**
- Repository PI (“collector”) obtains IRB approval for establishing and maintaining the repository
- Repository PI determines the conditions under which s/he will share specimens or data from the repository with Recipient Investigators
- Repository PI develops a “Usage Agreement” that describes those conditions
- Repository PI is responsible for maintaining a copy of the signed Usage Agreements

If Recipient Investigator agrees to those conditions, and the Repository PI and Recipient Investigator both sign the Usage Agreement, the Recipient Investigator does NOT need IRB approval – the Repository PI may provide the specimens or data based on the signed Usage Agreement alone.

The Recipient Investigator **DOES need IRB approval** in the following circumstances:

a) If the Recipient Investigator wants to use the specimens or data in a manner that goes beyond what is described in the Usage Agreement (e.g., get subject identifiers so that additional data items can be obtained from medical records), the Recipient Investigator must submit an IRB application for review and approval. The IRB application should specifically describe why the Recipient Investigator cannot do his/her study without going beyond the terms of use in the Usage Agreement.

b) If the Recipient Investigator is being funded by a funding source that requires evidence of IRB approval (e.g., NIH), the Recipient Investigator should submit an IRB application for review and approval. The Recipient Investigator should include with his/her IRB application a copy of the funding agency grant, and a copy of the signed Usage Agreement so that the IRB knows that the terms of the Usage Agreement will be followed. IRB approval of the Recipient’s use of the specimens or data will be classified as exempt from the federal regulations. The funding agency will be notified by the Division of Sponsored Programs (via the DHHS 310 form) that the PI has obtained IRB approval for an exempt project, and the PI will not have to submit continuing review applications for the duration of that grant.

Further information about establishing a formal specimen repository, along with sample usage agreements and additional information required by the IRB, may be found in a document called "Specimen/Data Repository Procedures at UI" on the IRB Policies and Guidance page. Investigators are encouraged to contact the Human Subjects Office for assistance before
submitting an application to establish a formal registry.

**Emergency Settings: Research in the Emergency Setting (Planned Emergency Research)**

The federal regulations for the protection of human subjects in research require informed consent, with a few narrow exceptions. FDA regulations in 21 CFR 50.24 provides a narrow exception to the requirement for informed consent from each human subject, or his or her legally authorized representative, prior to initiation of an experimental intervention. The Department of Health and Human Services (DHHS) also outlines waiver criteria for DHHS funded research at [61 FR 51531]. These documents establish a single standard for this class of research.

The exception to the requirement for informed consent would apply to a limited class of research activities involving human subjects who are in need of emergency medical intervention but who cannot give informed consent because of their life-threatening medical condition, and who do not have a legally authorized person to represent them. The intent of the new regulation is to allow research on life-threatening conditions for which available treatments are unproven or unsatisfactory and where it is not possible to obtain informed consent, while establishing additional protections to provide for safe and ethical studies.

Persons with life-threatening conditions who can neither give informed consent nor refuse enrollment are a vulnerable population. FDA recognizes that the lack of autonomy and inability of subjects to give informed consent requires additional protective procedures in the review, approval, and operation of this research. The exception from the informed consent requirement permitted by the rule is conditional upon documented findings by the IRB. Because these projects almost certainly represent situations of more than minimal risk and certain requirements are necessary to conduct this research at the UI, call the HSO for guidance if you receive funding to conduct this type of research project.

**Emergency Use of an Investigational Drug or Device**


*FDA defines that *emergency use* means the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval. [21 CFR 56.102(di)]*

**Obtaining an Emergency IND**

The emergency use of an unapproved investigational drug or biologic requires an IND. If the intended subject does not meet the criteria of an existing study protocol, or if an approved study protocol does not exist, the usual procedure is to contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company's IND.

The need for an investigational drug or biologic may arise in an emergency situation that does not allow time for submission of an IND. In such a case, FDA may authorize shipment of the test article in advance of the IND submission. Requests for such authorization may be made by telephone or other rapid communication means.

**Exemption from Prospective IRB Approval**

Emergency use is defined as the use of an investigational drug or biological product with a human subject in a life-threatening or severely debilitating situation in which no standard
acceptable treatment is available and in which there is not sufficient time to obtain IRB approval [21 CFR 56.102(d)]. The emergency use provision in the FDA regulations [21 CFR 56.104(c)] is an exemption from prior review and approval by the IRB. The exemption, which may not be used unless the subject is in a life-threatening or severely debilitating situation in which no standard acceptable treatment is available, allows for one emergency use of a test article without prospective IRB review. Life-threatening means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible. Severely debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

Not all emergency use requires an exemption from prospective IRB review. When there is time for prospective IRB approval, the University of Iowa IRB expects the investigator to complete a New Project application describing the emergency use. The application will be scheduled for review at the next IRB meeting (IRB-01 meets every week). The FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval. [21 CFR 56.104(c)] Therefore, if the first use does not have prospective review, the IRB notifies the investigator that if it is possible subsequent use of the agent will occur, a New Project application should be submitted for IRB review immediately following the first emergency use. The FDA acknowledges, however, that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

The investigator should notify the IRB-01 or IRB-03 chair prior to the emergency use, however, this notification should not be construed as IRB approval. The investigator is required to file a written report within five working days, and notifying the chair is used to initiate tracking to ensure that the investigator files this report as required by 21 CFR 56.104(c). The FDA regulations do not provide for expedited IRB approval in emergency situations. An IRB must either convene and give "full board" approval of the emergency use or, if the conditions of 21 CFR 56.102(d) are met and it is not possible to convene a quorum within the time available, the use may proceed without any IRB approval.

Some manufacturers will agree to allow the use of the test article, but their policy requires "an IRB approval letter" before the test article will be shipped. If it is not possible to convene a quorum of the IRB within the time available, the IRB-01 or IRB-03 chair will send the sponsor a written statement that the IRB is aware of the proposed use and considers the use to meet the requirements of 21 CFR 56.104(c). Although this is not an "IRB approval," the acknowledgment letter has been acceptable to manufacturers and has allowed the shipment to proceed.

**Exception From Informed Consent Requirement**

Even for an emergency use, the investigator is required to obtain informed consent of the subject or the subject's legally authorized representative unless both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:
(1) The subject is confronted by a life-threatening situation necessitating the use of the test article.

(2) Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject.

(3) Time is not sufficient to obtain consent from the subject’s legal representative.

(4) No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

If, in the investigator's opinion, immediate use of the test article is required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the clinical investigator should make the determination and, within five working days after the use of the article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. The investigator must notify the IRB within 5 working days after the use of the test article.

**Genetic Research**

DNA projects, by nature of their subject matter, are reviewed for the following information in addition to the standard required review. Genetic information is uniquely personal information and has the potential to influence employment, insurance, finance, education and possibly self-perception. Therefore, genetic information must be carefully maintained in order to protect against stigmatization, discrimination, or significant psychological harm to the subject.

IRB review considers the following issues in both the application and the Informed Consent Document, as applicable:

* Information that can be obtained from DNA samples in general, and the specific questions to be addressed in this study.

* The extent of subject and sample confidentiality if the sample and subsequent information will be part of a registry or database.

* The rights and limitations of subjects to require destruction of their sample and/or associated data at a future date. The rights and limitations of subjects to require that their sample and or associated data be stripped of any identifying information.

* Identifying information available to other researchers if their sample and/or associated data are part of a registry or database.

* Mechanisms for maintaining confidentiality in long-term studies, registries, or databases.

* Potential for commercial profit by the institution, investigator or sponsor from information gathered in this study.

* The availability or access to genetic counseling in cases where a study may reveal genetically important information (i.e., possessing genetic defects which could be passed on).

* Subjects must have the right to decline receiving genetic information.

In the absence of a specific authorization to maintain a DNA sample, DNA samples collected and stored or analyzed in connection with a research project shall be destroyed upon completion of the project or withdrawal of the individual from the project. This information must be clearly stated in the Informed Consent Document.

Before involving children in DNA research, the parent(s) or legal guardian(s) must review and sign the Informed Consent Document. The Informed Consent Document must give parents/guardians the option of whether or not they want the results (if available) of the genetic analysis disclosed to them. Whenever appropriate, the child's assent should be solicited. Upon reaching the age of majority, if the subject may request his or her information be disclosed that
should be included in the Consent Document. Investigators must follow the appropriate measures with regard to releasing such information (e.g., counseling, etc.). In some cases it may be possible to determine that some members of the family are not genetic relatives. Issues of genetic relationships (paternity or maternity, as could be hidden by adoption or donor fertilization) and other incidental information should not be revealed. The standard Informed Consent Document template contains suggested language for genetic research and for storing tissue or specimens for future use.

**HIPAA**

The Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA) became effective on 4/14/2003. The Privacy Rule provides standards for maintaining the privacy of individually identifiable health information. It applies only to individually identifiable health information that is maintained by a covered entity. If the health information is individually identifiable and if it is held by a covered entity, it is likely to be considered “protected health information.”

*What is a covered entity?*
A covered entity is any of the following:

a) a health plan,
b) a health care clearinghouse (billing service), or
c) a health care provider that transmits health information electronically.

*What is “protected health information” or PHI?*
PHI is health information that:

a) is transmitted or maintained in any form (electronic, oral, paper) by a covered entity AND
b) identifies the individual or could reasonably be used to identify the individual AND
c) 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.

*What kinds of information could identify or reasonably identify the individual?*
Any of the following information for the individual, relative, employer, or household member of the individual are examples:

- Name, street address, city, county, precinct, zip code, geocodes smaller than state
- Date of birth, ages > 89 years of age, or other dates such as diagnosis dates, procedure dates, admission or discharge dates
- Telephone numbers, Fax numbers, E-mail addresses, Social Security number, Medical record number
- Health plan beneficiary numbers, Account numbers, Certificate/license numbers
- Vehicle identifiers and serial numbers or license numbers, Device identifiers and serial numbers
- Web URLs, Internet Protocol (IP) address numbers, Biometric identifiers including finger/voice prints
- Full face photographic images and any comparable images
Is the University of Iowa a covered entity?
No. The University of Iowa is considered a “hybrid entity” in the world of HIPAA. This is because the UI is a single legal component with both covered (e.g. UI Health Care, student health, College of Dentistry) and non-covered functions (e.g. Lipid Research Center, College of Law, etc.). The hybrid entity designation limits the HIPAA liability for the institution. The covered components may use or disclose PHI for treatment, payment, or operations. Research is not treatment, payment or operations so the covered components may not use or disclose PHI for research except as permitted in the regulations.

What research use of PHI do the regulations permit?
The regulations permit the use of PHI for research under two conditions: 1) the investigator obtains a signed authorization from the patient, or 2) the investigator obtains a waiver of authorization from the IRB. At the University of Iowa, the authorization to use PHI is combined with the research informed consent document. Refer to the informed consent document template in the section called “Will My Health Information be Used During this Study?” for the authorization language. If you plan to look at, use, or create PHI for research purposes, a signed informed consent document that includes the “HIPAA” section authorizes the covered entity to disclose the PHI to the research team.

The waiver of authorization to use PHI for research purposes is separate from the waiver of elements of consent from 45CFR46. Like the DHHS waiver, the waiver of authorization to use PHI for research must be approved by the IRB or privacy board. Examples of research that might be eligible for a waiver include retrospective chart reviews or retrospective specimen studies. The New Project Application in HawkIRB includes questions to help the IRB decide whether or not the criteria for a waiver have been met for a given research project. These criteria include:
- The research could not practicably be conducted without the waiver AND
- The research could not practicably be conducted without access to and use of the PHI.
- The use or disclosure of the PHI involves no more than minimal risk to the privacy of individuals based on, at least, the presence of the following elements:
  a. The PI has an adequate plan to protect identifiers from improper use/disclosure
  b. The PI has an adequate plan to destroy identifiers at the earliest opportunity
  c. The PI gives adequate written assurance that the PHI will not be disclosed to others.

Examples of times you might look at, use, or create PHI for research purposes:
If you or a member of your research team within the conduct of a research protocol:
- Look at a clinic schedule, a medical chart, or an electronic record, to schedule subjects for a study visit or identify a diagnosis for subjects, OR
- Conduct research with an inpatient population, OR
- Conduct medical testing, OR
- Conduct research on the CRU, OR
- Conduct a retrospective or prospective chart review, OR
- Create or add information to an in-house database or registry for research use, OR
- Provide treatment through a research protocol, OR
- Collect medical records from an outside institution, OR
- Look at or use data from a QA/QI database, OR
- Compare information collected on a survey to information in the medical record then YOU are looking at, using or creating PHI for research purposes!
For more information about the HIPAA Privacy Rule, check out the HIPAA page on the HSO website.

At the UI:
- [UIHC HIPAA website](#)
- [University of Iowa HIPAA website](#)

Federal links:
- [HIPAA Privacy Rule Office of Civil Rights](#)
- [NIH Information for Researchers on the HIPAA Privacy Rule](#)
- [Privacy Rule Complete Regulation Text (45CFR 160 and 164, unofficial text)](#)

**International Research**

Human subjects research conducted by University of Iowa or VAHCS investigators (faculty, staff or students) in foreign countries remains under the UI purview and guidelines. Procedures normally followed outside the United States for research involving human subjects may differ from those set forth in federal and University policies. These may result from differences in language, cultural and social history, and social mores. In addition, national policies such as the availability of national health insurance, philosophically different legal systems, and social policies may make U.S. forms and procedures inappropriate. While the UI IRB cannot impose our standards for written documentation on other cultures, we do not relax our standards for ethical conduct of research or for a meaningful consent process.

Special attention should be given to local customs and to local cultural and religious norms in drafting written consent documents or proposing alternative consent procedures. Requests to review and waive some standard elements of domestic approvals may be considered. However, protections afforded subjects must approximate those provided to subjects in the United States. Research proposals for which this waiver may be reasonable should include explanations of cultural norms or conditions requiring such a waiver. For example, societies where no written language is used, societies where signatures might represent something quite different than what they represent in the United States.

The first step in the review process would be to make a determination about whether or not your project meets the definition of human subjects research. If you are unsure about whether or not your project would constitute human subjects research, you should contact the Human Subjects Office or contact the Chair of the appropriate IRB. This contact could be in the form of an e-mail describing your project in detail sent either to the Human Subjects Office (irb@uiowa.edu) or the IRB Chair of the appropriate IRB.

If your project does involve human subjects research, you will be required to submit an application via HawkIRB for IRB review and approval **prior** to the conduct of your research. In federally funded research, research activities in a foreign country may be approved if the procedures proscribed by a foreign institution are equivalent to those in the U.S. Research projects must have been approved by the local equivalent of an IRB before they are given final approval by the UI IRB. OHRP provides a listing of the laws, regulations, and guidelines that govern human subjects research in many countries around the world. Where there is no equivalent board or group, investigators must rely on local experts or community leaders to provide approval. The UI IRB will require documentation of this “local approval” before it gives final approval of your project.
**Investigational Drugs or Biologics**

**IND – Investigational New Drug**

Current Federal law requires that a drug be the subject of an approved marketing application before it is transported or distributed across state lines. Because a sponsor will probably want to ship the investigational drug to clinical investigators in many states, it must seek an exemption from that legal requirement. The IND is the means through which the sponsor technically obtains this exemption from the FDA.

During a new drug's early preclinical development, the sponsor's primary goal is to determine if the product is reasonably safe for initial use in humans, and if the compound exhibits pharmacological activity that justifies commercial development. When a product is identified as a viable candidate for further development, the sponsor then focuses on collecting the data and information necessary to establish that the product will not expose humans to unreasonable risks when used in limited, early-stage clinical studies.

FDA's role in the development of a new drug begins when the drug's sponsor (usually the manufacturer or potential marketer) having screened the new molecule for pharmacological activity and acute toxicity potential in animals, wants to test its diagnostic or therapeutic potential in humans. At that point, the molecule changes in legal status under the Federal Food, Drug, and Cosmetic Act and becomes a new drug subject to specific requirements of the drug regulatory system.

There are three IND types:

- **An Investigator IND** is submitted by a physician who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. A physician might submit a research IND to propose studying an unapproved drug, or an approved product for a new indication or in a new patient population.
- **Emergency Use IND** allows the FDA to authorize use of an experimental drug in an emergency situation that does not allow time for submission of an IND. It is also used for patients who do not meet the criteria of an existing study protocol, or if an approved study protocol does not exist.
- **Treatment IND** is submitted for experimental drugs showing promise in clinical testing for serious or immediately life-threatening conditions while the final clinical work is conducted and the FDA review takes place.

Once the IND is submitted to FDA, the sponsor must wait 30 calendar days before initiating any clinical trials. During this time, FDA has an opportunity to review the IND for safety to assure that research subjects will not be subjected to unreasonable risk. For more information on IND’s, refer to the following link: [FDA (CDER) website](https://www.fda.gov/Drugs/InformationOnDrugs/DevelopmentApprovalProcess/InvestigationalNewDrugs/). UI/VAHCS investigators conducting studies with an IND are required to submit documentation from the sponsor (either as a letter or email from the FDA or sponsor or indication on the commercial sponsor’s protocol) of the IND number assigned by the FDA. If the IND is an investigator held IND, the entire IND application and the 1571 are required. This documentation must be attached to the new project application in HawkIRB. IRB staff will check for this documentation and return protocols with inadequate or incomplete documentation of the IND.
Promotion and Charging for Investigational New Drugs
[Taken from 21 CFR 312.7]

Promotion. A sponsor or investigator, or any person acting on behalf of a sponsor or investigator, shall not represent in a promotional context (e.g. in advertisements, brochures or any recruitment media) that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including the dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution.

A sponsor or investigator shall not commercially distribute or test market an investigational new drug. In addition, an investigator should be aware that a sponsor cannot unduly prolong an investigation after finding that the results of the investigation appear to establish sufficient data to support a marketing application.

Charging. Charging for an investigational drug in a clinical trial under an IND is NOT permitted without the prior written approval of FDA. In requesting such approval, the sponsor shall provide a full written explanation of why charging is necessary in order for the sponsor to undertake or continue the clinical trial, e.g., why distribution of the drug to test subjects should not be considered by the sponsor to be part of the normal cost of doing business.

Investigators should include in the “Costs” section of the Informed Consent Document a statement that there will be no charges for the investigational new drug(s) used in the study. If this statement is not included in the informed consent document, the UI IRB will only allow its absence if the investigator attaches the prior written approval of the FDA to the sponsor to allow for test subject charges. This authorization to charge for an investigational drug under this section may be withdrawn by FDA if the agency finds that the conditions underlying the authorization are no longer satisfied. In this instance, it is the responsibility of the investigator to submit a modification to the informed consent document inserting the required statement as indicated above. In such cases where charges are allowed, sponsors are not allowed to commercialize the investigational new drug by charging a price larger than that necessary to recover costs of manufacture, research, development, and handling of the investigational drug. The investigator must be cognizant of this rule when participating in a clinical trial of an investigational new drug.

Treatment protocol or treatment IND. A sponsor or investigator may charge for an investigational drug for a treatment used under a treatment protocol or treatment IND provided:

1. There is adequate enrollment in the ongoing clinical investigations under the authorized IND;
2. Charging does not constitute commercial marketing of a new drug for which a marketing application has not been approved;
3. The drug is not being commercially promoted or advertised; AND
4. The sponsor of the drug is actively pursuing marketing approval with due diligence.

FDA must be notified in writing in advance of commencing any such charges, in an information amendment. Authorization for charging goes into effect automatically 30 days after receipt by FDA of the information amendment, unless the sponsor is notified to the contrary.
Investigational Use of FDA-approved Drugs or Biologics

The investigational use of approved, marketed products differs from the situation described above. "Investigational use" suggests the use of an approved product in the context of a clinical study protocol [see 21 CFR 312.3(b)]. When the principal intent of the investigational use of a test article is to develop information about the product's safety or efficacy, submission of an IND or IDE may be required. However, according to 21 CFR 312.2(b)(1), the clinical investigation of a marketed drug or biologic does not require submission of an IND if all six of the following conditions are met:

(i) it is not intended to be reported to FDA in support of a new indication for use or to support any other significant change in the labeling for the drug;
(ii) it is not intended to support a significant change in the advertising for the product;
(iii) it does not involve a route of administration or dosage level, use in a subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
(iv) it is conducted in compliance with the requirements for IRB review and informed consent;
(v) it is conducted in compliance with the requirements concerning the promotion and sale of drugs; and
(vi) it does not intend to invoke the exception for informed consent requirements [21 CFR 50.24].

Sponsor-Investigator (Investigator-Initiated) Research with Drugs or Biologics

The following information is intended to provide sponsor-investigators with information to guide them through the FDA requirements for sponsor-investigators who hold an IND. The federal regulations for INDs are found under 21 CFR 312. Responsibilities of sponsors and investigators are also contained in the International Conference on Harmonisation (ICH) Guidance for Industry, E6 Good Clinical Practice. For more information, review the FDA’s Center for Drug Evaluation and Research (CDER) web site www.fda.gov/cder.

This text is a synopsis of requirements specific to sponsor-investigators who hold INDs. It is intended to be a guide, but does not include the complete text of the regulations. Hyperlinks are included throughout the following text so that you may read the corresponding regulations. Sponsor-investigators must review and be familiar with the federal regulations before undertaking these responsibilities.

Sponsor-investigators are also required to follow all federal regulations and University of Iowa policies and guidance for Human Subjects research, and VAHCS requirements as applicable. University of Iowa policies and guidance for human subjects research are available in this Investigator’s Guide.

What is a Sponsor-Investigator?

When an Investigator holds an IND for the product being tested in a particular research study, he/she must also assume the role of the Sponsor, and is called a “Sponsor-Investigator.” The FDA defines a Sponsor-Investigator as “means an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The requirements
applicable to a sponsor-investigator under this part include both those applicable to an investigator and a sponsor.” [21 CFR 312.3]

What must the Sponsor-Investigator report to the FDA?
Sponsor-investigators have extensive reporting requirements under FDA regulations.

1. New protocol 21 CFR 312.30a
   Once the IND has been approved by the FDA, the sponsor-investigator must submit a new protocol for any study not contained in the IND application. The protocol can be submitted before or after IRB approval. The study may not begin until the protocol has been reviewed by the FDA and approved by the IRB.

2. Changes in the protocol 21 CFR 312.30b
   The following protocol changes must be submitted to the FDA.
   - For Phase 1 studies, any change that significantly affects the safety of subjects.
   - For Phase 2 and 3 studies, any change that significantly affects the safety of subjects, the scope of the investigation, or the scientific quality of the study.

3. New investigator 21 CFR 312.30c
   The addition of a new investigator must be reported to the FDA within 30 days of the investigator being added. The IND may not be shipped to the new investigator until the FDA has been notified.

4. Information amendments 21 CFR 312.31
   Any essential information that is not included in a protocol amendment, IND safety report, or annual report must be submitted to the FDA. Examples of essential information include new toxicology, chemistry, or other technical information. Information amendments should be submitted as necessary, but not more than every 30 days.

5. IND safety/adverse events reports 21 CFR 312.32
   An investigator shall promptly report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug. If the adverse effect is alarming, the investigator shall report the adverse effect immediately. [21 CFR 312.64]. Guides to adverse event reporting are indicated below:
   - **Unexpected fatal or life-threatening** experiences that are associated with the investigational drug must be reported to the FDA by fax or telephone as soon as possible, but no later than 7 days after the sponsor-investigator initially receives the information.
   - **Serious and unexpected adverse events** associated with the use of the drug that are not fatal or life-threatening must be submitted to the FDA as soon as possible, but no later than 15 days after the sponsor-investigator initially receives the information.

6. Annual reports 21 CFR 312.33
   The sponsor-investigator must submit a progress report to the FDA within 60 days of the anniversary date that the IND went into effect. The sponsor is also required under 21 CFR 312.33 to submit annual reports to the FDA on the progress of the clinical
investigations. [21 CFR 312.64]. The expected contents of the progress report are included in 21 CFR 312.33.

7. Withdrawal of an IND 21 CFR 312.38
Sponsor-investigators must inform the FDA of desire to withdraw an IND.

8. Discontinuation of an investigation 21 CFR 312.31(a)2
If the sponsor-investigator determines that an investigation drug presents an unreasonable and significant risk to subjects, she/he must discontinue the investigation within 5 working days after determining that the investigation should be discontinued. A report of the discontinuation of the investigation should be submitted to the FDA within 5 working days of the discontinuance.

9. Financial disclosure reports 21 CFR 312.57d
Any changes to financial disclosure information must be promptly reported to the FDA during the investigation and for 1 year following completion of the study.

What records must a sponsor-investigator maintain?

The sponsor-investigator is responsible for maintaining the following records during and for 2 years after the date a marketing application is approved for the drug for the indication for which it is being investigated. If no application is to be filed or if the application is not approved for such an indication, the sponsor-investigator is responsible for maintaining the following records until 2 years after the investigation is discontinued and FDA is notified. [21 CFR 312.62]. The sponsor-investigator must make these available to FDA inspectors at their request.

1. Drug accountability 21 CFR 312.57a
The sponsor-investigator must maintain records showing receipt, shipment, or other disposition of the investigational drug.

2. Financial interest 21 CFR 312.57b
The sponsor-investigator must maintain records showing any financial interests of any of the clinical investigators involved in the study (see also 21 CFR 54). The clinical investigator shall provide the sponsor with sufficient accurate financial information to allow an applicant to submit complete and accurate certification or disclosure statements. The clinical investigator shall promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following the completion of the study [21 CFR 312.64].

3. Case Histories 21 CFR 312.62b
The sponsor-investigator must maintain accurate case histories that record all observations and other data pertinent to the investigation on each subject who received the investigational drug and each subject who was employed as a control in the investigation. [21 CFR 312.62]. Case histories include the case report forms and supporting data such as signed and dated consent forms and medical records including, for example, progress notes.
of the physician, the individual’s hospital chart(s), and the nurses’ notes. The case history for each individual shall document that informed consent was obtained prior to participation in the study.

*What are the sponsor-investigator’s responsibilities as a sponsor?*

The sponsor-investigator carries all responsibilities toward co-investigators that are normally assigned to the sponsor.

1. **General responsibilities of sponsors** [21 CFR 312.50](https://www.accessdata.fda.gov/scripts/cder/indsearch/index.cfm)
   The sponsor-investigator is responsible for
   - selecting qualified investigators and providing them with the information they need to conduct an investigation properly.
   - ensuring proper monitoring of the investigation.
   - ensuring that the investigation is conducted in accordance with the general investigational plan and protocols contained in the IND.
   - maintaining an effective IND with respect to the investigations.
   - complying with FDA regulations with regard to the promotion and charging for investigational new drugs. See Chapter 9, Section IND – Investigational Drugs or Biologics, Sub-section Promotion and Charging for Investigational New Drugs above.
   - ensuring that FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug.

2. **Selection and monitoring of investigators** [21 CFR 312.53 – 312.56](https://www.accessdata.fda.gov/scripts/cder/indsearch/index.cfm)
   The sponsor-investigator is responsible for
   - selecting qualified investigators and monitors.
   - ensuring that the study drug is shipped only to participating investigators.
   - informing co-investigators of new observations with regard to the investigational drug and progress of the study.
   - reviewing on-going investigations, including assuring compliance of all investigators with the protocol, reviewing and evaluating safety and efficacy data of the investigational drug, and discontinuing studies that are deemed to pose an unreasonable and significant risk to subjects.

   The sponsor-investigator is responsible for maintaining study records, as described above.

4. **Inspection of sponsor’s records and reports** [21 CFR 312.58](https://www.accessdata.fda.gov/scripts/cder/indsearch/index.cfm)
   The sponsor-investigator must allow FDA employees access to all records and reports at their request. Drug Enforcement Administration and Department of Justice employees must be given access to records and reports involving controlled substances at their request.

5. **Disposition of unused supply of investigational drug** [21 CFR 312.59](https://www.accessdata.fda.gov/scripts/cder/indsearch/index.cfm)
   **If the investigation is terminated, suspended, discontinued, or completed, the** sponsor-investigator is responsible for assuring that all co-investigators return any unused supplies of the investigational drug to the sponsor, or otherwise provide for disposition of the
unused supplies of the drug under 21 CFR 312.59 [21 CFR 312.62]. The sponsor-investigator must maintain records of the disposition of the drug as described above.

What are the sponsor-investigator’s responsibilities as an investigator?
As an investigator, the sponsor-investigator has all the responsibilities of investigators in any clinical trial.

1. General responsibilities of investigators 21 CFR 312.60
   The sponsor-investigator is responsible for
   • ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations.
   • protecting the rights, safety, and welfare of subjects under the investigator’s care
   • ensuring the control of drugs under investigation.

2. Control of the investigational drug 21 CFR 312.61
   The sponsor-investigator must administer the investigational drug only to subjects under his/her direct supervision, or under the supervision of a sub-investigator responsible to the investigator. The sponsor-investigator must also ensure that the investigational drug is not given to any person not authorized to receive it.

3. Investigator recordkeeping and record retention 21 CFR 312.62
   The sponsor-investigator is responsible for maintaining adequate records of the disposition of the drug, including dates, quantity, and use by subjects. This is described above.

4. Investigator reports 21 CFR 312.64
   The sponsor-investigator must provide reports to the FDA as described above.

5. Assurance of IRB review 21 CFR 312.66
   The sponsor-investigator is responsible for
   • assuring that a qualified IRB will be responsible for initial and continuing review and approval of the investigation.
   • providing a letter or email from the FDA (as an attachment to the HawkIRB new project application) giving the IND number assigned by the FDA.
   • assuring that he/she will report to the IRB all changes and unanticipated problems involving risk to human subjects or others.
   • assuring that he/she will not make any changes in the investigation without prior IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

6. Inspection of investigator’s records and reports 21 CFR 312.68
   The sponsor-investigator must allow FDA employees access to all records and reports at their request. An investigator shall upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee to have access to, and copy and verify any records or reports made by the investigator pursuant to 21 CFR 312.62 [21 CFR 312.68]. The investigator is not required to divulge participant names unless the records of particular individuals require a more detailed study of the cases, or
unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained.

7. Handling of controlled substances  
   The sponsor-investigator must take adequate precautions to ensure the safe and secure handling of controlled substances. The investigator shall take adequate precautions, including storage of the investigational drug in a securely locked, substantially constructed cabinet, or other securely locked, substantially constructed enclosure, access to which is limited, to prevent theft or diversion of the substance into illegal channels of distribution.
Investigational Medical Devices
IDE – Investigational Device Exemption

An investigational device is a medical device which is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. Clinical investigations undertaken to develop safety and effectiveness data for medical devices must be conducted according to the requirements of the IDE regulations [21 CFR part 812]. An IDE study may not necessarily commence 30 days after an IDE submission to FDA. Certain clinical investigations of devices (e.g., certain studies of lawfully marketed devices) may be exempt from the IDE regulations [21 CFR 812.2(c)]. Unless exempt from the IDE regulations, an investigational device must be categorized as either "significant risk" (SR) or "nonsignificant risk" (NSR) – see the section below for more information. The determination that a device presents a nonsignificant or significant risk is initially made by the sponsor. The proposed study is then submitted either to FDA (for SR studies) or to an IRB (for NSR studies).

The IRB's SR/NSR determination has significant consequences for the study sponsor, FDA, and prospective research subjects. SR device studies must be conducted in accordance with the full IDE requirements [21 CFR part 812], and may not commence until 30 days following the sponsor's submission of an IDE application to FDA. Submission of the IDE application enables FDA to review information about the technical characteristics of the device, the results of any prior studies (laboratory, animal and human) involving the device, and the proposed study protocol and consent documents. Based upon the review of this information, FDA may impose restrictions on the study to ensure that risks to subjects are minimized and do not outweigh the anticipated benefits to the subjects and the importance of the knowledge to be gained. The study may not commence until FDA has approved the IDE application and the IRB has approved the study.

In contrast, NSR device studies do not require submission of an IDE application to FDA. Instead, the sponsor is required to conduct the study in accordance with the "abbreviated requirements" of the IDE regulations [21 CFR 812.2(b)]. Unless otherwise notified by FDA, an NSR study is considered to have an approved IDE if the sponsor fulfills the abbreviated requirements. The abbreviated requirements address, among other things, the requirements for IRB approval and informed consent, recordkeeping, labeling, promotion, and study monitoring. NSR studies may commence immediately following IRB approval.

Once the final SR/NSR decision has been rendered by the IRB (or FDA), the IRB must consider whether or not the study should be approved. In considering whether a study should be approved, the IRB should use the same criteria it would use in considering approval of any research involving an FDA regulated product [21 CFR 56.111]. FDA considers all SR studies to present more than minimal risk, and thus, full IRB review is necessary. In making its determination on approval, the IRB should consider the risks and benefits of the medical device compared to the risks and benefits of alternative devices or procedures.

Significant and Nonsignificant Risk Medical Device Studies

The Investigational Device Exemption (IDE) regulations [21 CFR part 812] describe two types of device studies, "significant risk" (SR) and "nonsignificant risk" (NSR). An SR device study is defined [21 CFR 812.3(m)] as a study of a device that presents a potential for serious risk to the health, safety, or welfare of a subject and

1. is intended as an implant; or
2. is used in supporting or sustaining human life; or
(3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or

(4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

An NSR device investigation is one that does not meet the definition for a significant risk study. NSR device studies, however, should not be confused with the concept of "minimal risk," a term utilized in the Institutional Review Board (IRB) regulations [21 CFR part 56] to identify certain studies that may be approved through an "expedited review" procedure. For both SR and NSR device studies, IRB approval prior to conducting clinical trials and continuing review by the IRB are required. In addition, informed consent must be obtained for either type of study [21 CFR part 50].

**Distinguishing Between SR and NSR Device Studies**

The effect of the SR/NSR decision is very important to research sponsors and investigators. SR device studies are governed by the IDE regulations [21 CFR part 812]. NSR device studies have fewer regulatory controls than SR studies and are governed by the abbreviated requirements [21 CFR 812.2(b)]. The major differences are in the approval process and in the record keeping and reporting requirements. The SR/NSR decision is also important to FDA because the IRB serves, in a sense, as the Agency's surrogate with respect to review and approval of NSR studies. FDA is usually not apprised of the existence of approved NSR studies because sponsors and IRBs are not required to report NSR device study approvals to FDA. If an investigator or a sponsor proposes the initiation of a claimed NSR investigation to an IRB, and if the IRB agrees that the device study is NSR and approves the study, the investigation may begin at that institution immediately, without submission of an IDE application to FDA.

If an IRB believes that a device study is SR, the investigation may not begin until both the IRB and FDA approve the investigation. To help in the determination of the risk status of the device, IRBs should review information such as reports of prior investigations conducted with the device, the proposed investigational plan, a description of subject selection criteria, and monitoring procedures. The sponsor should provide the IRB with a risk assessment and the rationale used in making its risk determination.

**SR/NSR Studies and the IRB: The NSR/SR Decision**

The assessment of whether or not a device study presents a NSR is initially made by the sponsor. If the sponsor considers that a study is NSR, the sponsor provides the reviewing IRB an explanation of its determination and any other information that may assist the IRB in evaluating the risk of the study. The sponsor should provide the IRB with a description of the device, reports of prior investigations conducted with the device, the proposed investigational plan, a description of patient selection criteria and monitoring procedures, as well as any other information that the IRB deems necessary to make its decision. The sponsor should inform the IRB whether other IRBs have reviewed the proposed study and what determination was made. The sponsor must inform the IRB of the Agency's assessment of the device's risk if such an assessment has been made. The IRB may also consult with FDA for its opinion.

The IRB may agree or disagree with the sponsor's initial NSR assessment. If the IRB agrees with the sponsor's initial NSR assessment and approves the study, the study may begin without submission of an IDE application to FDA. If the IRB disagrees, the sponsor should notify FDA
that an SR determination has been made. The study can be conducted as an SR investigation following FDA approval of an IDE application.

If the sponsor has an IDE number or the IRB requires an IDE, the investigator must submit to the IRB documentation of the assignment of an IDE number using the HawkIRB system. If the IDE is an investigator held IDE, the entire IDE application are required. This documentation must be attached to the new project application in HawkIRB. IRB staff will check for this documentation and return protocols with inadequate or incomplete documentation of the IDE.

Investigator-Initiated Research with Medical Devices

The following information is intended to provide sponsor-investigators with information to guide them through the FDA requirements for sponsor-investigators who hold an IDE. The federal regulations for IDEs are found under 21 CFR 812. For more information, review the FDA’s Center for Devices and Radiologic Health (CDRH) web site http://www.fda.gov/cdrh.

This is a synopsis of requirements specific to sponsor-investigators who hold IDEs. It is intended to be a guide, but does not include the complete text of the regulations. Hyperlinks are included throughout this document so that you may read the corresponding regulations. Sponsor-investigators must review and be familiar with the federal regulations before undertaking these responsibilities.

Sponsor-investigators are also required to follow all federal regulations and University of Iowa policies and guidance for Human Subjects research, and VAHCS requirements as applicable. University of Iowa policies and guidance for human subjects research are available in this Investigator’s Guide.

What is a Sponsor-Investigator?

When an Investigator holds an IDE for the product being tested in a particular research study, he/she must also assume the role of the Sponsor, and is called a “Sponsor-Investigator.” The FDA defines a Sponsor-Investigator as “an individual who both initiates and actually conducts, alone or with others, an investigation, that is, under whose immediate direction the investigational device is administered, dispensed, or used . . . . The obligations of a sponsor-investigator under this part include those of an investigator and a sponsor.” [21 CFR 812.3]

What must the Sponsor-Investigator report to the FDA and/or IRB? 21 CFR 812.150(a)]

Sponsor-investigators have extensive reporting requirements under FDA regulations.

1. Changes in the protocol 21 CFR 812.35

Changes to the investigational plan or manufacturing process must be submitted to the FDA for approval if they significantly affect the validity of study data, risk-benefit ratio, scientific soundness of the study, or the rights, safety, or welfare of subjects. These changes should be submitted to the FDA as a supplement to the IDE protocol and must be approved by the FDA before being implemented.

Changes that do not meet the above criteria (e.g., adding follow-up visits, changing secondary endpoints, etc.) should be submitted to the FDA within 5 working days of
implementation of the change. Minor changes to the purpose of the study, risk analysis, monitoring procedures, labeling, informed consent materials, and IRB information that do not affect the validity of study data, risk-benefit ratio, scientific soundness of the study, or the rights, safety, or welfare of subjects can be submitted with the annual report.

An investigator shall notify the sponsor and the reviewing IRB (21 CFR 56.108(a) (3) and (4)) of any deviation from the investigational plan to protect the life or physical well-being of a participant in an emergency. Such notice shall be given as soon as possible, but in no event later than 5 working days after the emergency occurred. Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human participants, FDA and IRB in accordance with [21 CFR 812.35(a)]. For more information, see Changes or Modifications during the Conduct of a Clinical Investigation; Final Guidance for Industry and CDRH Staff.

2. IDE safety/adverse device effects [21 CFR 812.150b]
   The sponsor-investigator must report all unanticipated adverse device effects to the FDA and the IRB within 10 working days of receiving the first notice of the event.

3. Withdrawal of IRB approval [21 CFR 812.150b]
   The sponsor-investigator must inform the FDA, all reviewing IRBs, and participating investigators of withdrawal of approval of an investigation or any part of an investigation by any reviewing IRB. This notification must occur within 5 working days after receipt of the withdrawal of approval.

4. Withdrawal of FDA approval [21 CFR 812.150b]
   The sponsor-investigator must notify all reviewing IRBs and participating investigators of any withdrawal of FDA approval. This notification must occur within 5 working days after receipt of the withdrawal of approval.

5. Current investigator list [21 CFR 812.150b]
   The sponsor-investigator must provide the FDA with a current list of investigators participating in the investigation. This list must be provided to the FDA every 6 months.

6. Annual reports [21 CFR 812.150b]
   The sponsor-investigator must submit a progress report to all reviewing IRBs at regular intervals, at least yearly. The first report must be within 60 days of the anniversary date that the IDE went into effect. For IDEs that have been determined to be significant risk, these reports must also be submitted to the FDA.

7. Recall and device disposition [21 CFR 812.150b]
   The sponsor-investigator must notify the FDA and all reviewing IRBs of any request that an investigator return, repair, or otherwise dispose of any units of a device. The notification must
occur within 30 working days after the request is made.

8. Discontinuation of an investigation 21 CFR 812.150b
   The sponsor-investigator must report the completion or termination of an investigation. These reports should be made by submitting a final report.
   For significant risk devices, the sponsor-investigator must notify the FDA within 30 working days and all reviewing IRBs within 6 months of the completion of the investigation.
   For non-significant risk devices, the sponsor must notify all reviewing IRBs within 6 months of completion of the study.

9. Informed consent 21 CFR 812.150b
   The sponsor-investigator must report to the FDA any use of the IDE without informed consent. This report must be submitted within 5 working days of receipt of notice of this use.

10. Significant risk device determinations 21 CFR 812.150b
    If an IRB determines that a device is significant risk, whereas the sponsor-investigator had proposed it to be a non-significant risk device, the sponsor-investigator must notify the FDA of this decision within 5 working days after learning of the IRB’s determination.

    In deciding whether or not a medical device is a significant risk, the IRB considers if the device:
    • Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a participant. [21 CFR 812.3(m)(1)].
    • Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a participant. [21 CFR 812.3(m)(2)].
    • Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a participant. [21 CFR 812.3(m)(3)].
    • Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject. [21 CFR 812.3(m)(4)].

11. Financial disclosure reports 21 CFR 812.43
    A clinical investigator shall disclose to the sponsor sufficient accurate financial information to allow the applicant to submit complete and accurate certification or disclosure statements. The investigator shall promptly update any changes to financial disclosure information and report it to the FDA during the investigation and for 1 year following completion of the study.

What records must a sponsor-investigator maintain?
   The sponsor-investigator is responsible for maintaining the following records during and for 2 years after completion or termination of the investigation or 2 years after the records are no longer needed to support a premarket approval application or a notice of completion of a product development protocol. 21 CFR 812.140d. The sponsor-investigator must make these available to FDA inspectors at their request.
1. Correspondence 21 CFR 812.140
The sponsor-investigator must maintain copies of all correspondence with other investigators, reviewing IRBs, monitors, and the FDA including required reports.

2. Financial interest 21 CFR 812.140
The sponsor-investigator must maintain records showing any financial interests of any of the clinical investigators involved in the study (see also 21 CFR 54).

3. Device records 21 CFR 812.140
A participating investigator shall maintain the following accurate, complete and current records relating to the investigator’s participation in an investigation. The sponsor-investigator must maintain records relating to the shipment, receipt, use (including adverse effects), and disposition of the device.

Additionally, for nonsignificant risk devices, the investigator must maintain
- the name and intended use of the device (type and quantity of the device, the dates of its receipt, and the batch number or code mark).
- a brief explanation of why the device is not a significant risk.
- the name and address of each investigator and the names of all persons who received, used, or disposed of each device.
- why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of
- a statement of the extent to which Good Manufacturing Practice (GMP) regulations will be followed in manufacturing the device (see also 21 CFR 820).

4. Case Histories 21 CFR 812.140
The sponsor-investigator must maintain accurate case histories that record all observations and other data pertinent to the investigation on each subject exposed to the investigational device. The case history for each individual shall document that informed consent was obtained prior to participation in the study.

An investigator or sponsor may withdraw from the responsibility to maintain records for the period required in 21 CFR 812.140(d) and transfer custody of the records to any other person who will accept responsibility for them under 21 CFR 812.140, including the requirements of 21 CFR 812.145 [21 CFR 812.140(e)]. Notice of this transfer shall be given to the FDA not later than 10 working days after transfer occurs.
What are the sponsor-investigator’s responsibilities as a sponsor?
The sponsor-investigator carries all responsibilities toward co-investigators that are normally assigned to the sponsor.

1. General responsibilities of sponsors 21 CFR 812.40
   The sponsor-investigator is responsible for
   a. selecting qualified investigators and providing them with the information they need to conduct an investigation properly.
   b. ensuring proper monitoring of the investigation.
   c. ensuring that IRB review and approval are obtained.
   d. submitting an IDE application to the FDA.
   e. ensuring that any reviewing IRB, FDA, and participating investigators are promptly informed of significant new information about an investigation.

2. Selecting and monitoring investigators 21 CFR 812.43 – 812.46
   The sponsor-investigator is responsible for
   a. selecting qualified investigators and monitors.
   b. ensuring that the investigational device is shipped only to participating investigators.
   c. obtaining investigator agreements.
   d. obtaining statements from participating investigators attesting to their commitment to the proper conduct of the investigation.
   e. obtaining accurate financial disclosure statements from participating investigators.
   f. providing participating investigators with the investigational plan.
   g. informing co-investigators of new observations with regard to the investigational device and progress of the study.
   h. reviewing on-going investigations, including assuring compliance of all investigators with the protocol, reviewing and evaluating safety and efficacy data of the investigational device, and discontinuing studies that are deemed to pose an unreasonable and significant risk to subjects.

3. Adverse device effects and study termination 21 CFR 812.46
   • The sponsor-investigator must immediately evaluate any unanticipated adverse device effect. If the sponsor-investigator determines that the device presents an unreasonable risk to subjects, the sponsor-investigator must terminate the study within 5 working days after making this determination, but not later than 15 working days after first receiving notice of the adverse effect.
   • If the device is significant risk, the sponsor-investigator may not resume a terminated investigation without IRB and FDA approval.
   • If the device is nonsignificant risk, the sponsor-investigator may not resume a terminated investigation without IRB approval.

4. Recordkeeping and record retention 21 CFR 812.140
   The sponsor-investigator is responsible for maintaining study records, as described above.

5. Inspection of sponsor’s records and reports 21 CFR 812.145
   The sponsor-investigator must allow FDA employees access to all records and reports at their request. An investigator who has authority to grant access shall permit authorized FDA employees, at reasonable times and in a reasonable manner, to enter and inspect any
establishment where devices are held (including any establishment where devices are manufactured, processed, packed, installed, used, or implanted or where records of results from use of devices are kept). [21 CFR 812.145(a)].

An investigator shall permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation. [21 CFR 812.145(b)].

An investigator shall permit authorized FDA employees to inspect and copy records that identify participants, upon notice that FDA has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the investigator to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading. [21 CFR 812.145(c)].

What are the sponsor-investigator’s responsibilities as an investigator?
As an investigator, the sponsor-investigator has all the responsibilities of investigators in any clinical trial.

1. General responsibilities of investigators 21 CFR 812.100
   An investigator may determine whether potential participants would be interested in participating in an investigation, but shall not request the written informed consent of any participant to participate, and shall not allow any participant to participate before obtaining IRB and FDA approval. [21 CFR 812.110].
   The investigator is responsible for providing a letter or an e-mail from the FDA (as an attachment to the HawkIRB system) giving the IDE number, if applicable, as assigned by the FDA.
   The sponsor-investigator is responsible for
   • ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable FDA regulations.
   • protecting the rights, safety, and welfare of subjects under the investigator’s care
   • ensuring the control of devices under investigation.

2. Compliance with protocol 21 CFR 812.110b
   The sponsor-investigator must conduct the investigation in accordance with the signed agreement, the investigational plan, FDA regulations, and IRB conditions. [21 CFR 812.110]

3. Device use and disposition 21 CFR 812.110c
   The sponsor-investigator must permit the use of an investigational device only with subjects under the investigator’s supervision. Upon completion or termination of a clinical investigation or the investigator’s part of an investigation, or at the sponsor’s request, an investigator shall return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs. [21 CFR 812.110]

4. Investigator recordkeeping and record retention 21 CFR 812.140a
   The sponsor-investigator is responsible for maintaining study records, as described above.

5. Investigator reports 21 CFR 812.150
   The sponsor-investigator must provide reports to the FDA as described above.

6. Inspection of investigator’s records and reports 21 CFR 812.145
The sponsor-investigator must allow FDA employees access to all records and reports at their request.

**Placebo-Controlled Trials**

If an investigator proposes a study in which a placebo is given for any length of time in lieu of an approved FDA indicated drug, the investigator must include risk management procedures in the research plan for the IRB for review. To the extent that the investigator demonstrates that the subjects' safety is monitored at all times and provisions are made for immediate rescue if needed, the IRB will consider approval of the study.

Once an approval is granted, the investigator is bound to follow the risk management procedures as with any other provision of the approved protocol. Use of placebos may be appropriate where the investigator demonstrates that:

- standard therapy is unavailable or is of unproved efficacy, or
- standard therapy possesses unacceptable side effects, or
- minimal harm may result from the use of placebo (e.g., ongoing disease has little adverse effect on the patient during the course of the trial and is reversible), or
- placebo itself may be an effective therapy, or
- the disease process is characterized by exacerbation and remission.

The risk management procedures should be in the written protocol, with the same level of detail as in the protocol itself. The following issues should be specified:

- the frequency of monitoring,
- whether monitoring is in person or by telephone,
- the criteria for managing a subject in the event of worsening, and
- how 24 hour-per-day, 7 day-per-week, medical care is made available in the event of questions, emergencies, worsening, or withdrawal from the protocol.

The IRB may make its decision based upon the extent to which the above factors are demonstrated and upon a relative weighing of these and other factors. In discussing potential harm from the use of placebos, the investigators must provide a procedure for adequate monitoring of subjects to ensure their safety.

**Pregnancy in Child (Minor) Subjects**

When a child is screened in a study or participating in study procedures that require a pregnancy test be administered, additional consent and assent information must be provided in the Informed Consent Document. The IRB has determined that children in research must be afforded the same rights they would normally have in a clinical setting with regard to the privacy of results from pregnancy testing. Thus, minors 12 years of age would have the choice as to whether or not pregnancy results would be shared with their parents/legal guardians. For children who have a positive pregnancy test and are less than 12 years of age, or if abuse is expected at any age, the proper authorities must be informed and parents or guardians will be informed of the pregnancy. Language to be included in the Informed Consent Document is provided in the Appendix section of the template Informed Consent Document in HawkIRB.

**Specimens – see Data/Specimen Collection Above**
State of Iowa Laws

Iowa state law on the legal age to consent to treatments or procedures (see Chapter 5, Section A for Individuals in the State of Iowa that meet the FDA and DHHS definitions of child and guardian)

Iowa state law provisions on mandatory reporting:

1. Current abuse of a dependent adult (see Iowa Code Chapter 235 B):

"Dependent adult" is defined in §235B.2(4) as follows:
"Dependent adult" means a person eighteen years of age or older who is unable to protect the person's own interests or unable to adequately perform or obtain services necessary to meet essential human needs, as a result of a physical or mental condition which requires assistance from another, or as defined by departmental rule.

2. Current child abuse (see §232.69)
Note: §232.69(2) refers to permissive reporters ("any other person (i.e., other than listed in (1)) who believes that a child has been abused may make a report").

3. Other reporting
The general licensing provisions for a number of health care professions (see Iowa Code Chapter 147) require reporting a wound or "other serious bodily injury" that is being treated by the person licensed under that chapter and that appears to have been received in connection with the commission of a criminal offense.

Reportable conditions (see §641--1.1-1.3 (139A))
Additional state laws provide for the notification and surveillance of reportable communicable and infectious diseases, poisoning and conditions. Of note, in Iowa these include cancer and birth defects with reporting to the State Health Registry located at UI. When it is possible that identification of a reportable condition may occur in the research setting, investigators must include this information and the reporting requirements in the informed consent document.

Intent to hurt self or others
Common law (not statute) generally requires that one report a demonstration of a current intent to hurt oneself or others.

1) Human Stem Cell Research and Cloning (Iowa Code 707C)

A person shall not intentionally or knowingly do any of the following:
• Perform or attempt to perform human reproductive cloning.
• Participate in performing or in an attempt to perform human reproductive cloning.
• Transfer or receive, in whole or in part, for the purpose of shipping, receiving, or importing, the product of human reproductive cloning.
Applicability of the laws of other states

In cases of human subjects research under the authority of the UI IRB(s) but conducted outside of the state of Iowa, the UI IRB confers with the UI Office of General Counsel regarding the applicability of other state, national, or international laws to the particular project. These cases are identified in the pre-review process of an application to the IRB and the advice of counsel is sought prior to the approval of the study. In general, the UI IRB will apply the law of the state in which the research is being conducted. For example, if a project involves children and one of the recruitment sites is in a bordering state, the laws of the bordering state will be evaluated to which individuals meet the DHHS and FDA definition of “children” at that site.

Surveys, Questionnaires, and Interview Studies

Not all survey, questionnaire, or interview research is minimal risk. For example, a survey or interview that asks questions about sensitive topics (e.g., childhood abuse, sexual functioning) likely to cause emotional stress or discomfort may require full IRB review. Some survey research may be classified as exempt from the regulations if the information obtained is recorded in a way that the subject cannot be identified (either directly or through a code numbers or link); in other words, if the research data are anonymous.

The term anonymous is sometimes confused with the term confidential. In human subjects research, anonymous means that at no time during the data collection could someone determine who provided the information. If a link existed at any time, even if the link is subsequently destroyed, the IRB cannot consider the information anonymous.

A survey or interview study may also be considered exempt from the regulations even when the data are not anonymous if the information being gathered could not reasonably place the subject at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, or reputation. The most common classification for survey, questionnaire, or interview research is expedited approval. If the study is not anonymous and contains information that, if known, could be damaging as described above, but it does not rise to the level of more than minimal risk, it may be given expedited approval. Although the New Project application gives the investigator the opportunity to indicate a classification, the chairs or his/her IRB member designee make the final determination as to the classification of exempt or expedited.

For minimal risk mail-out or web-based surveys or questionnaires, it may be appropriate to request that the chair or his/her IRB member designee waive the requirement for the subject's signature on an Informed Consent Document. When the subject's signature requirement is waived, generally the investigator provides all of the required elements of consent in a cover letter, with a statement that returning the survey or questionnaire will be considered voluntary agreement to participate. For additional information on waiver of signature, see Chapter 5.

Washout Issues in Drug Treatment Studies

When a subject is asked to stop taking some or all medications prior to beginning a drug treatment study, this is called a drug washout. Washouts are appropriate depending upon the disease to be studied and the nature of the proposed protocol. Washout studies require balancing the likelihood of harm, the effectiveness of monitoring, and the potential severity of the risk(s) to be avoided. When subjects are being washed out from a FDA approved and indicated drug, the individual investigator should clearly define the nature and degree of risk to the subjects and include risk management procedures in the research plan. To the extent that the investigator demonstrates that the subjects' safety is monitored at all times and provisions are made for immediate rescue if needed, the IRB will consider approval of the study. Once an approval is granted, the investigator is bound to follow the risk management procedures as with any other provision of the approved protocol. The risk management procedures should be in the written protocol, with the same level of detail as in the protocol itself. The following issues should be specified:

* careful definition as to when a subject would be withdrawn from the study,
* the frequency of monitoring,
* whether monitoring is in person or by telephone,
* the criteria for managing a subject in the event of worsening, and
* how 24 hour-per-day, 7 day-per-week, medical care is made available in the event of questions, emergencies, worsening, or withdrawal from the protocol.

Chapter 10 – Non-compliance with the Requirement of the Human Research Protection Program

In the federal regulations, non-compliance refers to failure to comply with the regulations, or the requirements or determinations of the IRB. Policies and procedures should cover serious non-compliance, continuing non-compliance, and non-compliance that is neither serious nor continuing, and corrective actions appropriate to the nature and degree of non-compliance.

Definitions of terms associated with noncompliance

What is noncompliance?
Noncompliance is failure to follow the federal regulations with respect to protection of human subjects in research or failure to follow the determinations of the IRB with respect to conduct of the research as approved by the IRB. For VA studies, this includes failure to follow the requirements of VHA Handbook 1200.5.

What is an allegation of noncompliance?
When information or suspected noncompliance comes to the attention of the IRB or an IRB Chair.

What is serious noncompliance?
Noncompliance that materially increases risks or that results in unexpected substantial harm to subjects or others. In addition the following instance(s) of noncompliance, as defined by OHRP, will always be determined as serious noncompliance:
- Non-Exempt human subjects research being carried out without IRB review and approval or without appropriate informed consent.
- Substantive modifications to IRB-approved research without IRB approval.

What is continuing noncompliance?
Any noncompliance that occurs repeatedly to the point of suggesting a pattern or an underlying problem. Continuing noncompliance may occur due to a lack of knowledge (unintentional) or due to deliberate choice to ignore regulations or determinations of the IRB (intentional).

Allegations of Noncompliance

The Principal Investigator bears the ultimate responsibility for the conduct of a research project. The investigator must comply with the requirements of the University of Iowa's Federalwide Assurance and with determinations of the IRB, as outlined in minutes and other correspondence. Information regarding noncompliance in human subjects studies may come to the attention of the IRB through several pathways. These include information contained in application forms, IRB reporting forms, monitoring reports, or reports from collaborators, employees, subjects, or others not directly involved in the research.

When information comes to the attention of the IRB outside of a full-board meeting, the Chair of the appropriate IRB reviews the allegations of noncompliance. The Chair makes a determination as to whether the alleged practices appear to (1) cause injury or any other unanticipated problems involving risks to subjects or others, or (2) constitute serious or continuing noncompliance with IRB determinations or federal regulations. In such cases, the Chair may choose to
suspend the study procedures, taking into consideration the welfare of currently enrolled subjects, pending an investigation and review by the full IRB. If an IRB Chair requests the research team suspend study procedures on a federally funded study, reporting to OHRP and the FDA (where applicable) may be required. The suspension of study procedures may be lifted either by the IRB Chair or the full IRB once a determination has been made based on the information gathered as a result of the investigation. If the Chair determines that the potential noncompliance did not involve any risk to subjects or others, and did not constitute serious or continuing noncompliance, the Chair may resolve the issue directly with the Principal Investigator and research team.

When potential noncompliance is first identified during a full-board review, the full-board makes a determination as to whether the alleged practices appear to (1) cause injury or any other unanticipated problems involving risks to subjects or others, or (2) constitute serious or continuing noncompliance with IRB determinations or federal regulations. In such cases, the full board may suspend the study procedures, taking into consideration the welfare of currently enrolled subjects, and determine how further investigation will be conducted according to the procedures indicated below.

In cases that involve allegations of research misconduct, the Chair contacts the UI Research Integrity Officer (RIO) for further action. This does not preclude the Chair or any member of the IRB from independently contacting the RIO about any allegation of scientific misconduct. Inquiries or investigations into research misconduct do not preclude IRB review and actions.

The following points outline procedures for investigating and resolving alleged noncompliance:

1. When made aware of an allegation of noncompliance, HSO staff immediately notifies the UI IRB Chair for the IRB of record and works with the Chair to compile any required background file information. If the alleged noncompliance involves a WIRB or study, the allegation is reported to an IRB-01 Chair who in turn immediately notifies the appropriate IRB of record.

2. The UI IRB Chair makes a determination as to whether to pursue the matter with the Principal Investigator via telephone call, e-mail, paper memo, or in person based on the nature and seriousness of the alleged noncompliance. The Chair may also choose to send an IRB Compliance Specialist to meet with research team members and review study materials as appropriate. The purpose of such contact is fact-finding, i.e. to determine if indeed there is noncompliance. Care is taken to maintain confidentiality when leaving messages for the Principal Investigator via voice mail or with secretarial and support staff. For WIRB studies, the UI IRB Chair coordinates the UI investigation with the IRB of record. Investigations are initiated within 5 working days of initial notification.

3. The UI Chair and/or Compliance Specialist document the outcome of any and all pertinent communications and discussions in writing, by either e-mail or paper memo with a copy to the IRB files. Such documentation should be factual and objective, and include timelines for resolution (e.g. meeting dates, response deadlines).

4. The UI Chair makes a decision based on the information gathered as to whether the allegation is credible.

5. If the UI Chair believes the allegation is credible, the UI Chair determines whether the noncompliance could possibly meet the definition of serious or continuing noncompliance. In making this decision, the Chair brings the issue to the appropriate Chairs’ meeting for discussion.

a) IRB Chairs meeting:

- Monitoring Reports with findings that require full-board review will be scheduled for discussion at the next available IRB Chairs meeting. The IRB Chairs will discuss agenda items for future IRB-01 Executive IRB Meetings, IRB-02 meeting, or IRB-03 meeting that will be considered for possible noncompliance (serious and / or continuing). If the Chair believes that the noncompliance is serious or continuing and that there is continuing risk of harm to current or future subjects, the Chair may
suspend research activities, taking into consideration the welfare of currently enrolled subjects, until review by the full board.

b) Prior to the IRB-01 Executive Committee Meeting or IRB-02(03) Full Board Meeting:

- IRB Chair contacts the Principal Investigator (PI) and grant-holder (if different from the PI) via e-mail to inform them of the issue of possible noncompliance and the required reporting for serious and/or continuing noncompliance.

- Send to the PI the following references:
  - Relevant Codes of Federal Regulation 21CFR56.108 (FDA); 45 CFR 46.103(b)(5) (Department of Health and Human Services).
  - University of Iowa Institutional Review Board Standard Operating Procedures available at http://research.uiowa.edu/hs/o/ (left hand column to open this document) sections IV Authority of the IRB, IX.D Noncompliance Investigation and Actions, IX.F.2 IRB Determinations Requiring Reporting, X.G Rebuttal or Appeal of UI IRB Decisions, XIX. Definitions of Noncompliance, Continuing Noncompliance, and Serious Noncompliance. The Principal Investigator may want to review other sections as well.
  - Guide for Human Subjects Research at the University of Iowa available at http://research.uiowa.edu/hs/o/ (see left hand column to open this document) Chapter 6 Section J Appeal of IRB Decisions, Chapter 7 Section C.6 Noncompliance, Chapter 10 Allegations of Noncompliance. The Principal Investigator may want to review other sections as well.

- The Monitoring Report is sent via e-mail to the PI in advance of the meeting to allow time for review and response. The PI will be asked to complete any required actions that did not require full-board review. The PI has 2 weeks to complete these required actions and, if desired, provide a response with any additional relevant information for the Executive Committee to review prior to the meeting.

c) Scheduling the Monitoring Report to an Executive Committee Meeting

- When the response is received from the PI, the Monitoring report can be scheduled for the next available Executive Committee meeting. If a meeting has already been scheduled, the report will only be scheduled to that meeting if there is space on the agenda and sufficient time to provide meeting materials to members prior to the meeting. If necessary, the administrative process will be initiated for scheduling the Monitoring Report to an IRB Executive Committee meeting.

- HSO Staff, in consultation with the IRB Chairs, arranges for the PI and IRB Executive Committee members to have the Monitoring Report, response from the PI and any other pertinent information (such as e-mail communication) available for review at least one week prior to the meeting according to standard procedures.

- IRB Chair sends a brief notice to the IRB Executive Committee members scheduled to attend the meeting stating that the specific findings in the Monitoring Report that are referred to full board will be considered for possible noncompliance (serious and/or continuing).

- Human Subjects Office (HSO) arranges for the PI and the grant-holder (if different from the PI) to attend the Executive IRB Meeting to address the Board and be available for questions regarding the issue of possible noncompliance.

- A primary reviewer is assigned to lead the discussion at the full board meeting. All IRB members including the primary reviewer receive appropriate materials such as monitoring report(s), communications with the Principal Investigator or other relevant individuals, and Reportable Events Forms (if applicable) for their review. Approved IRB applications, consent documents and other documentation from the project file may also be included as reference materials during the review and are distributed to all IRB members prior to the full board meeting. All IRB members are expected to review and be familiar with all materials.
d) **During the IRB Executive Committee Meeting:**
- Initial discussion of the findings in the Monitoring report and issues of possible noncompliance without the PI present.
- Invite the PI into the meeting to allow the opportunity to describe the issue of possible noncompliance.
- The IRB Executive members ask the PI questions and give the PI an opportunity to provide any new information that was not previously presented to the Board. PI is provided an opportunity for final comment before being asked to leave the meeting.
- The IRB Executive members have a final discussion and vote.
  1. The possible actions, include but are not limited to, that could be taken by the IRB include:
     - Suspension or termination of IRB approval of protocols that are found to be noncompliant with institutional policies and procedures, state laws, and/or federal laws or regulations, taking into consideration the welfare of currently enrolled subjects,
     - Compliance monitoring,
     - Letters of reprimand,
     - Restrictions on serving as an investigator on human subjects protocols,
     - Notification of currently enrolled subjects,
     - Providing additional information to past subjects,
     - Modification to research protocols,
     - More frequent continuing review or monitoring,
     - Changes in consent process or documents,
     - Requirement that currently enrolled subjects re-consent to participation,
     - Request more information prior to making a final decision,
     - Referral of the issue to other organizational entities such as UI legal counsel, risk management, or the research integrity officer, or
     - other actions as appropriate.
  2. The IRB determines which sanctions and/or requirements must be met for the study to proceed. If the investigator can meet these sanctions/requirements with simple concurrence, the IRB Chair determines when these are met and gives approval for the study to recommence. If sanctions or requirements require more than simple concurrence, the issue is returned to the full board for consideration of resumption of the research project.
  3. The IRB determines whether the noncompliance meets the definition of serious or continuing noncompliance.

e) **After the IRB Executive Committee Meeting:**
- Meeting Minutes are completed and provided to the PI according to the standard procedures.
- The Principal Investigator (and grant-holder, if different from the PI) receives the IRB Executive Committee meeting minutes via e-mail unless there was an open application in HawkIRB that was scheduled for the IRB meeting. If a HawkIRB application was scheduled to the meeting the minutes will be attached to the application in the usual manner.

f) **Appeal Process for Determinations of Serious and/or Continuing Noncompliance:**
- The PI may appeal IRB determinations of serious and/or continuing noncompliance. Such an appeal
must be submitted in writing to the Chair of Record listed on the Monitoring Report. The basis for the appeal must be new information that was not previously available or considered by the IRB during the meeting in which the determination was made. The investigator must provide a rationale for the appeal and any other relevant supporting documentation. The IRB Chair determines if the appeal contains new information and an adequate rationale. The IRB Chair determines whether or not the appeal will be reviewed by the Executive Committee.

• Appeals containing new information will be scheduled for review by the IRB at an Executive Committee meeting. If the appeal requires discussion or explanation beyond what is provided to the board in written format, the PI may be invited by the Chair to attend the Executive Committee meeting at which the appeal is presented. The PI is invited for the purpose of answering questions and participating in discourse with board members. The PI will leave prior to IRB discussion and vote on the issue(s). The IRB will notify the PI in writing via the meeting minutes of the discussion and vote on the appeal.

g) Notification process for Determinations of Serious and/or Continuing Noncompliance:

• If all avenues of the appeal process have been exhausted and the IRB Full Board upholds a Serious and/or Continuing Noncompliance determination the procedure for reporting to the appropriate institutional departments and offices, the institutional official, sponsors, and/or the appropriate regulatory agencies of events determined by the IRB to be serious or continuing non-compliance. The full board HSO staff in collaboration with the IRB Chair prepares a letter for signature by the IRB Chair(s) that contains the following information:
  1. The nature of the event (whether or not the event was an unanticipated problem involving risks to subjects or others, serious or continuing non-compliance, or a suspension or termination of approval of research or a combination of these events),
  2. The name of the institution conducting the research,
  3. The title of the research project and/or grant proposal in which the problem occurred,
  4. The name of the principal investigator on the protocol,
  5. The IRB number assigned to the research project and the number of any applicable federal award(s) such as grants, contracts, or cooperative agreements,
  6. A short summary of the project,
  7. A detailed description of the problem including the findings of the organization and the reasons for the IRB’s decision,
  8. Actions the institution is taking or plans to take to address the problem (e.g. revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, increase IRB monitoring of the project, etc.),
  9. Plans, if any, for any follow-up action.

• The full board HSO staff sends a copy of this letter no more than one month following the review and final determination by the convened IRB to:

Institutional Entities:

a) The UI Institutional Official (Office of the Vice President for Research),
b) Principal Investigator,
c) Division of Sponsored Programs (DSP) or Division of Sponsored Programs (CTO) depending on the funding source and which office handled the contract/grant. The DSP or the CTO then determine whether notification of the sponsor is required by contract or agreement and notifies the sponsor accordingly.
d) Departmental Executive Officer (DEO) of the principal investigator,
e) Dean of the College of the principal investigator,
f) Research Integrity Officer (RIO) if the event involved research misconduct.
Federal Agencies:

g) OHRP, if the study is subject to DHHS regulations or subject to a DHHS federalwide assurance,
h) FDA, if the study is subject to FDA regulations (21 CFR 50 and 56)
i) For VA research, the chair of the VA Research and Development Committee. This office then has the responsibility of forwarding the report to the Regional VA Office of Research Oversight.
j) If the study is conducted or funded by any Federal Agency other than DHHS that is subject to “The Common Rule” (see Definitions in Chapter XIX), the report is sent to OHRP or the head of the agency as required by the agency.

For VA Studies reports are also sent to:

k) Office of Research and Development
l) Regional VA Office of Research Oversight
m) VA Privacy Officer, when the report involves unauthorized use, loss, or disclosure of individually identifiable private information
n) VHA Information Security Officer when the report involves violations of VA information security requirements.

- Reporting to a regulatory agency does not occur if the event occurred at a site that was not subject to the direct oversight of the organization, and the agency has been notified of the event by the investigator, sponsor, another organization, or other mechanisms.

- The HSO Assistant Director can provide copies to others as deemed appropriate by the Institutional Official.

- For studies reviewed by WIRB, events of serious or continuing noncompliance are reported directly to WIRB and reporting is the responsibility of WIRB.

- Reporting of suspensions or terminations made by WIRB are the responsibility of WIRB.

Chapter 11 – Investigator Questions, Concerns and Suggestions

Staff in the HSO is available to investigators and their research team members to answer questions about the IRB review process. A staff listing along with their areas of expertise may be found on the HSO website. If the HSO is unable to help with your issue, you may also contact the Office of the Vice President for Research at 335.2119.
Definitions

**Agent of the Organization** – Agents include all individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility.

**Chair** – Chair or Vice-Chair, as designated on UI IRB roster submitted to OHRP, unless otherwise indicated.

**Children (Child)** –

*DHHS definition:* persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.

*FDA definition:* persons who have not attained the legal age for consent to treatments or procedures involved in clinical investigations, under the applicable law of the jurisdiction in which the clinical investigation will be conducted.

**For purposes of research conducted in Iowa, the term “child” as used in both the DHHS and FDA regulations is analogous to “minor” under Iowa Code and is viewed as “an unmarried person under the age of eighteen years.” (Based on Iowa Code §600A.2 (12))**

**Clinical Investigation** –

*FDA definitions:*

- any experiment that involves a test article and one or more human subjects and that is one of the following:
  - subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or
  - is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.
  - The term does not include experiments that are subject to the provision of 21CFR58, regarding nonclinical laboratory studies. (From 21 CFR 50.3(c); 21 CFR 56.102(c))

- any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For the purposes of this part, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice. (From 21 CFR 312.3(b))

*(Investigation):* a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device. (From 21 CFR 812.3(h))

**Coercion** - occurs when an overt or implicit threat of harm is intentionally presented by one person to another in order to obtain compliance. For example, an investigator might tell a prospective subject that he or she will lose access to needed health services if he or she does not participate in the research.

**Confidentiality** – the ethical or legal right that information is considered private and will be held secret unless consent is provided permitting disclosure.
**Conflict of Interest** – See [UI Operations Manual, Chapter 18.6](#) on Conflict of Interest in Research for Financial Conflict of Interest in Research definitions.

**For UI IRB members only, the following indicates a conflict of interest with a protocol under review:**

- a member of the research team;
- related to any member of the study team;
- identified as "key personnel" on a funding mechanism that supports the research project; or
- any other situation where the reviewer believes that another interest conflicts with his/her ability to deliberate objectively on a protocol.

**Continuing Noncompliance** – Any noncompliance that occurs repeatedly to the point of suggesting a pattern or an underlying problem. Continuing noncompliance may occur due to lack of knowledge (unintentional) or due to deliberate choice to ignore regulations or determinations of the IRB (intentional).

**Existing (Data, Documents, Records, Pathological or Diagnostic Specimens)** – Existing with regards to these materials means the items must be “on the shelf” or in existence at the time the project is submitted to the IRB for review.

**Federal Agency Other than DHHS that is subject to “The Common Rule”**

Any one of the following:

- Agency for International Development (22 CFR 225)
- Central Intelligence Agency (Executive Order)
- Consumer Products Safety Commission (16 CFR 1028)
- Department of Agriculture (7 CFR 1c)
- Department of Commerce (15 CFR 27)
- Department of Defense (32 CFR 219)
- Department of Education (34 CFR 97)
- Department of Energy (10 CFR 745)
- Department of Homeland Security (Public law 108-458 Sec. 8306)
- Department of Justice (28 CFR 46)
- Department of Transportation (49 CFR 11)
- Department of Veteran’s Affairs (38 CFR 16)
- Environmental Protection Agency (40 CFR 26)
- Housing and Urban Development (24 CFR 60)
- National Aeronautics and Space Administration (14 CFR 1230)
- National Science Foundation (45 CFR 690)
- Office of Science and Technology Policy (Adoption of policy)
- Social Security Administration (Public law 7.5.26)

**Guardian**

a person who is not the parent of a child, but who has been appointed by a court or juvenile court having jurisdiction over the child, to have a permanent self-sustaining relationship with the child and to make important decisions which have a permanent effect on the life and development of that child and to promote the general welfare of that child. A guardian may be a court or a juvenile court.

Unless otherwise enlarged or circumscribed by a court or juvenile court having jurisdiction over the child or by operation of law, the rights and duties of a guardian with respect to a child shall be as follows:

- To consent to marriage, enlistment in the armed forces of the United States, or medical,
psychiatric, or surgical treatment.

h. To serve as a guardian ad litem, unless the interests of the guardian conflict with the interests of the child or unless another person has been appointed guardian ad litem.

i. To serve as custodian, unless another person has been appointed custodian.

j. To make periodic visitations if the guardian does not have physical possession or custody of the child.

k. To consent to adoption and to make any other decision that the parents could have made when the parent-child relationship existed.

l. To make other decisions involving protection, education, and care and control of the child. [From Iowa Code 232.2(21)]

**Human subject** –
*DHHS definition*: a living individual about whom an investigator (whether professional or student) conducting research obtains a) data through intervention or interaction with the individual, or b) identifiable private information. (From 45 CFR 46.102.(d))

**FDA definitions (human participant)**:
-an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A participant may be either a healthy human or a patient. (From 21 CFR 50.3(g))

-(Subject): a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control A subject may be in normal health or may have a medical condition. (From 21 CFR 812.3(p))

**Identifiable Private Information** -
-private 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 (for example, a medical record). This information is considered individually identifiable if the identity of the subject is or may readily be ascertained by the investigator or associated with the information. (From 45 CFR 46.102(f)(2)

If information includes Protected Health Information (as defined later under Protected Health Information), identifiable information includes any of the following information for the individual, relative, employer, or household member of the individual:

- Name, street address, city, county, precinct, zip code, geocodes smaller than state
- Date of birth, ages > 89 years of age; or other dates such as diagnosis dates, procedure dates, admission or discharge dates
- Telephone numbers, fax numbers, e-mail addresses, social security numbers, medical record number
- Health plan beneficiary numbers, account numbers, certificate/license numbers
- Vehicle identifiers and serial numbers or license numbers, device identifiers and serial numbers
- Web URLs, Internet Protocol (IP) address numbers, biometric identifiers including finger/voice prints
- Full face photographic images and any comparable images.

**Interaction**
An interaction includes communication or interpersonal contact between investigator and participant.

**Intervention**
An intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the participant or the participant’s environment that are performed for research purposes.
Legally authorized representative (LAR)- an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

In studies involving children in the state of Iowa, the LAR is:
- the parent, OR
- the court-appointed guardian.

In non-VA studies involving cognitively impaired adults in the state of Iowa, the LAR is:
- the designated proxy (such as a Durable Power of Attorney for Health Care)
- the court-appointed guardian
- spouse
- adult child
- parent
- adult sibling.

In VA studies involving cognitively impaired adults, the LAR is:
- Health-care agent
- Legal guardian or special guardian
- Next-of-kin: a close relative of the subject 18 years of age or older, in the following priority:
  - Spouse
  - Child
  - Parent
  - Sibling
  - Grandparent
  - Grandchild
  - Close Friend

In studies that involve cognitively impaired adults, permission must be sought from the first existing person in the above lists, even if another relative is more conveniently available.

Minimal risk – 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 50.3(k))

In research involving prisoners – the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons. (45 CFR 46.303(d))

Minor modifications – modifications to a research project and/or consent documents that pose no additional risk to subjects (e.g. changes in title, co-investigator(s), funding sources). If the modification is an addition or modification of procedures they must fall into one of the categories eligible for expedited review. To be considered a minor modification, it must also maintain similar or increased safeguards to protect the subject.

Noncompliance – failure to follow the federal regulations with respect to protection of human subjects in research or failure to follow the determinations of the IRB with respect to conduct of the research as approved by the IRB. For VA studies, this includes failure to follow the requirements of VHA Handbook 1200.5.
**Nonscientist** - an individual who has little or no formal scientific or medical training or experience.

**Nonsignificant Risk (NSR) device investigation** - one that does not meet the FDA definition for a Significant Risk study.

**Privacy** – freedom from unauthorized intrusion or the state of being let alone and able to keep certain personal information to oneself.

**Protected Health Information (PHI)** – information that:
1. is transmitted or maintained in any form (electronic, oral, paper) by a covered entity, and
2. identifies the individual or could reasonably be used to identify the individual; and
3. 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 healthcare to an individual.

(From 45 CFR 160.103)

**Quorum** – a majority of voting members of an IRB, including at least one member whose primary expertise is in a nonscientific area.

**Research** - a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research even if they are a component of a larger non-research activity (e.g., instruction, demonstration.) (From 45 CFR 46.102(d))

The FDA defines research as a clinical investigation. Refer to the term “Clinical Investigation” in this section for the FDA definitions.

**Research Misconduct** – fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the research community for proposing, conducting, or reporting research. It does not include honest error or honest differences in interpretations or judgments of data or creative innovations that are nonetheless ethical, legal and meet professional standards.

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

**Serious adverse drug experience** – Any adverse drug experience (associated with the use of the drug) occurring at any dose that results in any of the following outcomes: death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed above. (from 21 CFR 312.32(a))

**Serious Noncompliance** – Noncompliance that materially increases risks or that results in unexpected substantial harm to subjects or others. In addition the following instance(s) of noncompliance, as defined by OHRP, will always be determined as serious noncompliance:
- Non-Exempt human subjects research being carried out without IRB review and approval or without appropriate informed consent.
- Substantive modifications to IRB-approved research without IRB approval.
**Significant Risk (SR) device study** - one that presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject. (From 21 CFR 812.3(m))

**Suspension** - By requirement of the convened IRB or an IRB Chair, a temporary halt to a selection of research activities being conducted under an IRB-approved project or a temporary halt to the IRB-approved project as a whole.

**Termination** - By requirement of the convened IRB, a permanent halt to some or all research activities in a previously approved IRB project.

**Test Article** – any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the Federal Food Drug and Cosmetic Act, or under sections 351 or 354-360F of the Public Health Service Act. (From 21 CFR 50.3(j) and 21 CFR 56.102(l))

**Unanticipated adverse device effect** – Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death the frequency, specificity or severity of which has not previously been identified in the investigational plan or application, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects. (from 21 CFR 812.3(s))

**Unanticipated problem involving risk to subjects or others** – Any problem or event that:
   a) was not expected given the nature of the research, the population under study and the approved procedures or protocol for conduct of the study,
   b) impacts the rights, safety, or welfare of subjects or others (e.g. those not directly involved in the research such as research staff or family members), and
   c) is related to the research intervention, research procedures, and/or conduct of the research study.

**Unexpected adverse drug experience** – Any adverse drug experience (associated with the use of the drug), the frequency, specificity or severity of which is not consistent with the current investigator brochure; or, if an investigator brochure is not required or available, the specificity or severity of which is not consistent with the risk information provided to subjects and the IRB. (from 21 CFR 312.32(a))

**Undue influence** - often occurs through an offer of an excessive or inappropriate reward or other overture in order to obtain compliance. For example, an investigator might promise psychology students extra credit if they participate in the research. If that is the only way a student can earn extra credit, then the investigator is unduly influencing potential subjects. If, however, she offers comparable non-research alternatives for earning extra credit, the possibility of undue influence is minimized.

**VA Research** - Research performed at the VAHCS and/or utilizing VAHCS resources, or performed by VAHCS employees or agents on VAHCS time.
IRB-01 PRIMARY REVIEWER CHECKLIST
New Projects

**Protocol & Primary Reviewer Identification**
Principal Investigator: 
IRB ID: 
Study Title: 
Primary Reviewer: 
Meeting Date: 

Please use this checklist when reviewing this protocol. Make notes in the space provided for leading the discussion with the full board. Please contact the investigator with your questions prior to the meeting date. If you see any significant problems with this study, please contact the IRB chair in advance of the meeting to alert him/her of your concerns.

### Primary Reviewer Self-Assessment

1. Do you, as the primary reviewer assigned to this project, have a **conflict of interest** with this project?  

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<thead>
<tr>
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<th>Yes</th>
<th>No</th>
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#### 1. Conflict of Interest Policy:
An IRB member may not vote on a project, and is not counted towards a quorum, when
1) s/he serves as a co-investigator or other member of the research team, or
2) an immediate family member (spouse or domestic partner and dependent children) serves as a co-investigator or other member of the research team, or
3) when s/he or an immediate family member (spouse or domestic partner and dependent children) has a **significant financial interest** with a project being reviewed.

2. Conflict of interest in research involves situations in which an investigator has a significant financial interest that may compromise, or have the appearance of compromising, professional judgment in the design, conduct, or reporting of research. The terms "investigator" and "significant financial interest" are defined below.

3. Investigators conducting research funded by the Public Health Service (including National Institutes of Health) and National Science Foundation, as well as those conducting studies regulated by the Food and Drug Administration, are subject to agency specific regulations (II-18.8 UI Operations Manual). These regulations set forth the obligations of investigators, sponsors and institutions for research involving significant financial or other conflicts of interest, and affected parties are advised to review the relevant regulations prior to submission of a research proposal or application.

   a) "Investigator" means the principal investigator and any other person, whether faculty, staff, or student, who is responsible for the design, conduct, or reporting of research. "Investigator" also includes the investigator's spouse and dependent children.

   b) "Significant financial interest" means anything of monetary value, including, but not limited to, salary or other payments for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options, or other ownership interests); and intellectual property rights (patents, copyrights, and royalties from such rights) held by an investigator or the investigator's immediate family (immediate family means spouse or domestic partner, and dependent children, individually or in aggregate, when such interest involves:

   i. Payments in excess of $10,000 (including salary, consulting fees, royalty or licensing payments from intellectual property, and honoraria and/or gifts) received within the past 12 months or anticipated for the next 12 months (excluding salary and other payments for services from the
ii. An equity interest in a publicly traded company worth more than $10,000 or more than 5 percent of the business entity as determined by reference to its publicly listed price (excluding mutual funds);

iii. Any equity interest if the value cannot be determined by reference to publicly listed prices (i.e., an equity interest in a privately held company, such as a start-up company);

iv. A position giving rise to a fiduciary duty, such as director, officer, partner, trustee, employee, or any other position of management; or

v. Intellectual property rights (patents or copyrights) or royalties from such rights whose value may be affected by the outcome of the research, including royalties distributable under University policy or any royalty-sharing agreements involving the University.

4. Personal agreements between sponsors and investigators, IRB members, or their immediate family members where the amount of compensation (consulting, board honoraria, or any other kind) could change depending on the outcome of a study or any other activity the faculty/IRB member performs as part of their University service are prohibited. In some cases, such arrangements are illegal under state law.

2. Do you think there is a need for someone with additional expertise (i.e. a consultant) to assist in the review of this protocol?

The need for a consultant should be made based on the scientific design of the study, the ethical issues of the study, the potential risks or benefits of the study, specific privacy and confidentiality concerns, or considerations relative to a particular study population.

If your answer to question #1 OR #2 is Yes, STOP HERE.
Call the Human Subjects Office at 335-6564 and/or the IRB chair as soon as possible to inform us of this conflict or need for a consultant.

Additional Notes or Comments:
<table>
<thead>
<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Section I; VI.14-15; VII.E</strong></td>
<td>3. Does the use of human subjects have research relevance?</td>
</tr>
<tr>
<td>Consider</td>
<td>Yes</td>
</tr>
<tr>
<td>• The use of human subjects in this project is relevant and appropriate to answer the questions being asked.</td>
<td></td>
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<tr>
<td>• The study design is appropriate to answer the questions being asked.</td>
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<tr>
<td>• The investigator has adequate access to the population under study to allow for recruitment of the required number of participants to conduct this study.</td>
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Points for discussion:

<table>
<thead>
<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
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<tbody>
<tr>
<td><strong>HawkIRB Entire Application</strong></td>
<td>4. Are there any ethical issues regarding the study’s design and conduct?</td>
</tr>
<tr>
<td>Consider</td>
<td>Yes</td>
</tr>
<tr>
<td>• Ethical issues may include but are not limited to the Belmont report principles: respect for persons (voluntary, fully informed consent), beneficence (obligation to protect subjects from harm and secure their well-being), and justice (benefits and burdens of research are fairly distributed).</td>
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<tr>
<td><strong>Section VIII: Risks</strong></td>
<td>5. Are risks (physical, emotional, financial, legal, social) to subjects minimized?</td>
</tr>
<tr>
<td>Consider</td>
<td>Yes</td>
</tr>
<tr>
<td>• 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 or (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.</td>
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<tbody>
<tr>
<td><strong>Section VIII: Risks; Section IX: Benefits</strong></td>
<td>6. Are risks to subjects reasonable in relation to anticipated benefits?</td>
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<tr>
<td>Consider</td>
<td>Yes</td>
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<tr>
<td>• Risks to subjects are reasonable in relation to</td>
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</table>
anticipated benefits (if any) to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

Points for discussion:

### HawkIRB Question | Checklist Question
---|---
**Question VIII.2** | 7. Are appropriate measures in place to provide the medical or psychological resources that subjects might require as a consequence of participating in this research (e.g. availability of emergency medical care, psychological counseling, etc.)?  
Yes ☐  No ☐  NA ☐

Points for discussion:

### HawkIRB Question | Checklist Question
---|---
**Sections VI: Subjects; VII.D.19-26** | 8. Is subject selection equitable?  
Consider:  
- *In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, cognitively or decisionally impaired persons, economically or educationally disadvantaged persons, students or other groups that require special consideration.*  
Yes ☐  No ☐

Points for discussion:

### HawkIRB Question | Checklist Question
---|---
**Section VIII.3-8** | 9. Are there procedures for monitoring safety?  
Consider:  
- *When appropriate, research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.*  
Yes ☐  No ☐

Points for discussion:
| HawkIRB Question | Checklist Question | | 
|---|---|---|---|
| **Questions X.1-X.3** | 10. Are there procedures for protecting the privacy of subjects?  
Consider:  
- When appropriate adequate provisions exist to protect the privacy of subjects. Privacy means freedom from unauthorized intrusion or the state of being let alone and able to keep certain personal information to oneself. | ☐ Yes ☐ | 
| **Sections VII.D.1-VII.D.7** | 11. Does the partial HIPAA waiver request described in Section VII.D.2-7 satisfy all of the criteria under section 164.512 of the Privacy Rule?  
Consider:  
This partial waiver of authorization for recruitment purposes satisfies the following criteria:  
(1) The use or disclosure of the requested information involves no more than a minimal risk to the privacy of individuals based on, at least, the presence of the following elements:  
(a) An adequate plan to protect the identifiers from improper use and disclosure  
(b) An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and  
(c) Adequate written assurances that the requested information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the requested information would be permitted by the Privacy Rule;  
(2) The research could not practicably be conducted without the waiver or alteration; and  
(3) The research could not practicably be conducted without access to and use of the requested information. | ☐ Yes ☐ ☐ NA | 

Points for discussion:
### HawkIRB Question | Checklist Question
---|---
**Questions X.4-6** | 12. Are there procedures for protecting the confidentiality of subject information?  
Consider:  
- *When appropriate, adequate provisions exist to protect subject confidentiality. Confidentiality means the ethical or legal right that information is considered private and will be held secret unless consent is provided permitting disclosure.*

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<th>Yes</th>
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Points for discussion:

### HawkIRB Question | Checklist Question
---|---
**Questions VII.A.1-10** | 13. If this research indicates that the investigator is the lead investigator of a multicenter study or the UI is the lead site of a multicenter study, is the management of information among sites adequate to ensure the protection of research subjects?  
Consider the adequacy of:  
- the procedures to identify and report unanticipated problems involving risks to subjects or others a) from the sites to the UI and b) from the UI to the sites,  
- the procedures that will be used to communicate protocol modifications from the UI to the other sites,  
- the procedures that will be used to communicate from the UI to the other sites any interim results,  
- the procedures that will be used to communicate from the UI to the other sites other new information which may impact a subject’s willingness to participate, or continue participating in the research

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<th>Yes</th>
<th>No</th>
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Points for discussion:

### 14. Should any of the following additional elements be included in the Consent?  
- If an element *is not present* in the consent and *should be* added, please select ‘yes’, and make sure to mention it during your review of the study at the meeting.  
- If an element *is not present* and *does not need to be* added select ‘no’ or ‘N/A’.  
- If an element is *present* in the consent and should remain, please select ‘yes’.  
- If an element *is present,* but *should not be,* select ‘no’ or N/A’ and make sure to mention it during your review of the study at the meeting.

*Consider:*  
- *Where appropriate, one or more of the following elements of information shall also be provided*
to each subject. Consider the nature of the research (i.e. clinical or physical intervention), the study design, the population under study (pregnant women or women capable of becoming pregnant, etc.), subject safety and welfare, as well as the relevance of the information in allowing the prospective subject to make an informed decision about participation.

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<tr>
<th>Indicate any items that are not in the submitted Informed Consent that you believe should be included:</th>
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<tbody>
<tr>
<td><strong>Section VIII</strong></td>
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<td><strong>Section VIII</strong></td>
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<td><strong>Section VIII; attached protocol</strong></td>
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<td><strong>Section VIII</strong></td>
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<td><strong>Section VIII</strong></td>
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<td><strong>Attached protocol</strong></td>
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<td><strong>Attached protocol</strong></td>
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### Questions VI.1; VI.6

Approximate number of subjects involved in the study (study-wide, at Iowa).

[Check to be sure this is included and matches the protocol information.]

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<th>Checklist Question</th>
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<td>15. For studies involving cognitively or decisionally impaired individuals, have the following points been considered?</td>
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<td>See U I Investigator’s Guide. PI should consider:</td>
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<td>• potential conflicts of interest when subjects cannot understand the difference between research and treatment;</td>
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<td>• subject’s potentially fluctuating capacity for consent;</td>
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<td>• how capacity to consent will be assessed;</td>
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<tr>
<td>• whether or not an Assent process should be used and if so, how assent should be obtained (e.g. written or verbal)</td>
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<tr>
<td>• measures for ensuring voluntary participation throughout the study.</td>
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Points for discussion:

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<th>Checklist Question</th>
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<tr>
<td>16. Does this research project involve any vulnerable populations of subjects?</td>
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<td>Consider:</td>
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<tr>
<td>• Vulnerable populations may include pregnant women, fetuses and neonates, children, prisoners, cognitively impaired individuals as well as others (e.g. students, mentally disabled persons, or educationally or economically disadvantaged persons) who are likely to be vulnerable to coercion or undue influence.</td>
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If Yes, are appropriate safeguards included in the protocol to protect their rights and welfare?

If No, to the above question, what additional safeguards do you recommend for the protection of the rights and welfare of these vulnerable subjects?
<table>
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<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
<th>Yes</th>
<th>No</th>
<th>NA</th>
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<tbody>
<tr>
<td>Questions VII.B.11-17; VII.E; Attachments list</td>
<td>17. If there is a grant application or industry protocol for this study, do the HawkIRB Application and the Informed Consent Document correspond to the grant application/protocol?</td>
<td>☐</td>
<td>☐</td>
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Points for discussion:

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<th>HawkIRB Question</th>
<th>Checklist Question</th>
<th>Yes</th>
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<th>NA</th>
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<tbody>
<tr>
<td>Section VII.B. 11-17; Section VIII: Risks; Attachments list</td>
<td>18. If there is a grant application or industry protocol for this study, do the risks described in the HawkIRB Application and the Informed Consent Document correspond to the grant application/protocol (and Investigator’s Brochure, if applicable, for a drug or device study)?</td>
<td>☐</td>
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Points for discussion:
### Questions VII.D.1-11

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<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
<th>Yes</th>
<th>No</th>
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<tr>
<td>Questions</td>
<td>19. Is the recruitment process (including telephone scripts, advertisements, brochures, letters, compensation) fully described, understandable, fair, honest, appropriate, and non-coercive and does not create undue influence? Consider: When the IRB reviews advertisements meant to be seen or heard by potential subjects, the IRB should ensure that the advertisements do not: -- state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and protocol, -- make claims, either explicitly or implicitly, that the drug, biologic, or device is safe and effective for the purposes under investigation, -- make claims, either explicitly or implicitly, that the drug, biologic, or device is known to be equivalent or superior to any other drug, biologic or device, -- use terms, such as “new treatment,” “new medication,” or “new drug” without explaining that it is investigational, -- promise “free medical treatment,” when the intent is only to say subjects will not be charged for taking part in the investigation, -- include exculpatory language, -- emphasize the payment or the amount to be paid, by such means as large or bold type.</td>
<td>No</td>
<td>Yes</td>
<td>NA</td>
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Points for discussion:

### Questions VII.D.8-18

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<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
<th>Yes</th>
<th>No</th>
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<tbody>
<tr>
<td>Questions</td>
<td>20. Do the circumstances of the consent process minimize the possibility of coercion or undue influence?</td>
<td>No</td>
<td>Yes</td>
<td>NA</td>
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Points for discussion:

### Questions VI.28-36

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<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
<th>Yes</th>
<th>No</th>
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<tbody>
<tr>
<td>Questions</td>
<td>21. In this research, is the legally effective informed consent of the subject or the subject’s legally authorized representative required? If yes, check all that apply:</td>
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<td></td>
<td>Subject</td>
<td>No</td>
<td>Yes</td>
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2014 V.1
### Checklist Question

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<th>Checklist Question</th>
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<tr>
<td><strong>Questions VI.16-17; VI.35; VII.D.29; Consent Document; Assent Document</strong></td>
<td>22. Does the consent process communicate the information in a language understandable to the subject population or their legally authorized representative?</td>
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This refers to all communication, including verbal explanations, instructions, and questions before and after the decision to take part, and is not limited to the consent document and recruitment materials.

Consider if some subjects are not native English speakers, is the information provided to the subjects in their language, for example, through the use of translators?

If there are subjects with language barriers due to cognitive, educational, or cultural limitations, the research team should communicate information to them in a language that these individuals can understand.

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<th>Yes</th>
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Points for discussion:

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<tr>
<td><strong>Questions VI.35; VII.D.29</strong></td>
<td>23. Do the circumstances of the consent process provide the prospective participant or the subject’s legally authorized representative sufficient opportunity to consider whether to participate?</td>
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<th></th>
<th>Yes</th>
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Points for discussion:
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<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
<th>Yes</th>
<th>No</th>
<th>NA</th>
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</table>
| **Section VII.B; Attachment list** | 24. If this is a study involving an investigational new drug(s), do the promotional materials (e.g. advertisements, brochures, recruitment media, etc.) represent the investigational new drug(s) in a manner that might indicate that the investigational new drug(s) is safe and/or effective for the purpose for which it is under investigation or do they promote the investigational new drug in any manner?  
Consider:  
A sponsor or investigator, or any person acting on behalf of a sponsor or investigator, shall not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution. 21 CFR 312.7(a) |     |    |   |
| **Points for discussion, if yes:** |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |     |    |   |
| **HawkIRB Question** | Checklist Question                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Yes | No | NA |
| **Section VII.B; Attachment list** | 25. If this is a clinical trial involving an investigational new drug(s), is it evident in the consent process that the subject does not have to pay for the investigational new drug(s)?  
Consider:  
Charging for an investigational drug in a clinical trial under an IND is not permitted without the prior written approval of FDA. In requesting such approval from FDA, the sponsor shall provide a full written explanation of why charging is necessary in order for the sponsor to undertake or continue the clinical trial, e.g. why distribution of the drug to test subjects should not be considered part of the normal cost of doing business. 21 CFR 312.7(d) |     |    |   |
<p>| <strong>Points for discussion, if no:</strong> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |     |    |   |</p>
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| Section VI: Subjects; VII.E.9-13 | 26. Is the compensation to subjects appropriate for this study? Consider the following:  
- Subject payments accrue as the study progresses and are not contingent upon the subject completing the entire study.  
- Any amount paid as a bonus for completing the study is reasonable and not so large as to unduly induce subjects to stay in the study when they might otherwise withdraw.  
- All information concerning payment, including the amount and schedule of payments, is set forth in the informed consent document.  
- Compensation for participation in a trial offered by a sponsor does not include a coupon good for a discount on the purchase price of the product once it has been approved for marketing. |

Points for discussion:

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| Questions VII.B.6-7 | 27. If subjects will receive a placebo in lieu of an approved, FDA-indicated drug, does one of the following apply? (Indicate) See U I Investigator’s Guide. PI should include  
- frequency of monitoring and whether monitoring is in person or by phone,  
- management criteria in event of worsening,  
- 24/7 availability for questions or emergencies.  
Placebo in lieu of an approved drug may be justified because (at least ONE must be checked):  
☐ standard therapy is unavailable or is of unproved efficacy,  
OR  
☐ standard therapy possesses unacceptable side effects,  
OR  
☐ minimal harm may result from the use of placebo (e.g., ongoing disease has little adverse effect on the patient during the course of the trial and is reversible),  
OR  
☐ placebo itself may be an effective therapy,  
OR  
☐ the disease process is characterized by exacerbation and remission. |
28. If subjects are being **washed out** from an approved FDA indicated drug, are procedures described per U of I policy (box)?

   *See UI Investigator’s Guide.* PI should include
   - when subject would be removed from study,
   - frequency of monitoring and whether monitoring is in person or by phone,
   - management criteria in event of worsening,
   - 24/7 availability for questions or emergencies.

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<th>HawkIRB Question</th>
<th>Checklist Question</th>
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| Questions VII.B.2-5 | 28. If subjects are being **washed out** from an approved FDA indicated drug, are procedures described per U of I policy (box)?<br>  *See UI Investigator’s Guide.* PI should include  
  - when subject would be removed from study,  
  - frequency of monitoring and whether monitoring is in person or by phone,  
  - management criteria in event of worsening,  
  - 24/7 availability for questions or emergencies. | Yes | No | NA |

Points for discussion:

29. Does this protocol require IRB review more than annually?

   Examples of when the IRB might consider review more frequently than annually may include:
   - a) Experimental therapies in which the clear potential for significant adverse experiences have been identified at the time of review; or 
   - b) Non-therapeutic projects based on risk information provided at the time of initial review; or 
   - c) Projects in which new information provided during the duration of the study (including at the time of continuing review) indicates a high probability of significant adverse experiences not previously reported; or 
   - d) Projects in which local or outside adverse experience reports create new concerns regarding the need for closer project scrutiny; or 
   - e) Projects where the UI IRB has concerns with regard to previous or potential serious or continuing noncompliance; or 
   - f) Other, as determined by the convened IRB.

   *In such cases, the IRB may consider granting approval for time periods less than one year, or for a limited number of subjects over*
a period not to exceed one year, or additional monitoring can be required.

Points for discussion:
30. For studies involving children, indicate the category below. Check whether or not the additional approval criteria within the shaded box are true. *(See questions VI.6-13 in HawkIRB)*

**Children** are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. Generally, for research with children in the state of Iowa, a child is an unmarried person under the age of 18. NOTE: If you are unsure of the applicable law where the research will be conducted, please call the Human Subjects Office (335-6564) for guidance.

**Minimal risk** means that the probability and magnitude of the 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 exams or tests.

**Assent** means a child’s affirmative agreement to participate in research. *(See questions VII.D.15 and VII. D.30-36 in HawkIRB)* In determining whether children are capable of assenting, the IRB should take into account the age, maturity, and psychological state of the children involved in the research. When soliciting the assent of children, the PI should consider the age of the subjects, their maturity, and their ability to read and comprehend a written document in deciding how the assent will be obtained (e.g. verbally or written.)

*(For the following items: See questions VII.E and VIII in HawkIRB)*

- [ ] Research not involving greater than minimal risk (45 CFR 46.404, 21 CFR 50.51)

  - a) No greater than minimal risk to children is presented in this research;
  - b) Adequate provisions are made for soliciting the permission of the parents or guardians;
    - The permission of one parent/guardian is required.
    - OR
    - The permission of both parents/guardians is required.
    - OR
    - The permission of the parents/guardians is waived.
  - c) Adequate provisions are made for soliciting the assent of the children;
    - (i) Assent is required of all children in this research
    - OR
    - (ii) Assent is required for some of the children in this research
    - OR
    - (iii) Assent is not required for any of the children in this research

  For (i) and (ii) above, should assent be documented? If so, describe the process below.

  For (ii) and (iii) above, describe below why assent is not required.

  Consider the following:
  - Children are not capable of providing assent because of their age, maturity, or psychological state;
  - The capability of children in this research is so limited that they could not reasonably be consulted;
The research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research;

The assent could be waived based on the criteria for a waiver of informed consent.

Points for discussion:
Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects (45 CFR 46.405, 21 CFR 50.52)

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<td><strong>a)</strong> More than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject or by a monitoring procedure that is likely to contribute to the subject’s well-being;</td>
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<tr>
<td><strong>b)</strong> The risk is justified by the anticipated benefit to the subjects;</td>
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<td><strong>c)</strong> The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches;</td>
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<td><strong>d)</strong> Adequate provisions are made for soliciting the permission of the parents or guardians;</td>
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<td><strong>The permission of one parent/guardian is required.</strong></td>
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<td>OR</td>
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<td><strong>The permission of both parents/guardians is required.</strong></td>
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<td>OR</td>
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<td></td>
<td><strong>The permission of the parents/guardians is waived.</strong></td>
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<tr>
<td><strong>e)</strong> Adequate provisions are made for soliciting the assent of the children;</td>
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<td></td>
<td><strong>(i) Assent is required of all children in this research</strong></td>
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<td>OR</td>
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<td><strong>(ii) Assent is required for some of the children in this research</strong></td>
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<td>OR</td>
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<td></td>
<td><strong>(iii) Assent is not required for any of the children in this research</strong></td>
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</tbody>
</table>

For (i) and (ii) above, should assent be documented? If so, describe the process below.

For (ii) and (iii) above, describe below why assent is not required. Consider the following:

- Children are not capable of providing assent because of their age, maturity, or psychological state;
- The capability of children in this research is so limited that they could not reasonably be consulted;
- The research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research;
- The assent could be waived based on the criteria for a waiver of informed consent.

Points for discussion:
Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition

(45 CFR 46.406, 21 CFR 50.53)

- a) More than minimal risk to children is presented by an intervention or procedure that does NOT hold out the prospect of direct benefit for the individual subject or by a monitoring procedure which is NOT likely to contribute to the subject’s well-being;
- b) The risk represents a minor increase over minimal risk;
- c) The intervention/procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
- d) The intervention/procedure is likely to yield generalizable knowledge about the subjects’ disorder or condition which is of vital importance for the understanding or amelioration of the subjects’ disorder or condition;
- e) Adequate provisions are made for soliciting the permission of BOTH parents/guardians unless one parent is deceased, unknown, incompetent, not reasonably available, or only one parent has responsibility for the care and custody of the child;
  OR
  - Permission of parents/guardians is waived.
- f) Adequate provisions are made for soliciting the assent of the children;
  - (i) Assent is required of all children in this research
  OR
  - (ii) Assent is required for some of the children in this research
  OR
  - (iii) Assent is not required for any of the children in this research

For (i) and (ii) above, should assent be documented? If so, describe the process below.

For (ii) and (iii) above, describe below why assent is not required. Consider the following:

- Children are not capable of providing assent because of their age, maturity, or psychological state;
- The capability of children in this research is so limited that they could not reasonably be consulted;
- The research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research;
- The assent could be waived based on the criteria for a waiver of informed consent.

Points for discussion:
Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (45 CFR 46.407, 21 CFR 50.54)

If the IRB does not believe the research meets the requirement of 404, 405, or 406, approval may be given only if:

(a) the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, and

(b) the Secretary of DHHS, after consultation with a panel of experts in pertinent disciplines and following opportunity for public review and comment has determined either

(1) that the research in fact satisfies the conditions of 404, 405, or 406, or

(2) the research presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children and the research will be conducted in accordance with sound ethical principles and adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.

Points for discussion:
31. For studies involving prisoners, indicate the category below. Check whether or not the additional approval criteria within the shaded box are true. *(See questions VI.13 VI.37-45 in HawkIRB)*

☐ Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects *(45 CFR 46.306(a)(2)(i)) (See Sections I, VII.E, VIII in HawkIRB)*

☐ Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects *(45 CFR 46.306(a)(2)(ii)) (See Sections I, VII.E, and VIII in HawkIRB.)*

☐ Research on conditions particularly affecting prisoners as a class *(for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his intent to approve such research *(45 CFR 46.306(a)(2)(iii)) (See Sections I and VII.E in HawkIRB.)*

☐ Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the intent to approve such research *(45 CFR 46.306(a)(2)(iv)) (See Sections I and VII.E in HawkIRB.)*

---

**45 CFR 46.305(a)**

*Approval may be given only if the IRB finds that:*

___(1) the research under review represents one of the categories of research permissible (above);

___(2) any possible advantages accruing to the prisoner through his/her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his/her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

___(3) the risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers;

___(4) procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected
randomly from the group of available prisoners who meet the characteristics needed for that particular research project;

(5) the information is presented in language which is understandable to the subject population;

(6) adequate assurance exists that parole boards will not take into account a prisoner’s participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and

(7) where the Board finds there may be a need for follow-up examinations or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners’ sentences, and for informing participants of this fact.

Points for discussion:
32. For studies involving pregnant women, human fetuses, or neonates, check whether or not the additional approval criteria are true in the relevant shaded box. (See questions VI.13 and VI.26-27 in HawkIRB.)

☐ Pregnant women or fetuses may be involved in research if all of the following conditions are met (45 CFR 46.204):

- (a) where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
- (b) the risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
- (c) any risk is the least possible for achieving the objectives of the research;
- (d) if the research holds out (1) the prospect of direct benefit to the pregnant woman, (2) the prospect of a direct benefit both to the pregnant woman and the fetus, or (3) no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, the woman’s consent is obtained;
- OR
- (e) if the research holds out the prospect of direct benefit solely to the fetus, then the consent of the pregnant woman and the father is obtained, except that the father’s consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest;
- (f) each individual providing consent under (d) or (e) above is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate; and
- (g) for children who are pregnant, assent and permission are obtained in accord with Subpart D for studies involving children;
- (h) no inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- (i) individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
- (j) individuals engaged in the research will have no part in determining the viability of a neonate.

☐ Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met (45 CFR 46.205a):

- (1) where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;
- (2) each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate;
- (3) individuals engaged in the research will have no part in determining the viability of a neonate; AND
46.205(b) if the neonate is of uncertain viability, until it has been ascertained whether or not a neonate is viable, the following additional conditions are met:

(1) the IRB determines (I) the research holds out the prospect of enhancing the probability of that survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or (ii) the purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and

(2) the legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent’s legally authorized representative is obtained in accord with Subpart A, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

OR 46.205(c) if the neonate is nonviable after delivery, all of the following additional conditions are met:

(1) vital functions of the neonate will not be artificially maintained;

(2) the research will not terminate the heartbeat or respiration of the neonate;

(3) there will be no added risk to the neonate resulting from the research;

(4) the purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and

(5) the legally effective informed consent of both parents of the neonate is obtained, except that the waiver and alteration provisions of Subpart A do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirement of this paragraph.

Points for discussion:
1. This study is:

☐ Minimal risk Describe:

☐ More than minimal risk

2. The IRB must determine whether the medical record had to be flagged to protect the subject’s safety by indicating participation in the study and the source of more information on the study. Should each subject’s VAHCS medical record be flagged for this study:

☐ No (complete one or more items below)

The IRB may consider not flagging the medical record because:

☐ Participation in the study involved only one encounter

☐ Participation in the study involved the use of a questionnaire or previously collected biological specimens.

☐ Identification as a subject in a this study would place the subject at greater than minimal risk. Describe:

☐ Yes Describe:

3. The IRB must prohibit paying subjects when the research is integrated with a patient’s medical care and when it makes no special demands on the patient beyond those of usual medical care.

Does the project propose payment to VA subjects?

☐ No

☐ Yes (complete section below)

Recommend permitting paying VA subjects because (choose and justify at least one option below):

☐ The research was not directly intended to enhance the diagnosis or treatment of the medical condition for which the subject was being treated, and when the standard of practice in affiliated non-VA institutions was to pay subjects in this situation. Describe:

OR

☐ The research was a multi-institutional study and subjects at collaborating non-VA institutions were paid for the same participation in the same study at the same rate proposed; Describe:

OR

☐ In the opinion of the IRB payment of subjects would be appropriate in other comparable situations; Describe:

OR
The subject incurred transportation expenses that would not be incurred in the normal course of receiving treatment and were not reimbursed by another mechanism. Describe:

4. Does this project propose to enroll subjects who are incompetent or those with impaired decision making capacity?

☐ No

☐ Yes (complete the section below)

For VA research, the IRB must determine and document the following:

a. Only incompetent persons or persons with impaired decision making capacity were suitable as subjects. Describe:

b. Competent persons were not suitable for the proposed research. Describe:

c. The investigator has demonstrated to the IRB that there is a compelling reason to include incompetent individuals or persons with impaired decision-making capacity as subjects. Provide comment on each of the following as it relates to this study:

   i. Incompetent persons or persons with impaired decision-making capacity were not being proposed as subjects simply because they were readily available. Describe:

   ii. The proposed research entailed no significant risks, tangible or intangible, or if the research presented some probability of harm, there had to be at least a greater probability of direct benefit to the subject. Describe:

   iii. The research did not impose a risk of injury, unless that research was intended to benefit that subject and the probability of benefit was greater than the probability of harm. Describe:

   iv. Procedures were devised to ensure that the subject’s legally authority representative is well informed regarding their roles and obligations to protect incompetent subjects or persons with impaired decision making capacity. Describe:

   v. Legally authorized representatives were told that their obligation was to try to determine what the prospective subject would do if competent, or if the prospective subject’s wishes could not be determined, what they thought was in the incompetent person’s best interest. Describe:
d. The IRB must determine the following when approving enrollment of those unable to consent for themselves. Provide protocol-specific information for each item below:

i. **Consent by a legally authorized representative** will be limited to situations where the prospective subject is incompetent or has impaired decision-making capacity, as determined and documented in the person’s medical record in a signed and dated progress note.
   Describe:

ii. **Determination that a subject is incompetent or has an impaired decision-making capacity** will be made by a legal determination or a determination by the practitioner, in consultation with the chief of service or Chief of Staff, after appropriate medical evaluation that the prospective subject lacks decision-making capacity and is unlikely to regain it within a reasonable period of time.
   Describe:

iii. **If** the determination that the prospective subject lacks decision-making capacity is based on a diagnosis of mental illness, the investigator will obtain consultation with a psychiatrist or licensed psychologist.
   Describe:

iv. **The** practitioner will explain the proposed research to the prospective subject when feasible.
   Describe:

v. **Subjects** will not be forced or coerced to participate in a research study.
   Describe:

5. Does this project allow non-veterans to be entered into the VA part of the protocol?

   ☐ No
   ☐ Yes

   Describe justification for why there is an insufficient number of veterans to complete this study:

6. Will informed consent be sought from each prospective subject or LAR?

   ☐ No – waiver has been requested and is appropriate

   ☐ Yes

7. Will informed consent be documented?

   ☐ No – waiver of documentation has been requested and is appropriate

   ☐ Yes

   a. Verify by checking below that the consent for this project includes the following:
A statement that in the event of a research-related injury the VA had to provide necessary medical treatment to a subject injured by participation.

A statement that a veteran-subject would not be required to pay for care received as a subject in a VA research project except in accordance with federal law and that certain veterans were required to pay co-payments for medical care and services provided by VA.

If non-veterans will be approved for inclusion in the VA portion of this study, the consent language indicates that regulations pertaining to the participation of veterans as subjects including indemnification for research-related injury pertain to the non-veteran as well.

The subject or the subject’s legally authorized representative will sign and date the consent document.

A witness to the subject’s signature or the subject’s legally authorized representative’s signature will sign and date the consent document.

If the sponsor or IRB requires a witness to the consenting process in addition to the witness to the subject’s signature and if the same person needed to serve both capacities, a note to that effect is placed under the witness’s signature line.

A copy of the signed and dated consent document is to be given to the person signing the consent document.

Consent is documented through the use of VA Form 10-1086.

If the IRB is allowing the short form of consent documentation, the IRB determined that:

The subject or the subject’s legally authorized representative will sign and date the consent document.

The witness will sign and date both the short form and a copy of the summary.

The person actually obtaining consent will sign and date a copy of the summary.

A copy of the signed and dated short form will be given to the subject or the subject’s legally authorized representative.

A copy of the summary will be given to the subject or the subject’s legally authorized representative.
IRB-02 PRIMARY REVIEWER CHECKLIST
New Projects

Protocol & Primary Reviewer Identification
Principal Investigator:
IRB ID:
Study Title:
Primary Reviewer:
Meeting Date:

Please use this checklist when reviewing this protocol. Make notes in the space provided for leading the discussion with the full board. Please contact the investigator with your questions prior to the meeting date. If you see any significant problems with this study, please contact the IRB chair in advance of the meeting to alert him/her of your concerns.

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<th>Primary Reviewer Self-Assessment</th>
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<tbody>
<tr>
<td>1. Do you, as the primary reviewer assigned to this project, have a conflict of interest with this project?</td>
<td>☐</td>
<td>☐</td>
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1. **Conflict of Interest Policy:**
   An IRB member may not vote on a project, and is not counted towards a quorum, when
   1) s/he serves as a co-investigator or other member of the research team, or
   2) an immediate family member (spouse or domestic partner and dependent children) serves as a co-investigator or other member of the research team, or
   3) when s/he or an immediate family member (spouse or domestic partner and dependent children) has a significant financial interest with a project being reviewed.

2. Conflict of interest in research involves situations in which an investigator has a significant financial interest that may compromise, or have the appearance of compromising, professional judgment in the design, conduct, or reporting of research. The terms "investigator" and "significant financial interest" are defined below.

3. Investigators conducting research funded by the Public Health Service (including National Institutes of Health) and National Science Foundation, as well as those conducting studies regulated by the Food and Drug Administration, are subject to agency specific regulations (II-18.8 UI Operations Manual). These regulations set forth the obligations of investigators, sponsors and institutions for research involving significant financial or other conflicts of interest, and affected parties are advised to review the relevant regulations prior to submission of a research proposal or application.

   c) "Investigator" means the principal investigator and any other person, whether faculty, staff, or student, who is responsible for the design, conduct, or reporting of research. "Investigator" also includes the investigator's spouse and dependent children.

   d) "Significant financial interest" means anything of monetary value, including, but not limited to, salary or other payments for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options, or other ownership interests); and intellectual property rights (patents, copyrights, and royalties from such rights) held by an investigator or the investigator's immediate family (Immediate family means spouse or domestic partner, and dependent children), individually or in aggregate, when such interest involves:

   vi. Payments in excess of $10,000 (including salary, consulting fees, royalty or licensing payments from intellectual property, and honoraria and/or gifts) received within the past 12 months or anticipated for the next 12 months (excluding salary and other payments for services from the University);

   vii. An equity interest in a publicly traded company worth more than $10,000 or more than 5 percent of the business entity as determined by reference to its publicly listed price (excluding mutual funds);

   viii. Any equity interest if the value cannot be determined by reference to
publicly listed prices (i.e., an equity interest in a privately held company, such as a start-up company);

ix. A position giving rise to a fiduciary duty, such as director, officer, partner, trustee, employee, or any other position of management; or

x. Intellectual property rights (patents or copyrights) or royalties from such rights whose value may be affected by the outcome of the research, including royalties distributable under University policy or any royalty-sharing agreements involving the University.

4. Personal agreements between sponsors and investigators, IRB members, or their immediate family members where the amount of compensation (consulting, board honoraria, or any other kind) could change depending on the outcome of a study or any other activity the faculty/IRB member performs as part of their University service are prohibited. In some cases, such arrangements are illegal under state law.

2. Do you think there is a need for someone with additional expertise (i.e. a **consultant**) to assist in the review of this protocol?

   The need for a consultant should be made based on the scientific design of the study, the ethical issues of the study, the potential risks or benefits of the study, specific privacy and confidentiality concerns, or considerations relative to a particular study population.

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<th>Yes</th>
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If your answer to question #1 OR #2 is Yes, STOP HERE.
Call the Human Subjects Office at 335-6564 and/or the IRB chair as soon as possible to inform us of this conflict or need for a consultant.
<table>
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<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
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</table>
| **Section I; VI.14-15; VII.E** | 3. Does the use of human subjects have research relevance? **Consider**  
- The use of human subjects in this project is relevant and appropriate to answer the questions being asked.  
- The study design is appropriate to answer the questions being asked.  
- The investigator has adequate access to the population under study to allow for recruitment of the required number of participants to conduct this study. |
| | Yes | No |

Points for discussion:

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<th>HawkIRB Question</th>
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| **HawkIRB Entire Application** | 4. Are there any ethical issues regarding the study’s design and conduct? **Consider**  
- Ethical issues may include but are not limited to the Belmont report principles: respect for persons (voluntary, fully informed consent), beneficence (obligation to protect subjects from harm and secure their well-being), and justice (benefits and burdens of research are fairly distributed). |
| | Yes | No |

Points for discussion:

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| **Section VIII: Risks** | 5. Are risks (physical, emotional, financial, legal, social) to subjects minimized? **Consider**  
- 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 or (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes. |
| | Yes | No |

Points for discussion:

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<th>Checklist Question</th>
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| **Section VIII: Risks; Section IX: Benefits** | 6. Are risks to subjects reasonable in relation to anticipated benefits? **Consider**  
- 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. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility. |
| | Yes | No |

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<tr>
<td>Question VIII.2</td>
<td>7. Are appropriate measures in place to provide the medical or psychological resources that subjects might require as a consequence of participating in this research (e.g. availability of emergency medical care, psychological counseling, etc.)?</td>
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| Sections VI: Subjects; VII.D.19-26 | 8. Is subject selection equitable? Consider:  
• In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, cognitively or decisionally impaired persons, economically or educationally disadvantaged persons, students or other groups that require special consideration. | ☐   | ☐  |

Points for discussion:

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| Section VIII.3-8 | 9. Are there procedures for monitoring safety? Consider:  
• When appropriate, research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects. | ☐   | ☐  |

Points for discussion:

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<th>HawkIRB Question</th>
<th>Checklist Question</th>
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| Questions X.1-X.3 | 10. Are there procedures for protecting the privacy of subjects? Consider:  
• When appropriate adequate provisions exist to protect the privacy of subjects. Privacy means freedom from unauthorized intrusion or the state of being let alone and able to keep certain personal information to oneself.  
• Researchers should be collecting the minimum private information needed to answer the research question. | ☐   | ☐  |

Points for discussion:

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<tr>
<td>Sections VII.D.1-VII.D.7</td>
<td>11. Does the partial HIPAA waiver request described in Section VII.D.2-7 satisfy all of the criteria under section 164.512 of the Privacy Rule?</td>
<td>☐</td>
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Consider:
This partial waiver of authorization for recruitment purposes satisfies the following criteria:
(1) The use or disclosure of the requested information involves no more than a minimal risk to the privacy of individuals based on, at least, the presence of the following elements:
(a) An adequate plan to protect the identifiers from improper use and disclosure
(b) An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
(c) Adequate written assurances that the requested information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the requested information would be permitted by the Privacy Rule;
(2) The research could not practicably be conducted without the waiver or alteration; and
(3) The research could not practicably be conducted without access to and use of the requested information.

Points for discussion:

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<td><strong>Questions X.4-6</strong></td>
<td>12. Are there procedures for protecting the confidentiality of subject information? Consider: • When appropriate, adequate provisions exist to protect subject confidentiality. Confidentiality means the ethical or legal right that information is considered private and will be held secret unless consent is provided permitting disclosure.</td>
<td>☐ Yes ☐ No</td>
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<td><strong>Questions VII.A.1-10</strong></td>
<td>13. If this research indicates that the investigator is the lead investigator of a multicenter study or the UI is the lead site of a multicenter study, is the management of information among sites adequate to ensure the protection of research subjects? Consider the adequacy of: • the procedures to identify and report unanticipated problems involving risks to subjects or others a) from the sites to the UI and b) from the UI to the sites, • the procedures that will be used to communicate protocol modifications from the UI to the other sites, • the procedures that will be used to communicate from the UI to the other sites any interim results, • the procedures that will be used to communicate from the UI to the other sites other new information which may impact a subject’s willingness to participate, or continue participating in the research</td>
<td>☐ Yes ☐ No ☐ NA</td>
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Points for discussion:
14. Should any of the following additional elements be included in the Consent? If an element is present in the consent, please select the appropriate option.

Consider:
- Where appropriate, one or more of the following elements of information shall also be provided to each subject. Consider the nature of the research (i.e. educational, psychological, or physical intervention), the study design, the population under study (pregnant women or women capable of becoming pregnant, etc.), subject safety and welfare, as well as the relevance of the information in allowing the prospective subject to make an informed decision about participation.

<table>
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<tr>
<th>Indicate any items that are not in the submitted Informed Consent that you believe should be included:</th>
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<tr>
<td><strong>Section VIII</strong></td>
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### Questions VI.28-36

15. For studies involving cognitively or decisionally impaired individuals, have the following points been considered?

   See U/I Investigator’s Guide. PI should consider:

   - potential conflicts of interest when subjects cannot understand the difference between research and treatment;
   - subject’s potentially fluctuating capacity for consent;
   - how capacity to consent will be assessed;
   - whether or not an Assent process should be used and if so, how assent should be obtained (e.g. written or verbal)
   - measures for ensuring voluntary participation throughout the study.

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<th>Yes</th>
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Points for discussion:

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### Questions VI.26-34

16. Does this research project involve any vulnerable populations of subjects?

   Consider:

   - Vulnerable populations may include pregnant women, fetuses and neonates, children, prisoners, cognitively impaired individuals as well as others (e.g. students, mentally disabled persons, or educationally or economically disadvantaged persons) who are likely to be vulnerable to coercion or undue influence.

   If Yes, are appropriate safeguards included in the protocol to protect their rights and welfare?

   If No, to the above question, what additional safeguards do you recommend for the protection of the rights and welfare of these vulnerable subjects?

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Points for discussion:

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### Attachments list

17. If there is a grant application or industry protocol for this study, do the HawkIRB Application and the Informed Consent Document correspond to the grant application/protocol?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>NA</th>
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Points for discussion:
<table>
<thead>
<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
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<tbody>
<tr>
<td><strong>Section VIII:</strong> Risks; Attachments list</td>
<td>18. If there is a grant application or industry protocol for this study, do the risks described in the HawkIRB Application and the Informed Consent Document correspond to the grant application/protocol?</td>
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Points for discussion:

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<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
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<tr>
<td><strong>Questions VII.D.1-11</strong></td>
<td>19. Is the recruitment process (including telephone scripts, advertisements, brochures, letters, compensation) fully described, understandable, fair, honest, appropriate, and non-coercive and does not create undue influence?</td>
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Consider the following issues regarding the recruitment process:

- should not state or imply a certainty of a favorable outcome or other benefits beyond what is outlined in the consent document and protocol;
- Should not make claims, either explicitly or implicitly, that the intervention or procedure is safe and effective for the purposes under investigation;
- Should not make claims, either explicitly or implicitly, that the methods used in the study are known to be equivalent or superior to any existing or commonly used methods.
- Should not use terms such as “new treatment” or “new method” without explaining that it is investigational.
- Should not promise “free services or testing,” when the intent is only to say subjects will not be charged for taking part in the investigation;
- Should not include exculpatory language;
- Should not emphasize the payment or the amount to be paid by such means as large or bold or underlined type.
-- include exculpatory language,
-- emphasize the payment or the amount to be paid, by such means as large or bold type.

Yes | No | NA |

Points for discussion:

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<tr>
<th>HawkIRB Question</th>
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<tr>
<td><strong>Questions VII.D.8-18</strong></td>
<td>20. Do the circumstances of the consent process minimize the possibility of coercion or undue influence?</td>
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Yes | No | NA |

Points for discussion:
### Questions

#### VI.28-36

<table>
<thead>
<tr>
<th>HawkIRB Question</th>
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<tr>
<td><strong>Questions VI.28-36</strong></td>
<td>21. In this research, is the legally effective informed consent of the subject or the subject’s legally authorized representative required?</td>
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<td>If yes, check all that apply:</td>
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<td>□ Subject</td>
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<td>□ Subject’s Legally Authorized Representative</td>
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<td>If no, please describe why this is not a requirement for approval:</td>
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<td>□ Waiver</td>
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<td>□ Alteration of Consent</td>
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<td>□ Other</td>
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<td>Points for discussion:</td>
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#### VI.16-17; VI.35; VII.D.29; Consent Document; Assent Document

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<thead>
<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
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<tbody>
<tr>
<td><strong>Questions VI.16-17; VI.35; VII.D.29; Consent Document; Assent Document</strong></td>
<td>22. Does the consent process communicate the information in a language understandable to the subject population or their legally authorized representative?</td>
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<td>This refers to all communication, including verbal explanations, instructions, and questions before and after the decision to take part, and is not limited to the consent document and recruitment materials.</td>
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<td>Consider if some subjects are not native English speakers, is the information provided to the subjects in their language, for example, through the use of translators.</td>
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<td>If there are subjects with language barriers due to cognitive, educational, or cultural limitations, the research team should communicate information to them in a language that these individuals can understand.</td>
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<td>Points for discussion:</td>
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#### VI.35; VII.D.29

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<th>HawkIRB Question</th>
<th>Checklist Question</th>
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<td><strong>Questions VI.35; VII.D.29</strong></td>
<td>23. Do the circumstances of the consent process provide the prospective participant or the subject’s legally authorized representative sufficient opportunity to consider whether to participate?</td>
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Points for discussion:
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<th>Checklist Question</th>
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<td><strong>Section VI:</strong> Subjects; VII.E.9-13</td>
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<td>24. Is the compensation to subjects appropriate for this study? Consider the following:</td>
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<td>• Subject payments accrue as the study progresses and are not contingent upon the subject completing the entire study.</td>
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<td>• Any amount paid as a bonus for completing the study is reasonable and not so large as to unduly induce subjects to stay in the study when they might otherwise withdraw.</td>
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<td>• All information concerning payment, including the amount and schedule of payments, is set forth in the informed consent document.</td>
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<td>• Compensation for participation in a study offered by a sponsor does not include a coupon good for a discount on the purchase price of the experimental product once it has been approved for marketing.</td>
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<td><strong>Entire application</strong></td>
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<td>25. Does this protocol require IRB review more than annually?</td>
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<td>Examples of when the IRB might consider review more frequently than annually may include:</td>
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<td>a) Study procedures in which the clear potential for significant adverse experiences have been identified at the time of review; or</td>
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<td>b) Non-therapeutic projects based on risk information provided at the time of initial review; or</td>
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<td>c) Projects in which new information provided during the duration of the study (including at the time of continuing review) indicates a high probability of significant adverse experiences not previously reported; or</td>
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<td>d) Projects in which local or outside adverse experience reports create new concerns regarding the need for closer project scrutiny; or</td>
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<td>e) Projects where the UI IRB has concerns with regard to previous or potential serious or continuing noncompliance; or</td>
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<td>f) Other, as determined by the convened IRB.</td>
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<td>In such cases, the IRB may consider granting approval for time periods less than one year, or for a limited number of subjects over a period not to exceed one year, or additional monitoring can be required.</td>
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<td>Points for discussion:</td>
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26. For studies involving children, indicate the category below. Check whether or not the additional approval criteria within the shaded box are true.  (See questions VI.6-13 in HawkIRB)

Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. Generally, for research with children in the state of Iowa, a child is an unmarried person under the age of 18. NOTE: If you are unsure of the applicable law where the research will be conducted, please call the Human Subjects Office (335-6564) for guidance.

Minimal risk means that the probability and magnitude of the 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 exams or tests.

Assent means a child’s affirmative agreement to participate in research.  (See questions VII.D.15 and VII. D.30-36 in HawkIRB) In determining whether children are capable of assenting, the IRB should take into account the age, maturity, and psychological state of the children involved in the research. When soliciting the assent of children, the PI should consider the age of the subjects, their maturity, and their ability to read and comprehend a written document in deciding how the assent will be obtained (e.g. verbally or written.)

(For the following items: See Sections VII.E and VIII in HawkIRB)

☐ Research not involving greater than minimal risk (45 CFR 46.404, 21 CFR 50.51)

- a) No greater than minimal risk to children is presented in this research;
- b) Adequate provisions are made for soliciting the permission of the parents or guardians;
  - The permission of one parent/guardian is required.
  - OR
  - The permission of both parents/guardians is required.
  - OR
  - The permission of the parents/guardians is waived.
- c) Adequate provisions are made for soliciting the assent of the children;
  - (i) Assent is required of all children in this research
  - OR
  - (ii) Assent is required for some of the children in this research
  - OR
  - (iii) Assent is not required for any of the children in this research

For (i) and (ii) above, should assent be documented? If so, describe the process below.

For (ii) and (iii) above, describe below why assent is not required.

Consider the following:

- Children are not capable of providing assent because of their age, maturity, or psychological state;
- The capability of children in this research is so limited that they could not reasonably be consulted;
- The research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research;
- The assent could be waived based on the criteria for a waiver of informed consent.

Points for discussion:
Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects (45 CFR 46.405, 21 CFR 50.52)

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<td>a) More than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject or by a monitoring procedure that is likely to contribute to the subject’s well-being;</td>
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<td>b) The risk is justified by the anticipated benefit to the subjects;</td>
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<td>c) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches;</td>
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<td>d) Adequate provisions are made for soliciting the permission of the parents or guardians;</td>
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<td>e) Adequate provisions are made for soliciting the assent of the children;</td>
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Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition
(45 CFR 46.406, 21 CFR 50.53)

- a) More than minimal risk to children is presented by an intervention or procedure that does NOT hold out the prospect of direct benefit for the individual subject or by a monitoring procedure which is NOT likely to contribute to the subject’s well-being;
- b) The risk represents a minor increase over minimal risk;
- c) The intervention/procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
- d) The intervention/procedure is likely to yield generalizable knowledge about the subjects’ disorder or condition which is of vital importance for the understanding or amelioration of the subjects’ disorder or condition;
- e) Adequate provisions are made for soliciting the permission of BOTH parents/guardians unless one parent is deceased, unknown, incompetent, not reasonably available, or only one parent has responsibility for the care and custody of the child;
  OR
    Permission of parents/guardians is waived.
- f) Adequate provisions are made for soliciting the assent of the children;
  - (i) Assent is required of all children in this research
    OR
  - (ii) Assent is required for some of the children in this research
    OR
  - (iii) Assent is not required for any of the children in this research

For (i) and (ii) above, should assent be documented? If so, describe the process below.

For (ii) and (iii) above, describe below why assent is not required. Consider the following:
- Children are not capable of providing assent because of their age, maturity, or psychological state;
- The capability of children in this research is so limited that they could not reasonably be consulted;
- The research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research;
- The assent could be waived based on the criteria for a waiver of informed consent.

Points for discussion:

Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (45 CFR 46.407, 21 CFR 50.54)

If the IRB does not believe the research meets the requirement of 404, 405, or 406, approval may be given only if:
- (a) the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, and
- (b) the Secretary of DHHS, after consultation with a panel of experts in pertinent disciplines and following opportunity for public review and comment has determined either
  - (1) that the research in fact satisfies the conditions of 404, 405, or 406, or
  - (2) the research presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children and the research will be conducted in accordance with sound ethical principles and adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.

Points for discussion:
27. For studies involving **prisoners**, indicate the category below. Check whether or not the additional approval criteria within the shaded box are true. *(See questions VI.13, VI.37-45 in HawkIRB)*

☐ Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects *(45 CFR 46.306(a)(2)(i)) (See Sections I, VII.E, VIII in HawkIRB)*

☐ Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects *(45 CFR 46.306(a)(2)(ii)) (See Sections I, VII.E, and VIII in HawkIRB)*

☐ Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his intent to approve such research *(45 CFR 46.306(a)(2)(iii)) (See Sections I and VII.E in HawkIRB)*

☐ Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the intent to approve such research *(45 CFR 46.306(a)(2)(iv)) (See Sections I and VII.E in HawkIRB)*

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**45 CFR 46.305(a)**

*Approval may be given only if the IRB finds that:*

___(1) the research under review represents one of the categories of research permissible (above);

___(2) any possible advantages accruing to the prisoner through his/her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his/her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

___(3) the risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers;

___(4) procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board
justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project; 

(5) the information is presented in language which is understandable to the subject population; 

(6) adequate assurance exists that parole boards will not take into account a prisoner’s participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have not effect on his or her parole; and 

(7) where the Board finds there may be a need for follow-up examinations or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners’ sentences, and for informing participants of this fact.

Points for discussion:
28. For studies involving **pregnant women, human fetuses, or neonates**, check whether or not the additional approval criteria are true in the relevant shaded box. *(See questions VI.13 and VI.26-27 in HawkIRB.)*

☐ **Pregnant women** or fetuses may be involved in research if all of the following conditions are met (45 CFR 46.204):

- (a) where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
- (b) the risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
- (c) any risk is the least possible for achieving the objectives of the research;
- (d) if the research holds out (1) the prospect of direct benefit to the pregnant woman, (2) the prospect of a direct benefit both to the pregnant woman and the fetus, or (3) no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, the woman’s consent is obtained; OR
- (e) if the research holds out the prospect of direct benefit solely to the fetus, then the consent of the pregnant woman and the father is obtained, except that the father’s consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest;
- (f) each individual providing consent under (d) or (e) above is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate; and
- (g) for children who are pregnant, assent and permission are obtained in accord with Subpart D for studies involving children;
- (h) no inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- (i) individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
- (j) individuals engaged in the research will have no part in determining the viability of a neonate.

☐ **Neonates of uncertain viability** and **nonviable neonates** may be involved in research if all of the following conditions are met (45 CFR 46.205a):

- (1) where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;
- (2) each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate;
- (3) individuals engaged in the research will have no part in determining the viability of a neonate; AND

46.205(b) **if the neonate is of uncertain viability**, until it has been ascertained whether or not a neonate is viable, the following additional conditions are met:
(1) the IRB determines that (i) the research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or (ii) the purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and

(2) the legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent’s legally authorized representative is obtained in accord with Subpart A, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

OR 46.205(c) if the neonate is nonviable after delivery, all of the following additional conditions are met:

(1) vital functions of the neonate will not be artificially maintained;
(2) the research will not terminate the heartbeat or respiration of the neonate;
(3) there will be no added risk to the neonate resulting from the research;
(4) the purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
(5) the legally effective informed consent of both parents of the neonate is obtained, except that the waiver and alteration provisions of Subpart A do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirement of this paragraph.

Points for discussion:
IRB PRIMARY REVIEWER CHECKLIST
(Prisoner Advocate)

Protocol & Primary Reviewer Identification
Principal Investigator:
IRB ID:
Study Expiration Date:
Primary Reviewer:
Meeting Date:

Please use this checklist when reviewing this protocol. Make notes in the space provided for leading the discussion with the full board. Federal regulations or UI policy references are boxed. Please contact the investigator with your questions prior to the meeting date. If you see any significant problems with this study, please contact the IRB chair in advance of the meeting to alert him/her of your concerns.

Primary Reviewer Self-Assessment

1. Do you, as the primary reviewer assigned to this project, have a conflict of interest with this project?
   
   1. Conflict of Interest Policy:
      An IRB member may not vote on a project, and is not counted towards a quorum, when
      1) s/he serves as a co-investigator or other member of the research team, or
      2) an immediate family member (spouse or domestic partner and dependent children) serves
      as a co-investigator or other member of the research team, or
      3) when s/he or an immediate family member (spouse or domestic partner and dependent
      children) has a significant financial interest with a project being reviewed.

2. Conflict of interest in research involves situations in which an investigator has a significant financial interest that may compromise, or have the appearance of compromising, professional judgment in the design, conduct, or reporting of research. The terms "investigator" and "significant financial interest" are defined below.

3. Investigators conducting research funded by the Public Health Service (including National Institutes of Health) and National Science Foundation, as well as those conducting studies regulated by the Food and Drug Administration, are subject to agency specific regulations (II-18.8 below). These regulations set forth the obligations of investigators, sponsors and institutions for research involving significant financial or other conflicts of interest, and affected parties are advised to review the relevant regulations prior to submission of a research proposal or application.

   a) "Investigator" means the principal investigator and any other person, whether faculty, staff, or student, who is responsible for the design, conduct, or reporting of research. "Investigator" also includes the investigator's spouse and dependent children.

   b) "Significant financial interest" means anything of monetary value, including, but not limited to, salary or other payments for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options, or other ownership interests); and intellectual property rights (patents, copyrights, and royalties from such rights) held by an investigator or the investigator's immediate family (Immediate family means spouse or domestic partner, and dependent children), individually or in aggregate, when such interest involves:
i. Payments in excess of $10,000 (including salary, consulting fees, royalty or licensing payments from intellectual property, and honoraria and/or gifts) received within the past 12 months or anticipated for the next 12 months (excluding salary and other payments for services from the University);

ii. An equity interest in a publicly traded company worth more than $10,000 or more than 5 percent of the business entity as determined by reference to its publicly listed price (excluding mutual funds);

iii. Any equity interest if the value cannot be determined by reference to publicly listed prices (i.e., an equity interest in a privately held company, such as a start-up company);

iv. A position giving rise to a fiduciary duty, such as director, officer, partner, trustee, employee, or any other position of management; or

v. Intellectual property rights (patents or copyrights) or royalties from such rights whose value may be affected by the outcome of the research, including royalties distributable under University policy or any royalty-sharing agreements involving the University.

4. Personal agreements between sponsors and investigators, IRB members, or their immediate family members where the amount of compensation (consulting, board honoraria, or any other kind) could change depending on the outcome of a study or any other activity the faculty/IRB member performs as part of their University service are prohibited. In some cases, such arrangements are illegal under state law.

2. Do you think there is a need for someone with additional expertise (i.e. a consultant) to assist in the review of this protocol?

   Yes ☐   No ☐

   The need for a consultant should be made based on the scientific design of the study, the ethical issues of the study, the potential risks or benefits of the study, specific privacy and confidentiality concerns, or considerations relative to a particular study population.

If your answer to question #1 OR #2 is Yes, STOP HERE. Call the Human Subjects Office at 335-6564 and/or the IRB chair as soon as possible to inform us of this conflict or need for a consultant.
3. **45 CFR 46.303 Definitions as used in this checklist:**
   (a) *Secretary* means the Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.

   (b) *DHHS* means the Department of Health and Human Services.

   (c) *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.

   (d) *Minimal risk* is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

4. **45 CFR 46.305 Additional duties of the Institutional Review Boards where prisoners are involved.**

   (a) In addition to all other responsibilities prescribed for Institutional Review Boards under this part, the Board shall review research covered by this subpart and approve such research only if it finds that:

   ___ (1) The research under review represents one of the categories of research permissible under §46.306(a)(2);

   ___ (2) Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

   ___ (3) The risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers;

   ___ (4) Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;

   ___ (5) The information is presented in language which is understandable to the subject population;

   ___ (6) Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and

   ___ (7) Where the Board finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners’ sentences, and for informing participants of this fact.
5. **45 CFR 46.306 Permitted research involving prisoners.**

(a) Biomedical or behavioral research conducted or supported by DHHS may involve prisoners as subjects only if:

___ (1) The institution responsible for the conduct of the research has certified to the Secretary that the Institutional Review Board has approved the research under §46.305 of this subpart;

AND

___ (2) In the judgment of the Secretary the proposed research involves solely the following:

___ (i) Study of the possible causes, effects, and processes of incarceration and of criminal behavior provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

___ (ii) Study of prisons as institutional structures or of prisoners as incarcerated persons provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

___ (iii) Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary has consulted with appropriate experts including experts in penology, medicine, and ethics and published notice in the FEDERAL REGISTER of his intent to approve such research; or

___ (iv) Research on practices both innovative and accepted which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research the study may proceed only after the Secretary has consulted with appropriate experts including experts in penology, medicine, and ethics and published notice in the FEDERAL REGISTER of the intent to approve such research.

6. **Does the use of human subjects have research relevance?** Yes No

The use of human subjects in this project is relevant and appropriate to answer the questions being asked. The study design is appropriate to answer the questions being asked.

Points for discussion:

7. **Are there any ethical issues regarding the study’s design and conduct?** Yes No

Ethical issues may include but are not limited to the Belmont report principles: respect for persons (voluntary, fully informed consent), beneficence (obligation to protect subjects from
harm and secure their well-being), and justice (benefits and burdens of research are fairly distributed).

Points for discussion:

8. Are risks (physical, emotional, financial, legal) to subjects minimized?  
   ☐ Yes  ☐ No
   
   **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 or (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

   Points for discussion:

9. Are risks to subjects reasonable in relation to anticipated benefits?  
   ☐ Yes  ☐ No
   
   **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. In evaluating risks and benefits, the IRB should consider only those risks and benefits that **may result from the research** (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

   Points for discussion:

10. Is subject selection equitable?  
    ☐ Yes  ☐ No
    
    **In making this assessment the IRB should take into account** the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

    Points for discussion:

11. Are there procedures for monitoring safety?  
    ☐ Yes  ☐ No
    
    **When appropriate, research plan makes adequate provision** for monitoring the data collected to ensure the safety of subjects.

    Points for discussion:

12. Are there procedures for protecting privacy and confidentiality?  
    ☐ Yes  ☐ No
    
    **When appropriate, adequate provisions exist** to protect the privacy of subjects and to maintain the confidentiality of data.

    Points for discussion:
13. For studies involving cognitively impaired individuals, have the following points been considered? □ Yes □ No □ NA

See U of I Investigator’s Guide to Human Subjects Review. PI should consider:
- potential conflicts of interest when subjects cannot understand the difference between research and treatment;
- subject’s potentially fluctuating capacity for consent;
- how capacity to consent will be assessed; and
- measures for ensuring voluntary participation throughout the study.

Points for discussion:

14. For studies involving children, indicate the category below. If applicable, check whether or not the additional approval criteria within the shaded box are true.

□ Research not involving greater than minimal risk (45 CFR 46.404)

If the IRB finds that no greater than minimal risk to children is presented, approval may be given only if adequate provisions are made for soliciting the assent of the children and the permission of at least one (1) parent/guardian. Minimal risk means that the probability and magnitude of the 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 exams or tests.

Points for discussion:

□ Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects (45 CFR 46.405)

If the IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject’s well-being, approval may be given only if the IRB finds that:

(a) the risk is justified by the anticipated benefit to the subjects, and
(b) the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches, and
(c) adequate provisions are made for soliciting the assent of the children and permission of at least one (1) parent/guardian.

Points for discussion:

□ Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition (45 CFR 46.406)

If the IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely
to contribute to the well-being of the subject, **approval may be given only if** IRB finds that:

- (a) the risk represents a minor increase over minimal risk, and
- (b) the intervention/procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations, and
- (c) the intervention/procedure is likely to yield generalizable knowledge about the subject’s disorder or condition which is of vital importance for the understanding or amelioration of the subject’s disorder or condition, and
- (d) adequate provisions are made for soliciting assent of the child and permission of both parents/guardians.

Points for discussion:

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**Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (45 CFR 46.407)**

If the IRB does not believe the research meets the requirement of 404, 405, or 406, **approval may be given only if**:

- (a) the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, and
- (b) the Secretary of DHHS, after consultation with a panel of experts in pertinent disciplines and following opportunity for public review and comment has determined either (1) that the research in fact satisfies the conditions of 404, 405, or 406, or (2) the research presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children and the research will be conducted in accordance with sound ethical principles and adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.

Points for discussion:
15. Secretary of DHHS has the authority to waive the applicability of some or all of the provisions of the DHHS regulations for the protection of human subjects to specific research activities or classes of research activities otherwise covered by the regulations. In a document published in the Federal Register on October 7, 2002 (67 FR 62432), the Secretary of DHHS sought public comment on a proposed waiver of the applicability of certain requirements of subpart C, 45 CFR part 46, to allow DHHS to conduct or support certain important and necessary epidemiologic research on prisoners that presents no more than minimal risk and no more than inconvenience to the prisoner subjects. The Secretary of DHHS specifically proposed waiving the applicability of 45 CFR 46.305(a)(1) and 46.306(a)(2) for certain research conducted or supported by DHHS that involves epidemiologic studies that meet the following criteria:

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<th>(1) In which the sole purposes are (choose one under (1)(i) or (1)(ii))</th>
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<td>(i) To describe the prevalence or incidence of a disease by identifying all cases,</td>
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<td>(ii) To study potential risk factor associations for a disease,</td>
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<td>(2) Where the institution responsible for the conduct of the research certifies to the Office for Human Research Protections, DHHS, acting on behalf of the Secretary, that the IRB approved the research and fulfilled its duties under 45 CFR 46.305(a)(2)–(7) and determined and documented that (Both points listed below must be applicable)</td>
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<td>(i) The research presents no more than minimal risk and no more than inconvenience to the prisoner subject</td>
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<td>AND</td>
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<td>(ii) Prisoners are not a particular focus of the research.</td>
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The range of studies to which the proposed waiver would apply includes epidemiological research related to chronic diseases, injuries, and environmental health. This type of research uses epidemiologic methods (such as interviews and collection of biologic specimens) that generally entail no more than minimal risk to the subjects. An example of an epidemiological study that could be permitted under the proposed waiver is one in which all persons with HIV, but with none of the known risk factors for HIV, are asked to participate in a study involving an interview, review of medical records, and collection of a blood specimen. The purpose of the study is to determine other 5 potential risk factors for HIV. All states with mandatory HIV reporting laws report these cases to the Centers for Disease Control and Prevention (CDC), DHHS. Each person who meets the study definition would be asked to participate, and prisoners could well be members of the potential study group. In order for the study to be approved under this waiver, the IRB would need to ensure that, among other things, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of the data.
Points for discussion:

16. *Approval may be given only if the IRB finds that:*

*45 CFR 46.305(a)*

- Yes ☐ No ☐ NA ☐

___(1) the research under review represents:

___ one of the categories of research permissible under 45 CFR 46.306(a)(2)

OR

___ the Epidemiology Waiver criteria - See 45 CFR 46.305(a)(2)-(7) listed below. The proposed waiver would require that such certification include the IRB’s determination and documentation that the research presents no more than minimal risk and no more than inconvenience to the prisoner-subject, and that prisoners are not a particular focus of the research.

___(2) any possible advantages accruing to the prisoner through his/her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his/her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

___(3) the risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers;

___(4) procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;

___(5) the information is presented in language which is understandable to the subject population;

___(6) adequate assurance exists that parole boards will not take into account a prisoner’s participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have not effect on his or her parole; and

___(7) where the Board finds there may be a need for follow-up examinations or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners’ sentences, and for informing participants of this fact.
# IRB-01 PRIMARY REVIEWER CHECKLIST

## CONTINUING REVIEW

### Protocol & Primary Reviewer Identification

<table>
<thead>
<tr>
<th>Principal Investigator:</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRB ID:</td>
</tr>
<tr>
<td>Study Expiration Date:</td>
</tr>
<tr>
<td>Primary Reviewer:</td>
</tr>
<tr>
<td>Meeting Date:</td>
</tr>
</tbody>
</table>

### Primary Reviewer Self-Assessment

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Do you, as the primary reviewer assigned to this project, have a <strong>conflict of interest</strong> with this project?</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

#### 1. Conflict of Interest Policy:

An IRB member may not vote on a project, and is not counted towards a quorum, when
1) s/he serves as a co-investigator or other member of the research team, or
2) an immediate family member (spouse or domestic partner and dependent children) serves as a co-investigator or other member of the research team, or
3) when s/he or an immediate family member (spouse or domestic partner and dependent children) has a **significant financial interest** with a project being reviewed.

#### 2. Conflict of interest in research involves situations in which an investigator has a significant financial interest that may compromise, or have the appearance of compromising, professional judgment in the design, conduct, or reporting of research. The terms "investigator" and "significant financial interest" are defined below.

#### 3. Investigators conducting research funded by the Public Health Service (including National Institutes of Health) and National Science Foundation, as well as those conducting studies regulated by the Food and Drug Administration, are subject to agency specific regulations (II-18.8 below). These regulations set forth the obligations of investigators, sponsors and institutions for research involving significant financial or other conflicts of interest, and affected parties are advised to review the relevant regulations prior to submission of a research proposal or application.

##### a) "Investigator" means the principal investigator and any other person, whether faculty, staff, or student, who is responsible for the design, conduct, or reporting of research. "Investigator" also includes the investigator's spouse and dependent children.

##### b) "Significant financial interest" means anything of monetary value, including, but not limited to, salary or other payments for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options, or other ownership interests); and intellectual property rights (patents, copyrights, and royalties from such rights) held by an investigator or the investigator's immediate family (Immediate family means spouse or domestic partner, and dependent children), individually or in aggregate, when such interest involves:

##### i. Payments in excess of $10,000 (including salary, consulting fees, royalty or licensing payments from intellectual property, and honoraria and/or gifts) received within the past 12 months or anticipated for the next 12 months (excluding salary and other payments for services from the University);

##### ii. An equity interest in a publicly traded company worth more than $10,000 or more than 5 percent of the business entity as determined by reference to its publicly listed price (excluding mutual funds);

##### iii. Any equity interest if the value cannot be determined by reference to
publicly listed prices (i.e., an equity interest in a privately held company, such as a start-up company);
iv. A position giving rise to a fiduciary duty, such as director, officer, partner, trustee, employee, or any other position of management; or
v. Intellectual property rights (patents or copyrights) or royalties from such rights whose value may be affected by the outcome of the research, including royalties distributable under University policy or any royalty-sharing agreements involving the University.

4. Personal agreements between sponsors and investigators, IRB members, or their immediate family members where the amount of compensation (consulting, board honoraria, or any other kind) could change depending on the outcome of a study or any other activity the faculty/IRB member performs as part of their University service are prohibited. In some cases, such arrangements are illegal under state law.

2. Do you think there is a need for someone with additional expertise (i.e. a consultant) to assist in the review of this protocol?

   The need for a consultant should be made based on the scientific design of the study, the ethical issues of the study, the potential risks or benefits of the study, specific privacy and confidentiality concerns, or considerations relative to a particular study population.

   □ Yes □ No

If your answer to question #1 OR #2 is Yes, STOP HERE.
Call the Human Subjects Office at 335-6564 and/or the IRB chair as soon as possible to inform us of this conflict or need for a consultant.
### Project Review -- Enrollment

<table>
<thead>
<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>VI.1 + VI.6</td>
<td>3. How many subjects are currently approved by the IRB for enrollment?</td>
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<td></td>
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<tr>
<td>CRII.1</td>
<td>4. How many subjects have been enrolled to date?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRII.1 - Enrollment Report</td>
<td>5. How many subjects have been enrolled since the last continuing review?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>CR.II.1&gt;(VI.1 + VI.6)</td>
<td>6. Does the number of subjects enrolled in this study exceed the maximum number of subjects approved by the IRB?</td>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>CRII.5</td>
<td>7. Has the project permanently stopped enrolling new subjects into the study?</td>
<td>Yes</td>
<td></td>
<td>No</td>
</tr>
</tbody>
</table>

**Points for Discussion:**

The following questions ask about certain populations of subjects that might be involved in this project. To determine the previous regulatory categorization, follow these steps:

A. Log-in to HawkIRB.
B. Type the IRB # of this protocol into the box in the upper right side of the main page (next to the “Go” button) and then hit “Go.” This will take you to the Project Summary page for the project.
C. Using the yellow tabs at the top of this page, choose “Approval.”
D. The most recently approved form for the project is listed at the top. By looking at Administrative Codes, you will see the most recent regulatory classifications.

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<th>No</th>
<th>N/A</th>
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<td>VI.6</td>
<td>8. Does this research project involve children (persons &lt; 18)?</td>
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<td></td>
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</tr>
<tr>
<td></td>
<td><em>Children</em> are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. Generally, for research with children in the state of Iowa, a child is an unmarried person under the age of 18. NOTE: If you are unsure of the applicable law where the research will be conducted, please call the Human Subjects Office (335-6564) for guidance.*</td>
<td></td>
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<tr>
<td>Project Summary Page: Approval</td>
<td>9. Is the regulatory classification regarding children in this research still accurate?</td>
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<td></td>
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<tr>
<td>VI.26-27</td>
<td>10. Does this project involve pregnant women, fetuses, or neonates?</td>
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<tr>
<td>Project Summary Page: Approval</td>
<td>11. Is the regulatory classification regarding pregnant women, fetuses, or neonates in this research still accurate?</td>
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<tr>
<td>HawkIRB Question</td>
<td>Review each of the following</td>
<td></td>
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<td>CR.I</td>
<td>14. Accrual or Recruitment Difficulties/Problems or Delays</td>
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<td>CR.II.5</td>
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<td>16. Research-related interventions</td>
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<td>17. Summary of the status of all subjects</td>
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<td>CR.III.1</td>
<td>18. Unanticipated problems involving risk to subjects or others.</td>
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<tr>
<td>CR.III.2</td>
<td>19. Description of unanticipated problems</td>
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<td>CR.III.3</td>
<td>20. Subject Complaints</td>
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<td>CR.III.4</td>
<td>21. Description of subject complaints</td>
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<td>CR.III.5</td>
<td>22. Subjects who withdraw</td>
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<td>CR.III.6</td>
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<td>CR.III.9</td>
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<td>CR.III.10</td>
<td>27. Competitive Continuation</td>
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<td>CR.III.11</td>
<td>28. Regulatory Correspondence</td>
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<tr>
<td>CR.III.12</td>
<td>29. Sponsor or funding agency monitoring</td>
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<td></td>
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</tr>
<tr>
<td>Attachments</td>
<td>30. Review attachments</td>
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</tr>
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Points for Discussion:

**Project Review – Approval of Continuing Review**
<table>
<thead>
<tr>
<th>HawkIRB</th>
<th>Checklist Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>II. 31</td>
<td>Do the PI and study team continue to have the appropriate expertise to conduct this research?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>VIII 32</td>
<td>Do the risks to subjects (physical, emotional, financial, legal, social, etc.) continue to be minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>VII.E VIII 33</td>
<td>Do the risks to subjects continue to be minimized, whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes?</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>
| VIII IX CR. III.1 34 | Do the risks to subjects remain reasonable in relation to anticipated benefits (if any) to subjects, and the importance of the knowledge that may reasonably be expected to result?  
*Consider:*  
- Review the summary of adverse experiences & unanticipated problems;  
- In evaluating risks and benefits, consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research); | ☐ | ☐ |
| I VI 35 | Does subject selection remain equitable?  
*Consider:*  
- The purposes of the research;  
- The setting in which the research will be conducted being particularly cognizant of the special problems of research involving vulnerable populations (children, prisoners, pregnant women, decisionally impaired persons, economically or educationally disadvantaged persons, students or other groups that require special consideration) | ☐ | ☐ |
| VIII 36 | Does the data and safety monitoring plan continue to be adequate for monitoring the data collected to ensure the safety of subjects (i.e. is it appropriate for the level of risk)?  
*Review all data safety or progress reports completed to date.* | ☐ | ☐ |
| X.1-3 37 | Do procedures for protecting the privacy of subjects remain adequate?  
*Privacy means freedom from unauthorized intrusion or the state of being let alone and able to keep certain personal information to oneself.* | ☐ | ☐ |
| X.4-6 38 | Do procedures for protecting the confidentiality of subject information remain adequate?  
*Confidentiality means the ethical or legal right that information is considered private and will be held secret unless consent is provided permitting disclosure.* | ☐ | ☐ |

Points for Discussion:
IRB-02 PRIMARY REVIEWER CHECKLIST
CONTINUING REVIEW

Protocol & Primary Reviewer Identification
Principal Investigator:
IRB ID:
Study Title:
Study Expiration Date:
Primary Reviewer:
Meeting Date:

Primary Reviewer Self-Assessment

1. Do you, as the primary reviewer assigned to this project, have a conflict of interest with this project?  

   1. Conflict of Interest Policy:  
      An IRB member may not vote on a project, and is not counted towards a quorum, when  
      1) s/he serves as a co-investigator or other member of the research team, or  
      2) an immediate family member (spouse or domestic partner and dependent children) serves  
      as a co-investigator or other member of the research team, or  
      3) when s/he or an immediate family member (spouse or domestic partner and dependent  
      children) has a significant financial interest with a project being reviewed.  
   2. Conflict of interest in research involves situations in which an investigator has a significant  
      financial interest that may compromise, or have the appearance of compromising,  
      professional judgment in the design, conduct, or reporting of research. The terms  
      "investigator" and "significant financial interest" are defined below.  
   3. Investigators conducting research funded by the Public Health Service (including National  
      Institutes of Health) and National Science Foundation, as well as those conducting studies  
      regulated by the Food and Drug Administration, are subject to agency specific regulations (II-  
      18.8 UI Operations Manual). These regulations set forth the obligations of investigators,  
      sponsors and institutions for research involving significant financial or other conflicts of  
      interest, and affected parties are advised to review the relevant regulations prior to  
      submission of a research proposal or application.  

      a) "Investigator" means the principal investigator and any other person, whether  
      faculty, staff, or student, who is responsible for the design, conduct, or reporting of  
      research. "Investigator" also includes the investigator's spouse and dependent  
      children.  
      b) "Significant financial interest" means anything of monetary value, including, but not  
      limited to, salary or other payments for services (e.g., consulting fees or honoraria);  
      equity interests (e.g., stocks, stock options, or other ownership interests); and  
      intellectual property rights (patents, copyrights, and royalties from such rights) held  
      by an investigator or the investigator's immediate family (Immediate family means  
      spouse or domestic partner, and dependent children), individually or in aggregate,  
      when such interest involves:  

      i. Payments in excess of $10,000 (including salary, consulting fees, royalty  
         or licensing payments from intellectual property, and honoraria and/or  
         gifts) received within the past 12 months or anticipated for the next 12  
         months (excluding salary and other payments for services from the  
         University);  
      ii. An equity interest in a publicly traded company worth more than $10,000  
          or more than 5 percent of the business entity as determined by reference  
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iv. A position giving rise to a fiduciary duty, such as director, officer, partner, trustee, employee, or any other position of management; or

v. Intellectual property rights (patents or copyrights) or royalties from such rights whose value may be affected by the outcome of the research, including royalties distributable under University policy or any royalty-sharing agreements involving the University.

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2. Do you think there is a need for someone with additional expertise (i.e. a consultant) to assist in the review of this protocol?

The need for a consultant should be made based on the scientific design of the study, the ethical issues of the study, the potential risks or benefits of the study, specific privacy and confidentiality concerns, or considerations relative to a particular study population.

If your answer to question #1 OR #2 is Yes, STOP HERE.
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## Project Review -- Enrollment

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<th>Checklist Question</th>
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</tr>
</thead>
<tbody>
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<td>CR.II.1 - Enrollment Report</td>
<td>5. How many subjects have been enrolled since the last continuing review?</td>
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<tr>
<td>CR.II.1&gt;(VI.6 + VI.6)</td>
<td>6. Does the number of subjects enrolled in this study exceed the maximum number of subjects approved by the IRB?</td>
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<td>CR.II.5</td>
<td>7. Has the project permanently stopped enrolling new subjects into the study?</td>
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### Points for Discussion:

The following questions ask about certain populations of subjects that might be involved in this project. To determine the previous regulatory categorization, follow these steps:

- Log-in to HawkiIRB.
- Type the IRB # of this protocol into the box in the upper right side of the main page (next to the “Go” button) and then hit “Go.” This will take you to the Project Summary page for the project.
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<td>VI.6</td>
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<td>Project Summary Page: Approval</td>
<td>9. Is the regulatory classification regarding children in this research still accurate?</td>
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<tr>
<td>VI.37</td>
<td>12. Does this project involve prisoners?</td>
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## Project Review – Study Progress

<table>
<thead>
<tr>
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<th>Review each of the following</th>
</tr>
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<tbody>
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<tr>
<td>CR.II.6</td>
<td>16. Research-related interventions</td>
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<td>CR.II.7</td>
<td>17. Reason study is being kept open</td>
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Points for Discussion:

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## Project Review – Approval of Continuing Review

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<tr>
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<tbody>
<tr>
<td>II</td>
<td>32. Do the PI and study team continue to have the appropriate expertise to conduct this research?</td>
<td>No</td>
<td>Discuss</td>
</tr>
<tr>
<td>VIII</td>
<td>33. Do the risks to subjects (physical, emotional, financial, legal, social, etc.) continue to be minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>VII.E</td>
<td>34. Do the risks to subjects continue to be minimized, whenever appropriate, by using</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Points for Discussion:
<table>
<thead>
<tr>
<th>VIII</th>
<th>procedures already being performed on the subjects for diagnostic or treatment purposes?</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>VIII IX CR. III.1</td>
<td>35. Do the risks to subjects remain reasonable in relation to anticipated benefits (if any) to subjects, and the importance of the knowledge that may reasonably be expected to result?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Consider:</td>
<td></td>
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<tr>
<td></td>
<td>• Review the summary of adverse experiences &amp; unanticipated problems;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• In evaluating risks and benefits, consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research);</td>
<td>Discuss</td>
</tr>
<tr>
<td>I VI</td>
<td>36. Does subject selection remain equitable?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Consider:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• The purposes of the research;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• The setting in which the research will be conducted being particularly cognizant of the special problems of research involving vulnerable populations (children, prisoners, pregnant women, decisionally impaired persons, economically or educationally disadvantaged persons, students or other groups that require special consideration)</td>
<td>Discuss</td>
</tr>
<tr>
<td>VIII</td>
<td>37. Does the plan to manage risks continue to be adequate to ensure the safety of subjects (i.e. is it appropriate for the level of risk)?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Review all progress reports completed to date.</td>
<td>Discuss</td>
</tr>
<tr>
<td>X.1-3</td>
<td>38. Do procedures for protecting the privacy of subjects remain adequate?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Privacy means freedom from unauthorized intrusion or the state of being let alone and able to keep certain personal information to oneself.</td>
<td>Discuss</td>
</tr>
<tr>
<td>X.4-6</td>
<td>39. Do procedures for protecting the confidentiality of subject information remain adequate?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Confidentiality means the ethical or legal right that information is considered private and will be held secret unless consent is provided permitting disclosure.</td>
<td>Discuss</td>
</tr>
</tbody>
</table>

Points for Discussion:
## Project Review – Verification & Approval Period

<table>
<thead>
<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
</table>
| **Entire Application** | 40. Do you think this project needs verification from sources other than the investigators that no material changes have occurred to since the previous IRB review? Consider verification if any of the following are true:  
  - This is a complex project involving unusual levels or types of risks to subjects;  
  - This is a project involving a vulnerable population;  
  - This is a project conducted by an investigator who previously failed to comply with IRB determinations; or  
  - This is a project where the continuing review application or reports from other sources have indicated that changes may have occurred without IRB approval.                                                                                       | ☐  | ☐  |
| **Entire Application** | 41. Does this project require IRB review more frequently than annually? Consider the following:  
  - Are there study procedures/interventions in which the clear potential for significant adverse experiences have been identified at the time of this review?  
  - Does the risk information provided in this application indicate the potential for significant adverse experiences?  
  - Is this a project in which it is likely that new information provided during the course of the study might indicate a high probability of significant adverse events not previously reported?  
  - Is this a project in which local or outside adverse experience reports might create new concerns regarding the need for closer project scrutiny?  
  - Is this a project where the IRB has concerns with regard to previous or potential serious or continuing noncompliance?                                                                                   | ☐  | ☐  |

Points for Discussion:
**IRB-01 PRIMARY REVIEWER CHECKLIST**

**MODIFICATIONS or CONTINUING REVIEW + MODIFICATIONS**

**Protocol & Primary Reviewer Identification**
Principal Investigator:
IRB ID:
Study Expiration Date:
Primary Reviewer:
Meeting Date:

**Primary Reviewer Self-Assessment**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Do you, as the primary reviewer assigned to this project, have a conflict of interest with this project?</td>
<td>☐ Yes ☐ No</td>
</tr>
</tbody>
</table>

1. **Conflict of Interest Policy:**
   An IRB member may not vote on a project, and is not counted towards a quorum, when
   1) s/he serves as a co-investigator or other member of the research team, or
   2) an immediate family member (spouse or domestic partner and dependent children) serves as a co-investigator or other member of the research team, or
   3) when s/he or an immediate family member (spouse or domestic partner and dependent children) has a significant financial interest with a project being reviewed.

2. Conflict of interest in research involves situations in which an investigator has a significant financial interest that may compromise, or have the appearance of compromising, professional judgment in the design, conduct, or reporting of research. The terms "investigator" and "significant financial interest" are defined below.

3. Investigators conducting research funded by the Public Health Service (including National Institutes of Health and National Science Foundation, as well as those conducting studies regulated by the Food and Drug Administration, are subject to agency specific regulations (II-18.8 below). These regulations set forth the obligations of investigators, sponsors and institutions for research involving significant financial or other conflicts of interest, and affected parties are advised to review the relevant regulations prior to submission of a research proposal or application.

   a) "Investigator" means the principal investigator and any other person, whether faculty, staff, or student, who is responsible for the design, conduct, or reporting of research. "Investigator" also includes the investigator's spouse and dependent children.

   b) "Significant financial interest" means anything of monetary value, including, but not limited to, salary or other payments for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options, or other ownership interests); and intellectual property rights (patents, copyrights, and royalties from such rights) held by an investigator or the investigator's immediate family (Immediate family means spouse or domestic partner, and dependent children), individually or in aggregate, when such interest involves:

   i. Payments in excess of $10,000 (including salary, consulting fees, royalty or licensing payments from intellectual property, and honoraria and/or gifts) received within the past 12 months or anticipated for the next 12 months (excluding salary and other payments for services from the University);

   ii. An equity interest in a publicly traded company worth more than $10,000 or more than 5 percent of the business entity as determined by reference to its publicly listed price (excluding mutual funds);

   iii. Any equity interest if the value cannot be determined by reference to publicly listed prices (i.e., an equity interest in a privately held company, such as a start-up company);
iv. A position giving rise to a fiduciary duty, such as director, officer, partner, trustee, employee, or any other position of management; or
v. Intellectual property rights (patents or copyrights) or royalties from such rights whose value may be affected by the outcome of the research, including royalties distributable under University policy or any royalty-sharing agreements involving the University.

4. Personal agreements between sponsors and investigators, IRB members, or their immediate family members where the amount of compensation (consulting, board honoraria, or any other kind) could change depending on the outcome of a study or any other activity the faculty/IRB member performs as part of their University service are prohibited. In some cases, such arrangements are illegal under state law.

2. Do you think there is a need for someone with additional expertise (i.e. a consultant) to assist in the review of this protocol?

The need for a consultant should be made based on the scientific design of the study, the ethical issues of the study, the potential risks or benefits of the study, specific privacy and confidentiality concerns, or considerations relative to a particular study population.

If your answer to question #1 OR #2 is Yes, STOP HERE.
Call the Human Subjects Office at 335-6564 and/or the IRB chair as soon as possible to inform us of this conflict or need for a consultant.
## Project Review -- Enrollment

<table>
<thead>
<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>VI.I + VI.6</td>
<td>3. How many subjects are currently approved by the IRB for enrollment?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>CRII.1</td>
<td>4. How many subjects have been enrolled to date?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>CRII.1 - Enrollment Report</td>
<td>5. How many subjects have been enrolled since the last continuing review?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>CR.II.1&gt;(VI. I + VI.6)</td>
<td>6. Does the number of subjects enrolled in this study exceed the maximum number of subjects approved by the IRB?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>CRII.5</td>
<td>7. Has the project permanently stopped enrolling new subjects into the study?</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

### Points for Discussion:

The following questions ask about certain populations of subjects that might be involved in this project. To determine the previous regulatory categorization, follow these steps:

A. Log-in to HawkIRB.

B. Type the IRB # of this protocol into the box in the upper right side of the main page (next to the “Go” button) and then hit “Go.” This will take you to the Project Summary page for the project.

C. Using the yellow tabs at the top of this page, choose “Approval.”

D. The most recently approved form for the project is listed at the top. By looking at Administrative Codes, you will see the most recent regulatory classifications.

<table>
<thead>
<tr>
<th>HawkIRB</th>
<th>Checklist Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>VI.6</td>
<td>8. Does this research project involve children (persons &lt; 18)? <strong>Children</strong> are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. Generally, for research with children in the state of Iowa, a child is an unmarried person under the age of 18. <strong>NOTE:</strong> If you are unsure of the applicable law where the research will be conducted, please call the Human Subjects Office (335-6564) for guidance.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Project Summary Page: Approval</td>
<td>9. Is the regulatory classification regarding children in this research still accurate?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>VI.26-27</td>
<td>10. Does this project involve pregnant women, fetuses, or neonates?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Project Summary Page: Approval</td>
<td>11. Is the regulatory classification regarding pregnant women, fetuses, or neonates in this research still accurate?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>VI.37</td>
<td>12. Does this project involve prisoners?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Project</td>
<td>13. Is the regulatory classification regarding prisoners in this research still</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>
Points for Discussion:

**PROJECT REVIEW -- MODIFICATIONS**

The recruitment process includes any documents (advertisements, brochures, letters, telephone scripts, etc.) that are meant to be seen or heard by potential subjects.

The consent process includes all communication with the subjects, including verbal explanations, instructions, and questions before and after the decision to participate and is not limited to the consent document and recruitment materials.

<table>
<thead>
<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>VII.13, VII.14, VII.21, &amp; attachments</td>
<td>14. Are changes being made to the recruitment process?</td>
<td>☐ Discuss</td>
<td>☐</td>
</tr>
<tr>
<td>VII.13, VII.14, VII.21, &amp; attachments</td>
<td>15. Does the recruitment process remain fully described, understandable, fair, honest, appropriate, non-coercive, and free from undue influence?</td>
<td>☐</td>
<td>☐ Discuss</td>
</tr>
<tr>
<td>VII.15, VII.19, VII.20, VII.21</td>
<td>16. Are changes being made to the consent process?</td>
<td>☐ Discuss</td>
<td>☐</td>
</tr>
<tr>
<td>VII.15, VII.19, VII.20, VII.21</td>
<td>17. Does the consent process remain fully described, understandable, fair, honest, appropriate, non-coercive, and free from undue influence?</td>
<td>☐</td>
<td>☐ Discuss</td>
</tr>
<tr>
<td>Consent</td>
<td>18. Are changes being made to the consenting materials?</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>
Consent
document &
application

19. Are the changes in the consenting materials consistent with those identified in the protocol amendment/application?

Application

20. Should currently enrolled subjects be notified of any changes described in this modification?

Points for Discussion:

---

**Project Review – Study Progress for Continuing Review + Modification**

<table>
<thead>
<tr>
<th>HawkIRB Question</th>
<th>Review each of the following</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR.I</td>
<td>21. Accrual or Recruitment Difficulties/Problems or Delays</td>
</tr>
<tr>
<td>CR.II.5</td>
<td>22. Permanently Stopped Enrolling</td>
</tr>
<tr>
<td>CR.II.6</td>
<td>23. Research-related interventions</td>
</tr>
<tr>
<td>CR.II.8</td>
<td>24. Summary of the status of all subjects</td>
</tr>
<tr>
<td>CR.III.1</td>
<td>25. Unanticipated problems involving risk to subjects or others.</td>
</tr>
<tr>
<td>CR.III.2</td>
<td>26. Description of unanticipated problems</td>
</tr>
<tr>
<td>CR.III.3</td>
<td>27. Subject Complaints</td>
</tr>
<tr>
<td>CR.III.4</td>
<td>28. Description of subject complaints</td>
</tr>
<tr>
<td>CR.III.5</td>
<td>29. Subjects who withdraw</td>
</tr>
<tr>
<td>CR.III.6</td>
<td>30. Number of withdrawals and reason</td>
</tr>
<tr>
<td>CR.III.7</td>
<td>31. Information that could affect subjects’ willingness to participate</td>
</tr>
<tr>
<td>CR.III.8</td>
<td>32. Description of new information</td>
</tr>
<tr>
<td>CR.III.9</td>
<td>33. Progress Report</td>
</tr>
<tr>
<td>CR.III.10</td>
<td>34. Competitive Continuation</td>
</tr>
<tr>
<td>CR.III.11</td>
<td>35. Regulatory Correspondence</td>
</tr>
<tr>
<td>CR.III.12</td>
<td>36. Sponsor or funding agency monitoring</td>
</tr>
<tr>
<td>Attachments</td>
<td>37. Review attachments</td>
</tr>
</tbody>
</table>

Points for Discussion:
### Project Review – Approval Criteria for Modification or Modification + Continuing Review

<table>
<thead>
<tr>
<th>HawkIRB</th>
<th>Checklist Question</th>
<th>Yes</th>
<th>No</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>II.</td>
<td>38. Do the PI and study team continue to have the appropriate expertise to conduct this research?</td>
<td>☐</td>
<td>☐</td>
<td>Discuss</td>
</tr>
<tr>
<td>VIII</td>
<td>39. Do the risks to subjects (physical, emotional, financial, legal, social, etc.) continue to be minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk?</td>
<td>☐</td>
<td>☐</td>
<td>Discuss</td>
</tr>
<tr>
<td>VII-E VIII</td>
<td>40. Do the risks to subjects continue to be minimized, whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes?</td>
<td>☐</td>
<td>☐</td>
<td>Discuss</td>
</tr>
<tr>
<td>VIII IX CR. III.1</td>
<td>41. Do the risks to subjects remain reasonable in relation to anticipated benefits (if any) to subjects, and the importance of the knowledge that may reasonably be expected to result?</td>
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<td>☐</td>
<td>Discuss</td>
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</table>
| Consider:  
- Review the summary of adverse experiences & unanticipated problems;  
- In evaluating risks and benefits, consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research); |
| I VI | 42. Does subject selection remain equitable? | ☐   | ☐  | Discuss |
| Consider:  
- The purposes of the research;  
- The setting in which the research will be conducted being particularly cognizant of the special problems of research involving vulnerable populations (children, prisoners, pregnant women, decisionally impaired persons, economically or educationally disadvantaged persons, students or other groups that require special consideration) |
| VIII | 43. Does the data and safety monitoring plan continue to be adequate for monitoring the data collected to ensure the safety of subjects (i.e. is it appropriate for the level of risk)? | ☐   | ☐  | Discuss |
| Review all data safety or progress reports completed to date. |
| X.1-3 | 44. Do procedures for protecting the privacy of subjects remain adequate? | ☐   | ☐  | Discuss |
| Privacy means freedom from unauthorized intrusion or the state of being let alone and able to keep certain personal information to oneself. |
| X.4-6 | 45. Do procedures for protecting the confidentiality of subject information remain adequate? | ☐   | ☐  | Discuss |
| Confidentiality means the ethical or legal right that information is considered private and will be held secret unless consent is provided permitting disclosure. |

Points for Discussion:
### Project Review – Verification & Approval Period (for Continuing Review only)

<table>
<thead>
<tr>
<th>HawkJRB</th>
<th>Checklist Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
</table>
| Entire Application | 46. Do you require verification that no material changes in the IRB approved study have occurred since the previous review?  

Consider verification if any of the following are true:  
- This is a complex project involving unusual levels or types of risks to subjects;  
- This is a project involving a vulnerable population;  
- This is a project conducted by an investigator who previously failed to comply with IRB determinations; or  
- This is a project where the continuing review application or reports from other sources have indicated that changes may have occurred without IRB approval. | ☐ | ☐ |
| | 47. Does this project require IRB review more frequently than annually?  

Consider the following:  
- Are there experimental therapies in which the clear potential for significant adverse experiences have been identified at the time of this review?  
- Is this a non-therapeutic project but the risk information provided during this review might indicate the potential for significant adverse experiences?  
- Is this a project in which it is likely that new information provided during the course of the study might indicate a high probability of significant adverse events not previously reported?  
- Is this a project in which local or outside adverse experience reports might create new concerns regarding the need for closer project scrutiny?  
- Is this a project where the IRB has concerns with regard to previous or potential serious or continuing noncompliance? | ☐ | ☐ |

**Points for Discussion:**
## Project Review – Verification & Approval Period

<table>
<thead>
<tr>
<th>HawkIRB</th>
<th>Checklist Question</th>
<th>Yes</th>
<th>No</th>
<th>Discuss</th>
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</table>
| Entire Application | 48. Do you require verification that no material changes in the IRB approved study have occurred since the previous review?  
Consider verification if any of the following are true:  
• This is a complex project involving unusual levels or types of risks to subjects;  
• This is a project involving a vulnerable population;  
• This is a project conducted by an investigator who previously failed to comply with IRB determinations; or  
• This is a project where the continuing review application or reports from other sources have indicated that changes may have occurred without IRB approval. |     |     |        |
| Entire Application | 49. Does this project require IRB review more frequently than annually?  
Consider the following:  
• Are there experimental therapies in which the clear potential for significant adverse experiences have been identified at the time of this review?  
• Is this a non-therapeutic project but the risk information provided during this review might indicate the potential for significant adverse experiences?  
• Is this a project in which it is likely that new information provided during the course of the study might indicate a high probability of significant adverse events not previously reported?  
• Is this a project in which local or outside adverse experience reports might create new concerns regarding the need for closer project scrutiny?  
• Is this a project where the IRB has concerns with regard to previous or potential serious or continuing noncompliance? |     |     |        |

Points for Discussion:
IRB-02 PRIMARY REVIEWER CHECKLIST

MODIFICATIONS or CONTINUING REVIEW + MODIFICATIONS

Protocol & Primary Reviewer Identification
Principal Investigator: 
IRB ID: 
Study Title: 
Study Expiration Date: 
Primary Reviewer: 
Meeting Date: 

<table>
<thead>
<tr>
<th>Primary Reviewer Self-Assessment</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Do you, as the primary reviewer assigned to this project, have a conflict of interest with this project?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Conflict of Interest Policy:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>An IRB member may not vote on a project, and is not counted towards a quorum, when</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) s/he serves as a co-investigator or other member of the research team, or</td>
<td></td>
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<tr>
<td>2) an immediate family member (spouse or domestic partner and dependent children) serves as a co-investigator or other member of the research team, or</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3) when s/he or an immediate family member (spouse or domestic partner and dependent children) has a significant financial interest with a project being reviewed.</td>
<td></td>
<td></td>
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<tr>
<td>2. Conflict of interest in research involves situations in which an investigator has a significant financial interest that may compromise, or have the appearance of compromising, professional judgment in the design, conduct, or reporting of research. The terms &quot;investigator&quot; and &quot;significant financial interest&quot; are defined below.</td>
<td></td>
<td></td>
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<tr>
<td>3. Investigators conducting research funded by the Public Health Service (including National Institutes of Health) and National Science Foundation, as well as those conducting studies regulated by the Food and Drug Administration, are subject to agency specific regulations (II-18.8 UI Operations Manual). These regulations set forth the obligations of investigators, sponsors and institutions for research involving significant financial or other conflicts of interest, and affected parties are advised to review the relevant regulations prior to submission of a research proposal or application.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) &quot;Investigator&quot; means the principal investigator and any other person, whether faculty, staff, or student, who is responsible for the design, conduct, or reporting of research. &quot;Investigator&quot; also includes the investigator's spouse and dependent children.</td>
<td></td>
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<td>b) &quot;Significant financial interest&quot; means anything of monetary value, including, but not limited to, salary or other payments for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options, or other ownership interests); and intellectual property rights (patents, copyrights, and royalties from such rights) held by an investigator or the investigator's immediate family (Immediate family means spouse or domestic partner, and dependent children), individually or in aggregate, when such interest involves:</td>
<td></td>
<td></td>
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<tr>
<td>i. Payments in excess of $10,000 (including salary, consulting fees, royalty or licensing payments from intellectual property, and honoraria and/or gifts) received within the past 12 months or anticipated for the next 12 months (excluding salary and other payments for services from the University);</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ii. An equity interest in a publicly traded company worth more than $10,000 or more than 5 percent of the business entity as determined by reference to its publicly listed price (excluding mutual funds);</td>
<td></td>
<td></td>
</tr>
<tr>
<td>iii. Any equity interest if the value cannot be determined by reference to</td>
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</tbody>
</table>
publicly listed prices (i.e., an equity interest in a privately held company, such as a start-up company);

iv. A position giving rise to a fiduciary duty, such as director, officer, partner, trustee, employee, or any other position of management; or

v. Intellectual property rights (patents or copyrights) or royalties from such rights whose value may be affected by the outcome of the research, including royalties distributable under University policy or any royalty-sharing agreements involving the University.

4. Personal agreements between sponsors and investigators, IRB members, or their immediate family members where the amount of compensation (consulting, board honoraria, or any other kind) could change depending on the outcome of a study or any other activity the faculty/IRB member performs as part of their University service are prohibited. In some cases, such arrangements are illegal under state law.

2. Do you think there is a need for someone with additional expertise (i.e. a consultant) to assist in the review of this protocol?

The need for a consultant should be made based on the scientific design of the study, the ethical issues of the study, the potential risks or benefits of the study, specific privacy and confidentiality concerns, or considerations relative to a particular study population.

☐ Yes  ☐ No

If your answer to question #1 OR #2 is Yes, STOP HERE.
Call the Human Subjects Office at 335-6564 and/or the IRB chair as soon as possible to inform us of this conflict or need for a consultant.
# Project Review -- Enrollment

<table>
<thead>
<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>VI.I + VI.6</td>
<td>3. How many subjects are currently approved by the IRB for enrollment?</td>
</tr>
<tr>
<td>CR.II.1</td>
<td>4. How many subjects have been enrolled to date?</td>
</tr>
<tr>
<td>CR.II.1 - Enrollment Report</td>
<td>5. How many subjects have been enrolled since the last continuing review?</td>
</tr>
<tr>
<td>CR.II.1 = (VI.1 + VI.6)</td>
<td>6. Does the number of subjects enrolled in this study exceed the maximum number of subjects approved by the IRB?</td>
</tr>
<tr>
<td>CR.II.5</td>
<td>7. Has the project permanently stopped enrolling new subjects into the study?</td>
</tr>
</tbody>
</table>

### Points for Discussion:

The following questions ask about certain populations of subjects that might be involved in this project. To determine the previous regulatory categorization, follow these steps:

A. Log-in to HawkIRB.

B. Type the IRB # of this protocol into the box in the upper right side of the main page (next to the “Go” button) and then hit “Go.” This will take you to the Project Summary page for the project.

C. Using the yellow tabs at the top of this page, choose “Approval.”

D. The most recently approved form for the project is listed at the top. By looking at Administrative Codes, you will see the most recent regulatory classifications.

<table>
<thead>
<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>VI.6</td>
<td>8. Does this research project involve children (persons &lt; 18)?</td>
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</tr>
<tr>
<td></td>
<td><strong>Children</strong> are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. Generally, for research with children in the state of Iowa, a child is an unmarried person under the age of 18. <strong>NOTE:</strong> If you are unsure of the applicable law where the research will be conducted, please call the Human Subjects Office (335-6564) for guidance.</td>
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<tr>
<td></td>
<td>9. Is the regulatory classification regarding children in this research still accurate?</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Go to Kid Appendix (Meeting Manual)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VI.26-27</td>
<td>10. Does this project involve pregnant women, fetuses, or neonates?</td>
<td></td>
<td></td>
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<td></td>
<td>Go to 12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Project Summary Page: Approval</td>
<td>11. Is the regulatory classification regarding pregnant women, fetuses, or neonates in this research still accurate?</td>
<td></td>
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<tr>
<td></td>
<td>Go to Preg Appendix (Meeting Manual)</td>
<td></td>
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<tr>
<td>VI.37</td>
<td>12. Does this project involve prisoners?</td>
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<td></td>
<td>Go to Next Section.</td>
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</tr>
</tbody>
</table>
Points for Discussion:

**PROJECT REVIEW -- MODIFICATIONS**

*The recruitment process includes any documents (advertisements, brochures, letters, telephone scripts, etc.) that are meant to be seen or heard by potential subjects.*

*The consent process includes all communication with the subjects, including verbal explanations, instructions, and questions before and after the decision to participate and is not limited to the consent document and recruitment materials.*

<table>
<thead>
<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>VII.D.13, VII.D.14, VII.D.21, &amp; Attachments</td>
<td>14. Are changes being made to the recruitment process?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VII.D.13, VII.D.14, VII.D.21, &amp; Attachments</td>
<td>15. Does the recruitment process remain fully described, understandable, fair, honest, appropriate, non-coercive, and free from undue influence?</td>
<td></td>
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<tr>
<td></td>
<td>Consider the following issues regarding the recruitment process:</td>
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<tr>
<td></td>
<td>• should not state or imply a certainty of a favorable outcome or other benefits beyond what is outlined in the consent document and protocol;</td>
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<tr>
<td></td>
<td>• Should not make claims, either explicitly or implicitly, that the intervention or procedure is safe and effective for the purposes under investigation;</td>
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<tr>
<td></td>
<td>• Should not make claims, either explicitly or implicitly, that the methods used in the study are known to be equivalent or superior to any existing or commonly used methods.</td>
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<td></td>
<td>• Should not use terms such as “new treatment” or “new method” without explaining that it is investigational.</td>
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<td></td>
<td>• Should not promise “free services or testing,” when the intent is only to say subjects will not be charged for taking part in the investigation;</td>
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<td></td>
<td>• Should not include exculpatory language;</td>
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<td></td>
<td>• Should not emphasize the payment or the amount to be paid by such means as large or bold or underlined type.</td>
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</tr>
<tr>
<td>VII.D.15, VII.D.19, VII.D.20, VII.D.21</td>
<td>16. Are changes being made to the consent process?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VII.D.15, VII.D.19, VII.D.20, VII.D.21</td>
<td>17. Does the consent process remain fully described, understandable, fair, honest, appropriate, non-coercive, and free from undue influence?</td>
<td></td>
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</tr>
<tr>
<td>VII.D.21</td>
<td>Consent Document</td>
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<tr>
<td>18. Are changes being made to the consenting materials?</td>
<td>Discuss</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consent Document &amp; Application</td>
<td>19. Are the changes in the consenting materials consistent with those identified in the protocol amendment/application?</td>
<td>Discuss</td>
<td></td>
</tr>
<tr>
<td>Application</td>
<td>20. Should currently enrolled subjects be notified of any changes described in this modification?</td>
<td>Discuss</td>
<td></td>
</tr>
</tbody>
</table>

Points for Discussion:

**Project Review – Study Progress for Continuing Review + Modification**

<table>
<thead>
<tr>
<th>HawkIRB Question</th>
<th>Review each of the following</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR.I</td>
<td>21. Accrual or Recruitment Difficulties/Problems or Delays</td>
</tr>
<tr>
<td>CR.II.5</td>
<td>22. Permanently Stopped Enrolling</td>
</tr>
<tr>
<td>CR.II.6</td>
<td>23. Research-related interventions ended</td>
</tr>
<tr>
<td>CR.II.7</td>
<td>24. Reason study is being kept open</td>
</tr>
<tr>
<td>CR.II.8</td>
<td>25. Summary of the status of all subjects</td>
</tr>
<tr>
<td>CR.III.1</td>
<td>26. Unanticipated problems involving risk to subjects or others.</td>
</tr>
<tr>
<td>CR.III.2</td>
<td>27. Description of unanticipated problems</td>
</tr>
<tr>
<td>CR.III.3</td>
<td>28. Subject Complaints</td>
</tr>
<tr>
<td>CR.III.4</td>
<td>29. Description of subject complaints</td>
</tr>
<tr>
<td>CR.III.5</td>
<td>30. Subjects who withdraw</td>
</tr>
<tr>
<td>CR.III.6</td>
<td>31. Number of withdrawals and reason</td>
</tr>
<tr>
<td>CR.III.7</td>
<td>32. Information that could affect subjects’ willingness to participate</td>
</tr>
<tr>
<td>CR.III.8</td>
<td>33. Description of new information</td>
</tr>
<tr>
<td>CR.III.9</td>
<td>34. Progress Report</td>
</tr>
<tr>
<td>CR.III.10</td>
<td>35. Competitive Continuation</td>
</tr>
<tr>
<td>CR.III.11</td>
<td>36. Regulatory Correspondence</td>
</tr>
<tr>
<td>CR.III.12</td>
<td>37. Sponsor or funding agency monitoring</td>
</tr>
<tr>
<td>Attachments</td>
<td>38. Review attachments</td>
</tr>
</tbody>
</table>

Points for Discussion:
### Project Review – Approval Criteria for Modification or Modification + Continuing Review

<table>
<thead>
<tr>
<th>HawkJIRB Question</th>
<th>Checklist Question</th>
<th>Yes</th>
<th>No</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>39. Do the PI and study team continue to have the appropriate expertise to conduct this research?</td>
<td>☐</td>
<td>☐</td>
<td>Discuss</td>
</tr>
<tr>
<td>VIII</td>
<td>40. Do the risks to subjects (physical, emotional, financial, legal, social, etc.) continue to be minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk?</td>
<td>☐</td>
<td>☐</td>
<td>Discuss</td>
</tr>
<tr>
<td>VII.E VIII</td>
<td>41. Do the risks to subjects continue to be minimized, whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes?</td>
<td>☐</td>
<td>☐</td>
<td>Discuss</td>
</tr>
<tr>
<td>VIII</td>
<td>42. Do the risks to subjects remain reasonable in relation to anticipated benefits (if any) to subjects, and the importance of the knowledge that may reasonably be expected to result?</td>
<td>☐</td>
<td>☐</td>
<td>Discuss</td>
</tr>
<tr>
<td></td>
<td>Consider:</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>• Review the summary of adverse experiences &amp; unanticipated problems;</td>
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<tr>
<td></td>
<td>• In evaluating risks and benefits, consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research);</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I VI</td>
<td>43. Does subject selection remain equitable?</td>
<td>☐</td>
<td>☐</td>
<td>Discuss</td>
</tr>
<tr>
<td></td>
<td>Consider:</td>
<td></td>
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<tr>
<td></td>
<td>• The purposes of the research;</td>
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<tr>
<td></td>
<td>• The setting in which the research will be conducted being particularly cognizant of the special problems of research involving vulnerable populations (children, prisoners, pregnant women, decisionally impaired persons, economically or educationally disadvantaged persons, students or other groups that require special consideration)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>VIII</td>
<td>44. Does the plan to manage risks continue to be adequate to ensure the safety of subjects (i.e. is it appropriate for the level of risk)?</td>
<td>☐</td>
<td>☐</td>
<td>Discuss</td>
</tr>
<tr>
<td></td>
<td>Review all progress reports completed to date.</td>
<td></td>
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</tr>
<tr>
<td>X.1-3</td>
<td>45. Do procedures for protecting the privacy of subjects remain adequate? Privacy means freedom from unauthorized intrusion or the state of being let alone and able to keep certain personal information to oneself.</td>
<td>☐</td>
<td>☐</td>
<td>Discuss</td>
</tr>
<tr>
<td>X.4-6</td>
<td>46. Do procedures for protecting the confidentiality of subject information remain adequate? Confidentiality means the ethical or legal right that information is considered private and will be held secret unless consent is provided permitting disclosure.</td>
<td>☐</td>
<td>☐</td>
<td>Discuss</td>
</tr>
</tbody>
</table>

Points for Discussion:
## Project Review – Verification & Approval Period (for Continuing Review only)

<table>
<thead>
<tr>
<th>HawkIRB Question</th>
<th>Checklist Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
</table>
| Entire Application | **47.** Do you think this project needs verification from sources other than the investigators that no material changes have occurred since the previous IRB review?  
Consider verification if any of the following are true:  
- *This is a complex project involving unusual levels or types of risks to subjects;*  
- *This is a project involving a vulnerable population;*  
- *This is a project conducted by an investigator who previously failed to comply with IRB determinations;* or  
- *This is a project where the continuing review application or reports from other sources have indicated that changes may have occurred without IRB approval.* | ☐   | ☐  |
| Entire Application | **48.** Does this project require IRB review more frequently than annually?  
Consider the following:  
- *Are there study procedures/interventions in which the clear potential for significant adverse experiences have been identified at the time of this review?*  
- *Does the risk information provided in this application indicate the potential for significant adverse experiences?*  
- *Is this a project in which it is likely that new information provided during the course of the study might indicate a high probability of significant adverse events not previously reported?*  
- *Is this a project in which local or outside adverse experience reports might create new concerns regarding the need for closer project scrutiny?*  
- *Is this a project where the IRB has concerns with regard to previous or potential serious or continuing noncompliance?* | ☐   | ☐  |

Points for Discussion:
University of Iowa Institutional Review Board
Prisoner Advocate Review Summary

IRB ID:

STUDY TITLE:

PRINCIPAL INVESTIGATOR:

☐ I have reviewed this study and find no issues related to the additional protections for research involving prisoners as subjects. I recommend approval.

The original finding that the study meets the requirements of 45 CFR 46.305 (a) (1-7 inclusive) and permitting this research under 45CFR46.306 (a)2( ) is not changed.

☐ I suggest the following revisions or clarifications to ensure the additional protections for research involving prisoners as subjects.

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

____________________________________________  Date
IRB-03 SUPPLEMENTAL PRIMARY REVIEWER CHECKLIST
STUDIES INVOLVING PTSD

1. The Secretary of Veterans Affairs has directed ORO to coordinate a comprehensive review of all VHA research studies involving individuals with PTSD.

2. The purpose of this review is to ensure appropriate (a) sensitivity to the PTSD study population; (b) consideration of relevant Food and Drug Administration (FDA) or Sponsor advisories, alerts, and warnings; (c) subject notification regarding such advisories, alerts, and warnings; and (d) review of risks associated with medications likely to be used in the PTSD study population.

3. Any study that involves PTSD will undergo additional review to ensure all safety measures are met for this population. This document will be completed as a supplemental to the Primary Reviewer Checklist and the IRB-03 VA Supplemental Primary Reviewer Checklist in the Full Board review of the research protocol.

   a. Does the protocol reflect consideration of the perspectives of individuals with PTSD and of providers experienced with PTSD. Specifically, does the study evidence adequate sensitivity to needs of individuals with PTSD?

      i. If so, please explain.
      ii. If not, how should the study be modified?

   b. Has the study’s design and implementation incorporated appropriate consideration of relevant FDA or Sponsor advisories, alerts, and warnings?

      i. If so, please explain.
      ii. If not, how should the study be modified?

   c. Have subjects been appropriately notified regarding such advisories, alerts, and warnings?

      i. If so, please explain.
      ii. If not, how should the study be modified?

   d. Have the risks associated with all study drugs been adequately evaluated relative to possible interactions with medications likely to be used by the persons in the study population?

      i. If so, please explain.
      ii. If not, how should the study be modified?
e. Has the study received scientific review by the VHA Office of Research and Development (ORD), the Department of Defense (DoD), or an agency of the Department of Health and Human Services (HHS)?
   
   i. If so, is there any indication that additional scientific review is warranted at this time?
   
   ii. If not, how was scientific review accomplished? Is there any indication that additional scientific review is warranted at this time?

f. Does the study as presently implemented satisfy all the criteria for IRB approval under the Federal Policy (Common Rule) for the Protection of Human Subjects at 38 CFR 16.111? Specifically,
   
   i. Are risks to subjects minimized and reasonable in relation to anticipated benefits? Specifically,
      
      • Has the most up-to-date information available from the scientific literature, the Sponsor, and the FDA been included in the risk/benefit analysis?

   ii. Is selection of subjects equitable? Specifically,
      
      • Do the burdens of participating in the research fall on those most likely to benefit from the research?
      • Are groups that are particularly vulnerable to research risks included or excluded appropriately?

   iii. Are the informed consent process and documentation of consent appropriate? Specifically,
      
      • Does the consent process ensure that prospective research subjects will understand the nature of the research and its reasonably foreseeable risks and discomforts?
      • Does the consent process include a discussion of alternatives to participation, including (where appropriate) the availability of the study interventions “off protocol”?
      • Is consent information provided in such a way that prospective subjects can knowledgeably and voluntarily decide whether or not to participate?

   iv. Is safety monitoring adequate? Specifically, does the protocol provide a plan for:
      
      • Monitoring adverse events?
      • Conducting a meaningful and systematic evaluation of adverse events?
      • Periodically reviewing the research to determine whether the risk/benefit ratio has shifted, there are unanticipated findings involving risks to subjects, and any new information should be provided to subjects?
• Determining whether the study should be continued in light of emerging information?

v. Are privacy and confidentiality provisions adequate? Specifically,

- Does the protocol adhere to ethical and VA standards for privacy and confidentiality?
- Does the protocol make appropriate provisions for protecting the confidentiality of the data?
- Are subjects provided with sufficient information about current and future data uses and data disclosures?
- Is an accurate and valid HIPPA Authorization for Research Use and Disclosure of Protected Health Information (PHI) obtained?

g. Is remuneration for participation modest, appropriate, and neither coercive nor unduly influential?

h. Does the protocol reflect consideration and implementation of special safeguards to protect the rights and welfare of research subjects who may be vulnerable to coercion?