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I. Institutional Authority

The Office of the Vice President for Research at the University of Iowa (UI) has established three internal IRBs and has agreements with one external IRB to review all human subjects research. These boards, the UI’s IRB-01, IRB-02, IRB-03 and the Western Institutional Review Board (WIRB) review projects in a wide range of medical, social and behavioral fields. The internal boards are required to meet at least once each year, although more frequent meetings are scheduled. Institutional oversight of the internal IRBs and the Human Research Protection Program is the responsibility of the Associate Vice President for Research: Regulatory Affairs/Institutional Official.
II. Mission & Purpose

As a principal element within the framework of the UI mission, the conduct of all research relates
directly to the overall mission of the UI. In particular, the Human Research Protection Program
(HRPP) oversees all such research involving human participants.

The mission of the UI IRBs is to assure that the rights and welfare of the human subjects are
adequately protected in research. To achieve this, UI IRBs advise investigators in designing
research projects in a manner to minimize potential harm to human subjects, review all planned
research involving human subjects prior to initiation of the research, approve research that meets
established criteria for protection of human subjects, and monitor approved research to ascertain that
human subjects are indeed protected.

The UI IRBs also inform and assist the UI and its researchers on ethical and procedural issues
related to the use of human subjects in research, to facilitate compliance with relevant regulations of
the United States Government and relevant state law, and to provide a framework suitable for
continued support by Government agencies, private foundations and the industry for research
involving human subjects at the UI.

Primary responsibility for assuring that the rights and welfare of the individuals involved are
protected continues to rest with principal investigators conducting the research. Others engaged in
the conduct of the research share this responsibility. Faculty who assign or supervise research
conducted by students or staff have an obligation to consider carefully whether those individuals are
qualified to safeguard adequately the rights and welfare of subjects.
III. Principles

A. General Principles

All human subjects research (see Human Subject and Research in Section XIX) conducted at the UI is guided by the ethical principles as set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research entitled “Ethical Principles and Guidelines for the Protection of Human Subjects of Research (Belmont Report)”.

B. Principles Governing Restricted-Access Research (from UI Operations Manual II.27.2)

1. Secret Research.
   No faculty or staff member, administrative officer, or student of The University of Iowa may utilize University facilities for the purpose of engaging in research, the purpose or results of which are not freely communicable.

2. Restricted-Access Research.
   Because The University of Iowa exists primarily for expanding and disseminating knowledge, research activities that are subject to indefinite suppression, censorship or control by a body outside the University, ordinarily are not, and should not be, conducted within the University. However, the University recognizes that, in some research fields, such as those involving the development of new chemicals and drugs for the enhancement of life, collaboration with industrial research groups may be necessary. In such circumstances, some aspects of research programs might be considered confidential for a limited period of time. Where the advancement of science and the proper protection of the rights of research investigators make restrictions on the access to research information unavoidable, it may be permitted, provided that public knowledge is available about the purposes of the research, the identity of the investigators, the amount and sources of funds to be expended, and the University facilities utilized in the research. Such exceptions must be individually approved by the Vice President for Research following consultation with the University Research Council.

   Unless specifically excepted by the Vice President for Research, the contents of a funded grant and the results obtained and any final grant report will be available for inspection one year after the completion of the final report on that grant or contract.

3. Industry-Sponsored Grant and Contract Agreements.
   To ensure that the University and the investigator are not subject to external control, results of the research must be able to be freely discussed in an appropriate forum (scholarly meeting or journal). However, to allow the sponsor the opportunity to protect any proprietary interest, following the completion of the project the sponsor will be given a period of 90 days' notice prior to dissemination of the results of the research. Long-term and collaborative projects in which premature release of preliminary results may be prejudicial to the outcome of the research may be excepted from this requirement for a reasonable but not unlimited time, with the specific approval of the Vice President for Research.
IV. The Authority of the IRB

A. Scope

All human subjects research carried out at the University or under its auspices must be reviewed and approved by an Institutional Review Board (IRB) prior to the start of the research. The IRBs are guided by the principles of the Belmont Report and the Common Rule in reviewing all human subjects protocols.

Authority for the IRB oversight of all federally-funded research is provided in the regulations of the Department of Health and Human Services (DHHS) at 45 CFR 46. Authority for IRB oversight of all research with products regulated by the Food and Drug Administration (FDA) is provided in 21 CFR 50. In addition, the UI Operations Manual mandates that all research and related activities involving the use of human subjects must be submitted for prior review by the appropriate University-designated IRB (Part II, Chapter 27.4).

The University of Iowa Chairs or HSO staff provides guidance and determination with regard to when an activity is human subjects research. Any project involving human subjects research is subject to the review and approval of the UI IRB. Requests for determinations may be submitted to the Chairs or HSO staff either verbally or in writing and the Chairs or HSO staff may respond either verbally or in writing with a determination.

University-designated IRBs review projects when:

1. the research is sponsored by this institution,
2. the research is conducted by or under the direction of any employee or agent of this institution in connection with his or her institutional responsibilities,
3. 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
4. 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
5. the research involves the use of this institution’s non-public information to identify or contact human subjects.

B. Authority

The authority conveyed to the IRBs includes the following:

1. review all research projects involving human subjects before the involvement of human subjects may begin;
2. require from investigators modifications in research protocols and Informed Consent Documents or recruitment materials as a condition for initial or continuation approval;
3. approve new research projects and the continuation of previously approved projects; disapprove the initiation of new research projects;
4. monitor the activities in approved projects including regularly scheduled continuing review at least every twelve months, verification of compliance with approved research protocols and informed consent procedures, and observe or have a third party observe the consent process;
5. develop mechanisms for prompt reporting to the IRB of any planned changes in approved projects prior to the implementation of those changes;
6. develop mechanisms for prompt reporting to the IRB of any unanticipated problems involving risks to subjects or others occurring in approved projects, or in other projects related in context to the approved projects;
7. suspend or terminate a previously approved project;
8. restrict aspects of a research study for the purpose of subject protection;
9. review and monitor the use of test articles (investigational drugs, biologicals and devices) for the purpose of treatment of serious or life-threatening illnesses.

C. Exempt Human Subjects Research

Federal regulations recognize certain types of human subjects research as being exempt from IRB oversight. The UI policy requires that all human subjects research be reviewed by the appropriate IRB. Research meeting the “exempt” criteria provided in federal regulations is confirmed by a UI IRB Chair (or his/her IRB member designee) review of a new project application. The principal investigator requests exemption when submitting this application.

The Chair or his/her IRB member designee takes this under consideration, but has the ultimate responsibility for making the decision whether the project meets the exempt criteria (see below). In making this determination, the Chair or his/her IRB member designee also considers any ethical issues including the possibility of coercion. When the Chair or his/her IRB member designee determines that the project does not qualify for exempt status, the application is returned to the investigator for revision and resubmission for consideration under either expedited or full board review.

Exemptions under 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) any 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 that is not 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. (see Definition of “Existing” in Section XIX)

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 payment for benefits or services under those programs.

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 are true, clinical investigations involving human participants are subject to IRB review under FDA regulations. The FDA exemption criteria are as follows:

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 XIX), 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 Section XV regarding Emergency use)
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.

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,
- Not involve significant physical invasions or intrusions upon the privacy interests of the subject,
- Has authorization or concurrence by the funding agency.

D. Authority of Institutional Officials

The Associate Vice President for Research: Regulatory Affairs as the designated Institutional Official has the authority to review decisions of the IRB. In the case of an approval decision, should the Associate Vice President for Research: Regulatory Affairs conclude that a project does not fully comply with policies or obligations of the UI, s/he may disapprove, suspend, or terminate the project on behalf of the institution. 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: Regulatory Affairs or any other officer/agency of the UI, state government, or federal government.

E. Undue Influence

Investigations of attempts to unduly influence any member of the UI internal IRB(s) or IRB Administrative Support staff focus on the protection of the independence of the IRB members and support staff so that they can function in the role of protecting research participants. Attempts to unduly influence the IRB can be reported in the following manner.

When an HSO staff member experiences undue influence, s/he should report such an occurrence to the Director of the Human Subjects Office or to the IRB Administrator. These reports of undue influence go to the Associate Vice President for Research: Regulatory Affairs. If the staff member feels that undue influence is coming from either the Director of the Human Subjects Office or the IRB Administrator, s/he reports the occurrence to the Associate Vice President for Research: Regulatory Affairs directly. If the staff member feels the undue influence is coming from any of the above individuals in the reporting chain, the staff member can report the incident to the UI Ombudsperson (See UI OM Part VI, Chapter 2).
When an IRB member experiences undue influence, s/he should first report the occurrence to the IRB chair of the IRB of which s/he is a member. The IRB chair can then notify the Director of the Human Subjects Office or the IRB Administrator. The report then goes to the Associate Vice President for Research: Regulatory Affairs. If the IRB member feels that the undue influence is coming from the IRB chair, the Director of the Human Subjects Office, or the IRB Administrator, the IRB member reports directly to the Associate Vice President for Research: Regulatory Affairs. If the IRB member experiences undue influence from any of the above reporting chain, the IRB member can report the incident to the UI Ombudsperson (See OM Part VI, Chapter 2).

Parties to whom the reports are made will evaluate the allegation and will determine a course of action to be taken. Actions can include additional investigation, internal resolution, or referral to the appropriate dean, the Vice President for Research, the Provost, or the Department of Human Resources.
V. Relationship of UI IRBs to Other Entities

A. Compliance with Federal Regulations

The UI (represented by the Office of the Vice President for Research) has filed a Federalwide Assurance (FWA) with the Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP) affirming that the University is in compliance with 45 CFR 46. This assurance applies to all research involving human subjects funded by federal agencies subscribing to the Common Rule. The full text of the FWA is available in hard copy by contacting the Human Subjects Office (HSO), and is posted on the HSO website (http://www.research.uiowa.edu/hso/).

In studies involving products regulated by the Food and Drug Administration regulations, the UI IRB-01 complies with the requirements set forth in 21 CFR 11, 21 CFR 50, 21 CFR 56, 21 CFR 312, 21 CFR 812, and 21 CFR 814, Subpart H.

B. Relationship with the Iowa City Veterans Affairs Medical Center

Under a Memorandum of Understanding (MOU) between the UI IRB-03 and the Iowa City Veterans Affairs Medical Center (VAMC), the UI provides IRB review for human subjects research conducted at the VAMC. The agreement specifies that IRB-03 operates under the conditions of the UI FWA and obligates IRB-03 to operate under any additional VAMC-specific regulations or policies. A copy of this document is available upon request from the Human Subjects Office. Projects reviewed on behalf of the VAMC receive the same IRB review as those conducted at the UI.

1. Research and Development Committee

Research to be undertaken by or under the direction of the VAMC, or research that involves VAMC patients requires review and approval by both IRB-03 and the VAMC Research and Development Committee (R&D Committee).

Completion of the UI IRB-03 review and associated IRB findings and actions is documented on a VA form 10-1223, and IRB approval letter, and IRB minutes for full board studies and sent to the VAMC research office and VA Principal Investigator. The deliberations of the VAMC R&D Committee are not shared with IRB-03 unless there are specific subject protection issues raised by the Committee. Should such issues arise, the R&D Committee notifies the IRB in writing following its deliberations. If the IRB agrees that the issue(s) are related to subject protection, the IRB will require the PI to revise the application to address the identified issue(s). The Principal Investigator notifies the R&D Committee when any study, including those involving investigational drugs, has been terminated. Once IRB-03 and the VAMC R&D Committee have reviewed and approved the new research project, the Human Subjects Office releases the project to the Principal Investigator.

2. VA Pharmacy Service
It is the responsibility of the VA Principal Investigator to inform the VA pharmacy service of the following:

- IRB and R&D Committee approval when the study involves pharmacy services through the use of VA Form 10-1223.
- A signed copy of VA Form 10-1086 (Informed Consent Document) to document each subject’s consent to participate in a study.
- Termination of a study involving investigational drugs (notice is to Chief, Pharmacy Service).

C. Relationship with the Western Institutional Review Board (WIRB)

Under a contract between UI and the Western Institutional Review Board (WIRB), WIRB provides IRB review and oversight for all research that meets the first condition:

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

WIRB provides IRB review and oversight for research that meet all of the following conditions:

2. 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.

3. The protocol for the project was designed and written by the sponsor.

4. The sponsor holds all INDs/IDEs for the protocol.

5. The only sponsor of the research is a for-profit entity/company.

6. The UI investigator has not previously submitted the study to another UI IRB. Only new projects as of November 1, 2005 are eligible for WIRB review. No transfers of projects already submitted to IRB-01 are allowed.

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.
5. Research performed at the VAMC and/or utilizing VAMC resources, or performed by VAMC employees or agents on VAMC time.

The primary function of WIRB is to perform all IRB functions in compliance with applicable federal and state regulations or laws in order to protect the rights and welfare of human subjects. The primary function of the UI is coordination of application materials to be submitted and coordination of other UI committee review prior to submission to WIRB for review. By contract, WIRB notifies
the UI HSO of any WIRB termination or suspension of a study, instances of serious or continuing
noncompliance, initiation of for-cause audits, targeted regulatory inspections or other matters that
may impact the UI’s compliance with applicable regulations and laws governing human subjects
research.

The UI has the contractual right to withhold any protocol from WIRB review and keep it for review
and oversight by IRB-01. The UI may decide to retain these 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. This determination is made by a UI IRB Chair.

D. Cooperative Research

In the conduct of cooperative research projects, each institution (or entity) is responsible for
safeguarding the rights and welfare of human subjects and for complying with any applicable
cooperative research projects which involve more than one institution. To avoid duplication of
review efforts by IRBs, the UI can choose to conduct joint reviews, rely upon the review of another
qualified IRB, or make other arrangements to establish oversight responsibilities. The UI makes a
determination about whether or not a cooperating outside institution is also engaged in human
subjects research (i.e. in collaboration with the UI.) This determination is made by the UI Chair
based on the outside institution’s role and whether that role meets any of the criteria for “engaged in
research” as defined in OHRP guidance of October 16, 2008..

1. When the outside institution is determined to be engaged and 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. Under limited circumstances, when the UI 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, UI may choose to extend its FWA to cover the
outside institution’s role in this single project.

2. When the outside institution is determined to be engaged, but is not receiving federal funding for
this study through a subcontract with the UI, the UI IRB requires that the research be conducted
under either another entity’s IRB oversight or the UI IRB takes on oversight of the research. In
the former instance, the UI 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.

3. When the outside institution is determined to be engaged as described in 1 or 2 above, and 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, the UI may choose to
sign an IRB Authorization Agreement or other equivalent agreement to make the non-local IRB
the IRB of record for that particular project. When this occurs and the research is federally funded, the outside IRB is added to the UI FWA.

The final determination to enter into any agreements described in this section is made by the Institutional Official.
E. Review of Human Subjects Research Activities by Other HRPP Committees and Administrative Offices

UI IRBs coordinate reviews with other HRPP components as described below. None of these entities are a formal part of the UI IRB structure, but there is communication between the entities regarding status of review and/or conditions of approval.

1. The UI Health Care Pharmacy and Therapeutics Sub-Committee (P&T)

This sub-committee has been established to provide the UI Health Care administration and its clinical leadership with information and advice concerning the proper use of drugs and related products. The mission of this committee is to a) promote evidence-based, best practice standards in the formulary decision-making process to assure clinical efficacy, patient safety, and cost-effective prescribing within UI Health Care, b) review policies and procedures related to proper medication administration to assure medications are administered safely and appropriately, c) facilitate education of healthcare providers and students regarding medication-related issues, d) assure that medications are prescribed appropriately safely, and effectively through medication use evaluation processes, e) assure compliance with JCAHO, FDA, and other regulatory guidelines related to medication use, f) review and support investigational medication studies to ensure patient safety and adherence to UI Health Care policies, and g) evaluate and assess point-of-care and other technology systems and processes to effectuate safe, prompt, and efficient prescribing in both the inpatient and ambulatory care settings.

P&T must review a research protocol if it involves the administration of investigational new drugs or drugs that are given off label. Additionally, if a study involves either FDA-approved drugs that are given as a component of a research protocol or any other substance that is ingested, injected, or applied to the body, the study must be reviewed by P&T.

It is not a requirement that an investigator have P&T approval prior to UI IRB review. However, P&T must review research studies using drugs as described above before final approval is granted by the UI IRB. To prevent delays in the total review process, at its discretion, the UI IRB may allow concurrent review by the UI IRB and P&T and defer release of the study contingent upon receipt and review of P&T deliberations. If P&T review is completed after the UI IRB review, the UI IRB Chair reviews any P&T comments. If the Chair believes the suggested changes are appropriate and qualify as minor modifications (see Minor Modifications in Section XIX), the UI IRB Chair reviews these through an expedited process. If changes exceed minor modifications, the UI IRB Chair refers the application back to the full board for review prior to final approval.

Protocols to be reviewed by WIRB must have prior P&T approval.

P&T approval is not required prior to emergency use of an investigational drug. A copy of the information submitted to the IRB is forwarded to P&T for its review and records.
P&T has the following procedure to avoid the appearance of a conflict of interest by those members of the Subcommittee and its consultative subcommittees who may have financial relationships with a pharmaceutical or medical device company (or a parent or subsidiary firm) which markets a product that is being considered for use at the UIHC:

1. At the start of each meeting, the Chair of the Pharmacy & Therapeutics Subcommittee (or the Chair of the various consultative subcommittees) will make the following disclosure announcement: “Any member who has a potential conflict of interest due to a financial relationship (whether current, prospective, or having occurred within the past two years) with a pharmaceutical or medical device company (or a parent or subsidiary firm) or a vendor providing pharmaceutical products or services is hereby requested to disclose that such a relationship exists prior to participating in discussions involving that company’s products or those products marketed by a head-to-head competitor firm. Members are further asked to abstain from voting in these instances.”

2. If a member has a financial relationship with a company as described in the disclosure announcement, s/he is requested to declare this fact at the time s/he discusses the product or the product of a direct competitor. The member will then refrain from voting on that issue.

3. The minutes of the meeting will state that the Chair made the disclosure announcement, and any disclosure declarations made by the members will be duly recorded, as will be the fact that the same members refrained from voting on the issues previously identified.

4. In order to allow the Chair to corroborate the disclosure declarations made by members of the subcommittee, s/he will have available a file which records each member’s financial relationships with pharmaceutical or medical device companies or a vendor providing pharmaceutical products or services. This file will be kept in the possession of the Chair, but will be made available to a Chair pro tem whenever the Chair is absent.

5. Subcommittee members will at least annually provide to the Chair of his/her respective subcommittee(s) a Disclosure Report which lists the names of those pharmaceutical or medical device companies or a vendor providing pharmaceutical products or services (or parent or subsidiary firms) with which a financial relationship exists. A financial relationship shall be considered to exist if the member has:

   a. A personal investment in the company.
   b. Received grant support for research during the past two years or has a grant pending.
   c. Received a gift, honorarium, or consultant fee equal to or exceeding $35.00 during the past two years.

   The following is offered as guidance regarding mutual funds:
   a. College Retirement Equities Fund (CREF) and general purpose mutual funds may be excluded from disclosure.
b. Mutual funds that focus on pharmaceuticals, the delivery of pharmaceutical products or services, or healthcare services that could be construed as a potential conflict of interest should be disclosed.

Funds received by a member on behalf of the member’s department do not constitute a financial relationship and therefore, need not be included in the Disclosure Form.

2. Medical Radiation Protection Committee (MRPC)

The MRPC operates under the auspices of the UI Radiation Protection Executive Committee. The MRPC is charged with ascertaining that all experimental or research uses of radioactive materials and/or ionizing radiation in or on human beings conform to the currently accepted radiation protection regulations and practices, and the UI Radioactive Material License on file with the Iowa Department of Public Health. The committee reviews studies involving x-ray, use of radioisotopes, and lasers. This committee also serves as the UI’s Radioactive Drug Research Committee.

The MRPC has developed a checklist for investigators to use to determine whether a project needs to be reviewed by the committee. It is not a requirement that an investigator have MRPC approval prior to UI IRB review. However, if MRPC review is required, the MRPC must review the study before final approval is granted by the UI IRB. To prevent delays in the total review process, at its discretion, the UI IRB may allow concurrent review by the UI IRB and the MRPC and defer release of the study contingent upon receipt and review of MRPC determinations. If MRPC review is completed after the UI IRB review, the UI IRB Chair reviews any MRPC comments. If the Chair believes the suggested changes are appropriate and qualify as minor modifications, the UI IRB Chair reviews these through an expedited process. If changes exceed minor modifications, the UI IRB Chair refers the application back to the full board for review prior to final approval.

Protocols to be reviewed by WIRB must have prior MRPC approval.

No member of the MRPC is allowed to vote on any protocols on which s/he is listed as an investigator or co-investigator.

3. Institutional Biosafety Committee (IBC)

The Institutional Biosafety Committee is responsible for ensuring that recombinant DNA activities comply with the National Institutes of Health (NIH) guidelines. The principal investigator is required to submit a registration document to the Environmental Health and Safety Office for all recombinant DNA experiments that are not exempted from the NIH guidelines. The registration document must be reviewed and approved by the IBC prior to the initiation of the research. The IBC will not review projects involving gene therapy until after the NIH Recombinant DNA Advisory Committee (RAC) has completed or waived its review of the protocol.

The IBC notifies the UI IRB of its approval of projects using recombinant DNA, but deliberations of the IBC are not shared with the UI IRB unless there are specific subject protection issues raised by the IBC. To prevent delays in the total review process, at its discretion, the UI IRB may allow concurrent review by the UI IRB and the IBC and defer release of the study contingent upon receipt of the UI IRB SOP Page 19 of 95
of IBC approval. If IBC review identifies specific subject protection issues after UI IRB review has occurred, the UI IRB Chair reviews these issues. If the Chair believes the suggested changes are appropriate and qualify as minor modifications, the UI IRB Chair reviews these through an expedited process. If changes exceed minor modifications, the UI IRB Chair refers the application back to the full board for review prior to final approval.

Protocols requiring IBC review are retained for review by IRB-01 and are not sent to WIRB regardless of industry sponsorship.

If an IBC member is the investigator, or a spouse or dependent child of the member involved in the project under review, or is part of the investigator's staff, he/she must recuse him/herself from reviewing and voting on the protocol.

4. Holden Comprehensive Cancer Center Protocol Review & Monitoring Committee

All cancer clinical trials at the UI Holden Comprehensive Cancer Center (HCCC) must be reviewed and approved by the Protocol Review and Monitoring Committee (PRMC). No investigator may have access to HCCC patients or resources without approval of the PRMC. All HCCC intramural studies, industry trials, or cooperative group studies require sanctioning by the PRMC.

The purpose of the PRMC review is to:

1. conduct a scientific review (oncologic science, pharmacy & therapeutic science, and biostatistical science) of all proposed and ongoing institutional cancer clinical research;

2. monitor all clinical cancer research protocols for sufficient progress;

3. terminate those cancer protocols that are not achieving goals in a reasonable time frame; determine prioritization of patient referrals to competing protocols.

It is a requirement that an investigator have PRMC approval prior to UI IRB or WIRB review.

A PRMC member who is an investigator or consultant on a protocol being reviewed by the PRMC is required to identify their relationship to the protocol. They will be excused from the room while the protocol is being discussed and the vote taken.

If the PRMC Chair is an investigator or consultant on a protocol, the co-Chair will take over and the Chair will leave the meeting. In the event both the Chair and co-Chair have conflict of interest regarding the same protocol, the HCCC Director will Chair the meeting.

When a statistician has helped in the development of a protocol under consideration, an alternate statistician should review the protocol.

5. Conflict of Interest in Research Committee
The Conflict of Interest in Research Committee (CIRC) is appointed by the Vice President for Research. The CIRC is made up of faculty and staff representing the diversity of academic and research disciplines of the UI.

The CIRC reviews those cases in which an Investigator has disclosed a significant financial conflict of interest (see Definitions in Chapter XIX).

The CIRC recommends management strategies to the Vice President for Research. Management strategies are developed and implemented to address investigator financial interest and to assure that the Investigator may satisfy his/her research obligations in an objective manner and to avoid and/or mitigate concerns of bias as well as to protect the rights and welfare of research subjects. Management strategies that may be considered in addressing conflicts range from no action required other than disclosure, to that of disqualification of the Investigator from participating in the project, as well as others.

Review of the study by the UI IRB is contingent upon UI IRB receipt and review of the CIRC management strategy which has been accepted and signed by the Investigator. The UI IRB has the authority to revise the management strategy if they determine it will increase protection for human subjects. Any such revisions are communicated to the Associate Vice President for Research: Regulatory Affairs. When a conflict of interest is identified in an ongoing study, the IRB (or IRB Chair) will ask the Principal Investigator to voluntarily halt enrollment until a management plan has been reviewed and approved by the IRB. If the Principal Investigator does not agree to voluntary halt of enrollment, the study will be referred to the next IRB meeting for consideration of suspension of study enrollment until a management plan is reviewed and approved by the IRB.

It is a requirement that an investigator have a signed CIRC management plan prior to WIRB review. No individual who holds a significant financial interest in a project may participate in the review of its management strategy.

6. Institute for Clinical and Translational Science Research Protocol Review Committee (CRU)

The Institute for Clinical and Translational Science Research Protocol Review Committee (CRU) reviews all protocols that propose to use the CRU. Each protocol is evaluated for scientific merit and utilization of CRU resources. Two ad hoc reviewers also critique the protocols.

The deliberations of this committee are not shared with the UI IRB unless there are specific subject protection issues raised by the CRU Advisory Committee. Should such issues arise, the CRU notifies the IRB-01 Chair in writing following its deliberations. If the Chair agrees that the issue(s) are related to subject protection, the Chair will require the PI to submit a modification to address the identified issue(s). It is not a requirement to obtain CRU Advisory Committee approval prior to final approval by the UI IRB.
The CRU may not be chaired by the CRU Program Director or the Associate/Assistant Program Director. Individuals receiving salary support from the CRU grant shall not be voting members of the CRU. Members of the CRU are excused from the meeting if protocols they are participating in are being discussed.
7. Nursing Research Committee

The Nursing Research Committee must give its approval for research to be done within the Department of Nursing. This committee is charged with assuring that the rights and welfare of patients and nursing personnel are protected. The Nursing Research Committee reviews studies that involve (a) the participation of patients or nursing staff, (b) procedures not normally part of the regular patient care or nursing activities of the unit or clinic, and (c) the development of instruments or procedures.

The deliberations of this committee are not shared with the UI IRB unless there are specific subject protection issues raised by the Nursing Research Committee. Should such issues arise, the Nursing Research Committee notifies the IRB-01 Chair in writing following its deliberations. If the Chair agrees that the issue(s) are related to subject protection, the Chair will require the PI to submit a modification to address the identified issue(s). It is not a requirement to obtain Nursing Research Committee approval prior to final approval by the UI IRB.

8. Cooperating Schools Program

The Cooperating Schools Program (CSP) is a University-wide service to facilitate the placement of research projects conducted by faculty, staff, and students in public schools throughout Iowa. The purpose of the CSP is to provide information to assist researchers with obtaining permission to conduct research in Iowa public schools. This program was instituted at the request of school administrators charged with the responsibility of approving research projects in their schools. It is not a requirement to obtain Cooperating Schools Program approval prior to final approval by the UI IRB.
9. External Support

In addition to the IRB review process, all human research with external support (funds, drugs, or devices) must be processed through one of two University administrative offices, depending on the source of support:

(1) For projects with government, foundation, or voluntary health agency support:  
The Division of Sponsored Programs (DSP)  
100 Gilmore Hall  
Note: Funding is not released until IRB approval has been obtained.

or,

(2) For projects with corporate support:  
The Clinical Trials Office (CTO)  
201 Gilmore Hall  
Note: IRB approval is not released until contract has been finalized.

The UI Operations Manual (OM) specifies operating procedures with regard to UI research conducted with funding from external sponsors. In particular, proposals for sponsored research must be submitted under signature of the Principal Investigator (PI) and approved in turn by the appropriate departmental executives for the PI and investigators, the PI’s collegiate dean, and the Office of the Vice President for Research (OVPR) prior to submission to the sponsoring agency (OM 27.1.c.(1)). The OVPR has responsibility for approval of all sponsored research applications including budgets, budget revisions, and final agreements (OM 27.2.c.(5)). Both the DSP and CTO may act as liaisons in negotiating and managing agreement terms and conditions for sponsored research. Corporate or industry contracts cannot be entered into in the name of the department or individual investigators, but rather must be in the name of the UI (OM 27.7.a). Sponsorship of research within the UI setting may be awarded as a grant, cooperative agreement, or contract.
F. Federal and State Legal Requirements

Federal

The UI IRB-01 operates as a Privacy Board as described in the Standards for Privacy of Individually Identifiable Health Information (the Privacy Rule) (45 CFR 160 and 164) of the Health Insurance and Portability and Accountability Act (HIPAA) when research involves Protected Health Information (see definition in XIX) as described in this act.

State (Iowa)

See Iowa state law on the legal age to consent to treatments or procedures (see Definitions in XIX 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 (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 (§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 (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.

4. Reportable conditions (§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.

5. 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.

A person shall not intentionally or knowingly do any of the following:

a. Perform or attempt to perform human cloning.
b. Participate in performing or in an attempt to perform human cloning.
c. Transfer or receive a cloned human embryo for any purpose.
d. Transfer or receive, in whole or in part, any oocyte, human embryo, fetus, or human somatic cell, for the purpose of human cloning.

This section shall not restrict areas of scientific research not specifically prohibited, including in vitro fertilization; the administration of fertility-enhancing drugs; or research in the use of nuclear transfer or other cloning techniques to produce molecules, deoxyribonucleic acid, tissues, organs, plants, animals other than humans, or cells other than human embryos.

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.
VI. The Membership of the UI IRBs

A. Appointment of Members

The Associate Vice President for Research: Regulatory Affairs (Institutional Official) appoints all UI IRB-01 and IRB-02 Chair(s) (see VII.A), members and alternates. The length of appointment is at the discretion of the Associate Vice President for Research: Regulatory Affairs.

The VA Medical Center Director appoints VA representatives to IRB-03 for a period of three years and may re-appoint them indefinitely. The IRB Chair(s) are appointed by the VA Medical Center Director for a term of one year and may be re-appointed indefinitely.

B. Regular Members

Each UI IRBs has at least five members including at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. UI IRB members are selected with varying backgrounds of expertise, experience, and diversity to promote complete and adequate review of research activities commonly conducted by the institution. Each UI IRB includes at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

IRB-03 includes two or more VA representatives as voting members and at least one of the VA representatives has scientific expertise. VA representatives serve as full members of the IRB and review non-VA research matters coming before the IRB. VA Research and Development administration officials are prohibited from serving as voting members of IRB-03 including, but not limited to the Associate Chief of Staff for Research and Development (ACOS) and the Administrative Officer for Research and Development (AO/R&D).

Membership rosters are maintained by the IRB Administrator and reviewed on an ongoing basis by the UI IRB Chairs and HSO Director to assure that expertise and experience is representative of the research under review including expertise with vulnerable populations including, but not limited to those with mental disabilities or impaired decision-making capacity. When a deficiency is identified, the IRB Administrator conducts directed recruitment of individuals with the needed expertise or experience. Recommendations may come from the UI IRB Chairs, other UI IRB members, or academic unit Deans, Directors, or Officers. Recommendations are reviewed with the Institutional Official who makes the final offer of membership.

C. Responsibilities

Responsibilities of members include reviewing human subject application materials in advance of meetings and being prepared to discuss issues related to human subjects protections, serving as primary reviewer when requested by the Chair, and having an understanding of the specific requirements of human subjects regulations. In addition to application materials distributed to all members, the Primary reviewer responsibilities include reviewing materials as described in section X.D.1.
UI IRB members serve at the discretion of the Associate Vice President for Research: Regulatory Affairs. Members who do not adequately fulfill their responsibilities as judged by the UI IRB Chair may be asked to step down from UI IRB membership by the Associate Vice President for Research: Regulatory Affairs.

D. Compensation of UI IRB Members

The OVPR provides no compensation to members of the UI IRBs with the exception of parking vouchers provided to community members to cover the cost of parking during meetings of the UI IRB. Individual UI Colleges are expected to provide members in proportion to the amount and type of research submitted by their faculty, staff, and students. The UI colleges may independently choose to provide support at either their departments and/or to individuals to meet this expectation. The home units of the Chairs receive compensation for their time commitment to the UI IRBs.

E. Member Liability

UI IRB members function as employees and agents of the UI. As such, when acting in accordance with the UI IRB Standard Operating Procedures, their actions are covered by the UI general liability coverage.

F. Alternate IRB Members

Alternate IRB members, if appointed, are designated for a specific member or members. Alternate IRB members are selected to assure comparable qualifications to the primary member based on discipline, expertise, and/or education and professional experience as appropriate. If both the alternate IRB member and the primary IRB member attend a meeting, only one of these two may vote. In these cases, the minutes reflect who is in attendance as a voting IRB member.

G. Non-Voting Members

The Associate Vice President for Research: Regulatory Affairs may, at his/her discretion, recruit non-voting (ex officio) members from among the academic or administrative staff of the UI whose presence at the meetings of the UI IRBs would aid the IRBs in conducting their duties. These members may take part in all meetings of the IRBs, participate in the discussions, and make recommendations to influence decisions, but they may not vote on the decisions. Non-voting members are not included in determining or establishing a quorum (see Quorum in Section XIX) at the meetings. UI IRB meeting minutes reflect the presence of non-voting members.

H. Consultants/Ad hoc Reviewers

At its discretion, the UI IRBs may invite scientists or non-scientists from within or outside the UI, who have special expertise, to function as consultants and ad hoc reviewers of a project application. These individuals have access to all documents submitted to the UI IRB relevant to the specific project under review, may participate in the deliberations and make recommendations on the project, but may not vote.
I. Conflict of Interest

No UI IRB member, consultant, or ad hoc reviewer may participate in the IRB review of any project in which the member has a conflict of interest (see Conflict of Interest in Section XIX) or any other relationship that may be inappropriate for objective review, except to provide information requested by the board. The individual can be a member of a UI IRB; however, he/she cannot participate in the review and approval process for any project in which he/she has a conflict of interest. This conflict of interest policy includes all types of review. (i.e. review by expedite procedures, review by a convened IRB, review of unanticipated problems involving risks to participants or others, or review of noncompliance with the regulations or requirements of the IRB.) In cases where the assigned initial reviewer has a conflict of interest, that study application is re-assigned to another reviewer or taken to full board. When the investigator-member has a conflicting interest, he or she may be present at UI IRB meetings, like any investigator, only to provide information requested by the board. He or she must be absent from the meeting room during the subsequent discussion and voting phases of the review and may not vote (e.g., agree, disagree, abstain) on the study. The absent member is not counted towards a quorum when the vote on the study in question is taken. Minutes document that these requirements have been met.
VII. Management of the UI IRB Process

A. UI IRB Chairs

Each UI IRB has a Chair(s), and at the discretion of the Associate Vice President for Research: Regulatory Affairs/Institutional Official, a Vice Chair. These individuals are respected, active members of the University community who are well-informed in regulations relevant to the use of human subjects in research. The Associate Vice President for Research: Regulatory Affairs appoints the Chair(s) based on their experience in human research protections, professional discipline(s) and achievements, educational background, and their availability to commit the appropriate amount of time and effort to the UI IRB program. The term of service is at the discretion of the Associate Vice President for Research: Regulatory Affairs. The Chairs are evaluated formally on an annual basis in meetings with the Associate Vice President for Research: Regulatory Affairs. The Chairs’ activities are also monitored on an ongoing basis during regular Chairs’ meetings with the Associate Vice President for Research: Regulatory Affairs, the HSO administration and through periodic reports of UI IRB application activity.

Whenever a Chair or Vice Chair is not available to conduct UI IRB business, s/he may designate a board member to assume his/her responsibilities during the period of his/her absence. An IRB Chair designee will be a named member of the IRB roster and will undergo a period of supervision and training for a minimum of three months directly related to the designee’s specific role by the IRB Chair prior to assuming designation responsibilities.

Responsibilities of the Chairs include:

- determining the type of review for initial, continuing review, and modification applications (exempt, expedited, full board) based on regulatory criteria,
- conducting expedited reviews and approvals,
- assigning primary reviewers for and running full board meetings,
- reviewing minutes,
- reviewing specific revisions to protocols/consent documents that are required as conditions of approval,
- signing the application form certifying project approval,
- reviewing reports of unanticipated problems involving risks to subjects or others,
- suspension of research procedures,
- referral to convened IRB for consideration of termination of research procedures.

Reports of unanticipated problems involving risks to subjects or others, of instances involving serious or continuing noncompliance, or of suspension or termination of a research project are made under signature of the Chairs according to the policy in Section IX.F.2 below.

In addition, the Chairs serve as resources for investigators and UI IRB members regarding issues related to University and federal policies.

B. Administrative Support - The Human Subjects Office
The UI Human Subjects Office (HSO), a unit within the Office of the Vice President for Research and reporting to the Associate Vice President for Research: Regulatory Affairs, has been established to support the IRB process. The HSO:

1. assists the UI IRBs in preparing for and monitoring IRB meetings;
2. maintains files on all human subjects research (including copies of all correspondence between the IRB and investigators) that takes place at the UI;
3. maintains databases for tracking studies;
4. assists with preparation of meeting minutes;
5. maintains files of minutes of full board meetings;
6. screens research applications for completeness prior to initiating the IRB review process;
7. acts as a resource for investigators on general regulatory information, guidance with forms, and assistance in preparing an application for IRB review;
8. maintains the institution’s Federalwide Assurance, the IRB membership rosters, and a resume for each IRB member;
9. provides staff support to the IRBs for all written correspondence;
10. sends notices of approval, study closure (other than closure of the study by the investigator) for externally sponsored projects to the UI DSP or the CTO;
11. generates and sends reminder notices to investigators of upcoming continuing reviews;
12. maintains information on federal regulations relating to human subjects research;
13. provides education regarding the IRB process and regulations to the University community;
14. maintains a human subjects research monitoring program;
15. coordinates submission of application materials required by WIRB;
16. checks the short form consent process for compliance with regulatory requirements;
17. maintains all correspondence between the IRB and the R&D Committee.

C. Resources

The UI provides adequate personnel, facilities and equipment to support the operation of the UI IRBs and HSO in performing the functions described in this document.
VIII. UI IRB Organization

A. IRB-01

All research projects involving human subjects which do not meet the criteria for review by WIRB (see V.D) are reviewed by IRB-01 (identified as IRB-01-NR by DHHS, indicating no restriction) when any of the following conditions apply:

1. The study is conducted in or involves patients or staff of UI Health Care.

2. The PI is from the College of Dentistry, Medicine, Pharmacy, Public Health, or the Department of Communication Sciences and Disorders in the College of Liberal Arts.

3. The PI is from the College of Nursing and the project involves physical or physiological interventions exceeding minimal risk (see Minimal Risk in Section XIX).

4. The study involves the use or creation of Protected Health Information (PHI) as defined by the federal Health Insurance Portability and Accountability Act (HIPAA).

5. The study is not a VA study (see definition in XIX.)

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.

B. IRB-02

Any research project involving human subjects, regardless of its source of funding, is reviewed by IRB-02 (identified as IRB-02-XM by DHHS, indicating no membership expertise in the medical sciences) when any of the following conditions apply.

1. The PI is from the College of Liberal Arts (except for those from the Department of Communication Sciences and Disorders), Education, Business Administration, Law, Engineering, or Nursing.

2. The PI is from the College of Nursing and the project involves physical or physiological interventions that do not exceed minimal risk.

IRB-02 does not review VA Studies or FDA-regulated research.

Policy issues and reports of noncompliance are reviewed during regular full board meetings.
C. IRB-03

IRB-03 provides IRB review for the Iowa City VAMC pursuant to the agreement referenced in Section V.B. When this board is convened at least one of the VA members must be present during any review and a licensed physician must be a voting member for research reviewed involving an FDA-regulated article.

C. Referral Between UI IRBs

The UI IRB Chair may, at his/her discretion, refer the review of a research project to the other UI IRB if he/she determines a) there is a conflict of interest among the investigator(s) and board member(s), or b) more appropriate expertise lies in the other board. However, research projects involving the VAMC, FDA-regulated research or that include physical or physiologic interventions involving more than minimal risk may not be referred to IRB-02, and projects involving VAMC must be reviewed by IRB-03.
IX. Functions of the UI IRB

A. Scope of Review

After initial review of applications by the HSO for completeness (Section X.B), UI IRB convened or expedited review of applications is conducted to:

1. consider the scientific or scholarly design to determine that the use of human subjects is relevant and appropriate to answer the questions being asked;
2. consider ethical issues with regard to the study’s design and conduct;
3. determine that the proposed recruitment and enrollment plan, including the inclusion and exclusion criteria used afford selection of subjects from the population that is equitable given the potential benefits and risks of the research;
4. identify the risks associated with the research, as distinguished from the risks of therapies the subjects would receive even if not participating in research;
5. identify level of risk;
6. determine that the risks are minimized to the extent possible by using procedures consistent with sound research design and which do not unnecessarily expose subjects to risks, and when appropriate, by using procedures which are already performed on subjects for non-research diagnostic or treatment purposes;
7. identify the probable benefits to be derived from the research;
8. determine that the risks are reasonable in relation to the anticipated benefits to subjects, if any, and the importance of the knowledge to be gained, considering only those risks and benefits that may result from the research;
9. assure that potential subjects are provided with an accurate and fair description of the risks or discomforts and the anticipated benefits;
10. require informed consent be sought and documented from each prospective subject or their legally authorized representative, or determine to waive these requirements according to appropriate regulatory requirements;
11. determine intervals of periodic review;
12. where appropriate, determine that adequate plans are in place for data and safety monitoring;
13. determine the adequacy of the provisions to protect the privacy of subjects and to maintain the confidentiality of the data;
14. where the subjects are likely to be members of a vulnerable population, determine that appropriate additional safeguards are in place to protect the rights and welfare of these subjects;
15. For VA Studies,
   a. determine whether the medical record for a subject has to be flagged to protect the subject’s safety by indicating participation in the study and the source of more information on the study. IRB-03 may determine that a record should not be flagged if
      1. Participation in the study involves only one encounter
      2. Participation in the study involves the use of a questionnaire or previously collected biological specimens.
      3. Identification as a subject in a particular study (if the study does not involve greater than minimal risk) would place the subject at greater than minimal risk.
   b. permit non-veterans to be entered into research only when there are insufficient veterans available to complete the study.
c. prohibit paying subjects for participation when the research is integrated with their medical care and when it makes no special demands on the subject beyond those of usual medical care.

d. allows payment of subjects only when one of the following is true:
   1. The research is not directly intended to enhance the diagnosis or treatment of the medical condition for which the subject is being treated, and when the standard of practice at The University of Iowa is to pay subjects in this situation.
   2. The research is a multi-institutional study and subjects at collaborating non-VA institutions are paid for the same participation in the same study at the same rate proposed.
   3. In the opinion of the IRB payment of subjects would be appropriate in other comparable situations.
   4. The subject will incur new transportation expenses that would not have been incurred in the normal course of receiving treatment and will not be reimbursed by another mechanism.

B. Special Consideration for Projects Involving Vulnerable Populations

The UI IRB considers certain groups of human subjects to be particularly vulnerable in a research setting. The UI IRB considers additional protections for research activities involving pregnant women, human fetuses and neonates, prisoners, children, and persons with impaired decision-making capacity. The UI IRB may also consider additional protections for those who are educationally or economically disadvantaged, students, or other groups that require special consideration. In reviewing these research projects, the UI IRB ascertains that the inclusion of the vulnerable population is adequately justified and that safeguards are implemented to minimize risks unique to each population.

Requests for approval of federally funded research that exposes children to risks that do not meet one of the above criteria must be submitted to the United States Secretary of Health and Human Services for review and approval. Determinations of approval by the UI IRB of federally funded research involving prisoners are reported to the DHHS Office of Human Research Protections (OHRP).

Requests for approval for a clinical investigation under FDA oversight that exposes children to risks that do not meet one of the above criteria must be submitted to the Commissioner of Food and Drugs for review and approval.

The UI IRB must have present at its meeting a designated prisoner advocate in order to review projects involving the use of prisoners in research. The Chair or his/her IRB member designee may approve new studies limited to retrospective review of prisoners’ records and minor modifications using expedited review procedures after review and comment by the prisoner advocate.

For VA studies, in order for IRB-03 to approve research involving persons with impaired decision-making capacity, IRB-03 finds and documents in the minutes or IRB records the following:
Only incompetent persons or persons with impaired decision making capacity are suitable as participants.

Competent persons are not suitable for the proposed research.

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 participants.

Incompetent persons or persons with impaired decision-making capacity are not being proposed as participants simply because they are readily available.

The research does not impose a risk of injury, unless that research is intended to benefit that participant and the probability of benefit is greater than the probability of harm.

Procedures have been devised to ensure that legally authorized representatives are well informed regarding their roles and obligations to protect incompetent participants or persons with impaired decision making capacity.

Legally authorized representatives will be told that their obligation is to try to determine what the prospective participant would do if competent, or if the prospective participant's wishes cannot be determined, what they think is in the incompetent person's best interest.

For VA studies, in order for IRB-03 to approve research involving adults unable to consent:

- Consent by a legally authorized representative must 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.
- The determination that a participant is incompetent or has an impaired decision-making capacity has to be made by a legal determination or a determination by the practitioner, in consultation with the chief of service, after appropriate medical evaluation indicates that the prospective subject lacks decision-making capacity and is unlikely to regain it within a reasonable period of time.
- Consultation with a psychiatrist or licensed psychologist has to be obtained if the determination that the prospective subject lacks decision-making capacity is based on a diagnosis of mental illness.

The following restrictions also apply to VA studies (IRB-03) with respect to vulnerable populations:

- Research involving fetuses cannot be approved.
- Research involving in vitro fertilization cannot be approved.
- Research involving prisoners as subjects cannot be approved unless a waiver has been granted by the Chief Research and Development Officer.
- Research involving children as subjects cannot be approved unless:
  - A waiver is granted by the Chief Research and Development Officer.
  - The study presents no greater than minimal risk.
  - The study meets all requirements of Subpart D of the DHHS or FDA regulations.
  - The Medical Center Director certifies that the facility is able to respond to pediatric emergencies.
  - If a contractor or a non-VA employee conducts the research, the individual or entity performing the research has appropriate liability insurance.
- Research involving pregnant women as subjects cannot be approved unless:
  - The research includes adequate provisions to monitor the risks to the subject and the fetus.
Adequate consideration is given to the manner in which prospective subjects are going to be selected.

Adequate provision is made to monitor the actual consent process by procedures such as:

- Overseeing the process by which individual consents are secured either by:
  - Approving enrollment of each individual.
  - Verifying, perhaps through sampling, that approved procedures for enrollment of individuals into the activity were being followed

- Monitoring the progress of the activity and intervening, as necessary, through such steps as visits to the activity site and continuing evaluation to determine if any unanticipated risks have arisen.

C. Suspension or Termination of IRB Approval

The UI IRB has the authority to suspend or terminate approval of human subjects research that is not being conducted in accordance with the UI IRB’s requirements or that has been associated with unexpected serious harm to subjects. The UI IRB also has the authority to suspend or terminate research being conducted under the oversight of WIRB. Any suspension or termination of approval includes a statement of the reasons for the IRB’s action and is reported in writing within 5 working days to the investigator, the investigator’s DEO, the Office of the Vice President for Research, and the Division of Sponsored Programs/Clinical Trials Office (when the study is externally funded). Suspension or termination of a WIRB-approved project is reported within 5 working days to the reviewing IRB.

Suspensions implemented by an IRB chair will be reported to and reviewed by the convened IRB. The IRB may take actions, within its authority, as deemed appropriate. When suspending or terminating IRB approval on an urgent basis, the IRB (or IRB chair for suspensions):

- consider actions to protect the rights and welfare of currently enrolled participants.
- consider whether procedures for withdrawal of enrolled participants considered their rights and welfare.
- consider whether participants should be informed of the termination or suspension.
- require any adverse events or outcomes to be reported to the IRB.

Notifications are made in accordance with Section IX.F.

D. Noncompliance Investigations and Actions

Please review to the UI Investigator’s Guide Chapter 10 – Non-compliance with the Requirement of the Human Research Protection Program for information related to this issue.
E. Review of Unanticipated Problems involving Risks to Subjects or Others

1. Unanticipated problems involving risk to subjects or others are reported to the IRB by UI investigators on the Reportable Events Form (REF) as required in Section XI.C. Information on this form indicates whether or not the investigator believes the reported event is an unanticipated problem involving risks to subjects or others. The process for review of these REFs is as follows: The IRB chair compares the content of the REF with the previously approved project materials such as applications, informed consent documents, 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 (See Definition in Section XIX).

2. If the chair agrees the event meets the definition of an unanticipated problem involving risk 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.
   a. If the event represents minimal risk of harm, the Chair reviews and signs the report through the HawkIRB system.
   b. If the event represents more than minimal risk of harm to subjects enrolled under the UI study, the report is referred for full board review.

3. 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 the Reportable Events Form (REF), communications with the Principal Investigator or other relevant individuals, approved IRB application, consent documents and other documentation from the project files as appropriate, prior to the full board meeting. All IRB members are expected to review and be familiar with all materials. The convened IRB makes a determination whether the event is an unanticipated problem involving risk to subjects or others. If the determination made by the convened IRB differs from that made by the IRB chair, the determination of the convened IRB supersedes that made by the IRB chair. When a quorum of IRB members is present, and after discussion, the IRB shall vote recommended actions.

4. The IRB or IRB Chair may take any of the following actions or other actions as appropriate:
   • Modification of the protocol,
   • Modification of the consent document,
   • Providing additional information to current subjects – this is done whenever the information relates to the subject’s willingness to continue participation,
   • Providing additional information to past subjects,
   • Requiring current subjects to re-consent to participation,
   • More frequent continuing review or monitoring (this can include observation of the research or consent process),
   • Requiring additional training of the investigator,
   • Notification of investigators at other sites,
   • Suspension or termination of the research as described in Section IX. C above,
   • Obtaining additional information

5. The IRB sends written notification of actions taken to the PI. Reports to other entities are made in accordance with procedures described in Section IX.F
F. Reporting

1. Maintaining FWA and UI IRB Registration

The HSO maintains the FWA and IRB registrations for IRB-01 and IRB-02 and notifies OHRP of any changes in the FWA or IRB membership as they occur.

IRB staff maintains a list of the IRB members (IRB rosters) for each IRB that include the following information:
- The information required by 45 CFR 46.103(b)(3) and 21 CFR 56.115(a)(5).
- Whether the member is a primary member or alternate member.
- The primary members whom each alternate member could substitute.

2. IRB Determinations Requiring Reporting

The following policy outlines 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:
- suspensions or termination of IRB-approval of research (see Definitions in Chapter XIX),
- serious or continuing non-compliance (see Definitions in Chapter XIX), or
- unanticipated problems involving risks to subjects or others (see Definitions in Chapter XIX)

Following an IRB determination of any of the above, 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:
- 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),
- The name of the institution conducting the research,
- The title of the research project and/or grant proposal in which the problem occurred,
- The name of the principal investigator on the protocol,
- The IRB number assigned to the research project and the number of any applicable federal award(s) such as grants, contracts, or cooperative agreements,
- A short summary of the project,
- A detailed description of the problem including the findings of the organization and the reasons for the IRB’s decision,
- 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.),
- 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:**
- The UI Institutional Official (Office of the Vice President for Research),
- Principal Investigator,
- Division of Sponsored Programs (DSP) or Clinical Trials Office (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.
- Departmental Executive Officer (DEO) of the principal investigator,
- Dean of the College of the principal investigator,
- Research Integrity Officer (RIO) if the event involved research misconduct.

**Federal Agencies:**
- OHRP, if the study is subject to DHHS regulations or subject to a DHHS federalwide assurance,
- FDA, if the study is subject to FDA regulations (21 CFR 50 and 56)
- 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.
- 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:
- Office of Research and Development
- Regional VA Office of Research Oversight
- VA Privacy Officer, when the report involves unauthorized use, loss, or disclosure of individually identifiable private information
- 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.

For studies reviewed by WIRB, unanticipated problems involving risks to subjects or others are reported directly to WIRB and reporting is the responsibility of WIRB.
X. Operations of the UI IRBs

A. Scheduling of Meetings

IRB-01 is scheduled to meet once or twice each week. A meeting is held each week with a primary purpose of reviewing New Project applications and modifications requiring full board review. In addition, on an every-other-week basis, an additional meeting is held for the primary purpose of conducting continuing reviews. Although each type of meeting has a designated primary focus, any issue requiring full board review may be brought to any of the weekly meetings. In addition, IRB-01 Executive Committee full board meetings are held on an as-needed basis throughout the year. IRB-02 is scheduled to meet the second and fourth week of the month. IRB-03 meetings are scheduled once per month.

HSO staff, when assigning protocols to full board IRB meetings makes an initial assessment of the member expertise in relation to the particular protocols requiring review. For protocols involving vulnerable populations or requiring other expertise, HSO staff schedules these protocols to meetings with IRB members having knowledge about or experience in working with vulnerable populations. The IRB chair, or their designee, when assigning primary reviewers to protocols, also assesses the expertise of the IRB membership and can take actions as indicated in Section X.D.1 if s/he determines additional expertise is required. If a Chair designee assigns primary reviewers to protocols, the IRB Chair will grant final approval of all primary reviewer assignments.

Individual meetings of either board may be cancelled by the Chair due to a) insufficient 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.

B. Submission of Applications

All applications for review are submitted electronically via the UI electronic application and database system, HawkIRB, using smart-form technology. Applications are initially screened in the HSO for completeness before assignment to the appropriate UI IRB. A complete submission for IRB review includes the following items as applicable:

1. HawkIRB application form,
2. written protocol (including the DHHS-approved protocol or sponsor protocol),
3. reports of prior investigations that provide relevant information to this review,
4. proposed Informed Consent Document(s) or other consenting materials,
5. sample Informed Consent Document(s) (for example the DHHS or other sponsor sample consent if available),
6. recruitment materials (including direct advertising materials),
7. survey instruments,
8. grant application,
9. investigator’s brochure,
10. other materials specific to the proposed study (e.g., sponsor correspondence with a regulatory agency such as the FDA regarding test item risk, etc.).
If the application is incomplete or otherwise not fully prepared for review, it is returned to the investigator or a request is made for necessary changes or to provide additional information. HSO staff contacts the investigator or members of the research team via HawkIRB requesting clarification of protocol issues or revisions in the application and/or associated document(s) prior to referral to the IRBs.

Once a complete packet of information has been received, it is assigned a UI IRB ID number. This unique number remains with the study and is never reassigned to a different study.

C. Determination of Type of Review

The Chair or his/her IRB member designee reviews the entire application and makes a determination as to whether the project constitutes human subjects research and, if so, the type of review (full board review, expedited review, or exempt). All applications are assigned to full board review unless (1) they meet the criteria listed in Section X.E or (2) they meet the criteria listed in Section IV.C. All projects involving the use of investigational drugs, devices, or biologics for which an IND/IDE is required receive full board review.

D. Full Board Review Process

1. Primary Reviewer Assignment

The Chair, or their designee, assigns primary reviewers in advance of a full board meeting. If a Chair designee assigns primary reviewers, the Chair will provide final approval of the Primary Reviewer assignments to any given IRB agenda. The Chair may, at his/her discretion, serve as the Primary Reviewer. In selecting the Primary Reviewer, consideration is given to the individual’s knowledge of the subject area embodied in the proposal. If, in the opinion of the IRB Chair, the IRB membership for a scheduled meeting does not include someone with the relevant scientific or scholarly expertise to conduct an in-depth review of a particular protocol, the Chair may take any of the following actions: 1) re-assign the particular protocol to another meeting where an IRB member with appropriate expertise will be in attendance and can act as the primary reviewer, 2) invite another member of the IRB with appropriate expertise (not otherwise scheduled to that meeting) to attend the meeting as primary reviewer, or 3) invite a consultant with the appropriate expertise to attend the meeting as the primary reviewer. If the IRB chair chooses to invite a consultant to be the primary reviewer, the consultant would act under the procedures for consultants as described in Section VI. H.

For initial, continuing review and modification reviews, the primary reviewer reviews the application, the proposed Informed Consent Document(s) and Assent Documents, sample Informed Consent Documents (for example from DHHS or other sponsor when available), DHHS-approved protocol (if one exists), recruitment materials (including direct advertising materials), and if applicable, the grant application, study protocol, and investigator’s brochure. In addition, for continuing review applications, the primary reviewer reviews the complete project application, which includes all materials previously reviewed by the UI IRB under expedited or full board review, and reports of unanticipated problems involving risks to subjects or others.
The Primary Reviewer may contact the investigator in advance of or during the board meeting for additional information or clarification. The primary reviewer leads the discussion of the application under review. The primary reviewer may not have a conflict of interest (see Conflict of Interest in Section XIX) regarding the project under review and is expected to notify the Chair of any conflict.

Primary Reviewers are provided a worksheet to document no conflict of interest and to ensure that all criteria for approval of research have been fulfilled.

2. Use of Consultants

At the time of preliminary review of a project application, the UI IRB Chair or Primary Reviewer may determine that the study requires further review by a consultant with expertise outside of the current UI IRB membership. This determination may 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.

Upon identifying the need for a consultant review, the Chair and/or Primary Reviewer in consultation with the Chair will identify a consultant based on the particular issues to be addressed. The Chair will determine that the consultant does not have a conflict of interest based on the definition provided in Section XIX. For issues requiring only simple clarification, a written set of questions will be developed for submission to the consultant or the completion of a primary reviewer checklist may be required of the consultant. A signed confidentiality agreement will be required from the consultant prior to completing the review process. The consultant’s written response to these questions will be provided to the full UI IRB for review at the time of the convened meeting. For issues requiring more than simple clarification, the consultant may also be asked to review the project application in its entirety and complete a primary reviewer checklist and be invited to attend the full board meeting during the review of that particular study. The consultant will leave prior to the final vote by the UI IRB. Documentation of the discussion with the consultant will be included in the meeting minutes.

3. Notification of Meetings and Distribution of Materials

The agenda and application materials are distributed to all UI IRB members scheduled to attend a meeting, the UI general counsel (ex-officio member of IRB-01 and IRB-02), and identified consultants, if applicable sufficiently in advance of the meeting date to allow time for review, generally a week in advance. The agenda indicates the date, time, and place of the meeting. For full board meetings, all attending UI IRB members, the UI general counsel, and identified consultants, if applicable, receive a printed copy of the application form, the application form updated with changes (for modification reviews), approved Informed Consent Document(s) and Assent Document(s) and newly proposed consent document(s) and Assent document(s), recruitment materials (including direct advertising materials), other proposed correspondence with subjects (if applicable), progress or status reports for continuing reviews, and other materials as determined by the Chair. The Primary Reviewer receives materials as described in X.D.1. In addition, all UI IRB members and the UI general counsel may review the entire application and associated materials online through HawkIRB at any time. All IRB members scheduled to attend a meeting are expected to review all
materials in sufficient depth to discuss the information at the convened meeting.

4. Urgent Review of Applications

Urgent review procedures may be invoked only under unusual circumstances. This does not include urgency that is a result of negligence or delay on the part of the investigator or his/her staff to submit human subjects applications in a timely fashion.

On occasion, however, an investigator is faced with an immediate deadline beyond his or her control. If the Chair permits urgent review of a protocol, the materials are distributed as soon as possible to UI IRB members to allow sufficient time for review prior to the meeting. The investigator may be required to attend the meeting to answer any questions that arise.

5. Meeting Procedures

The UI IRB meeting is called to order when a quorum of members is in attendance. A quorum consists of more than half of the primary members and must include at least one non-scientist. The meeting ends or is suspended whenever a quorum of members is no longer present. If a prisoner advocate is present, s/he counts as a primary member and the number of members required for a quorum may change. The quorum is monitored throughout the meeting by a Sr. HSO Full Board staff member or the UI IRB Chair.

At the discretion of the Chair and/or primary reviewer, the investigator(s) may be invited to attend the meeting for the purpose of additional clarification or discussion. The investigator(s) is (are) required to leave the meeting for subsequent discussion and voting.

At the discretion of the Chair, voting may be by written ballot or a show of hands. The official meeting minutes record a motion from the board and the number of votes which agree or disagree with the motion as well as the number abstaining. In the event a member of the UI IRB elects to cast no vote, the minutes record such and identify the individual who did not vote. A vote of approval by a member means that member has determined that risks to subjects are minimized; risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result; selection of subjects is equitable, informed consent will be sought from each subject or their legally authorized representative (or waived in accordance with the criteria listed in XIII.B); informed consent will be appropriately documented (or waived in accordance with the criteria listed in XIII.C); when appropriate, there are adequate provisions to protect the privacy of subjects and maintain the confidentiality of data; and when some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect their rights and welfare.

A majority vote of the members present at the meeting is required for approval. Investigators are notified in writing of the decision of the UI IRB and any changes required.

6. Meeting Minutes

Minutes are generated that record the following information:
- which IRB (IRB-01, IRB-02, or IRB-03) reviewed the project;

- attendance at each meeting including those members or alternate members who participated through videoconference or teleconference, and documentation that those members not physically present received all pertinent materials prior to the meeting and were able to participate in all discussions.

- indication by name when members absent themselves from the meeting due to a conflicting interest on individual agenda items and the reason for absenting themselves, or indication by name that a member was not present for discussion and voting on individual agenda items;

- the vote on actions taken by the IRB including the number, for, against and abstaining;

- Separate deliberations for each action, where applicable;

- actions taken by the board including determinations as required by federal regulations and protocol-specific findings justifying those determinations for waiver or alteration of the consent process, research involving pregnant women, human fetuses, and neonates, research involving prisoners, and research involving children;

- justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample informed consent document;

- the basis for requiring changes in or disapproving research;

- the length of time of an approval;

- a written summary of the discussion of controverted issues and their resolution;

- specific comments relevant to inclusion of certain populations;

- whenever a significant risk/non-significant risk determination is made, the rationale for significant risk/non-significant risk device determinations.

- 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.

- For IRB-03, if the convened IRB approves research contingent on specific minor conditions and the IRB Chair, or another IRB member designated by the Chair, approves the modifications, the approval by the Chair or designee is documented in the minutes of the first IRB meeting that is convened after the date of approval. IRB-03 minutes are available for review within three weeks of the meeting date. After approval by the IRB, the minutes cannot be altered by anyone including a higher authority.
7. Tabled Studies

When a study is tabled at a meeting (i.e. the majority vote agrees with a motion to table), the study, after the investigators have addressed the IRB requirements, must be returned to a full board IRB meeting for review. The Full Board Meeting Procedures described above are followed for these protocols. Additional materials distributed to members for tabled studies include the minutes from the previous meeting and any response to those minutes from the investigators.

At least one member of the IRB and one member of the HSO staff who attended the previous review will be in attendance at the rescheduled meeting to answer questions. Any IRB member who attended the initial review of the tabled study may also attend the meeting at which the tabled study is scheduled for re-review. When more than one member attends from the same rostered membership line, one of the members is designated as the voting member by the IRB Chair, and the other is a non-voting member. When possible, the primary reviewer from the previous review will be assigned as the primary reviewer for the study at the re-scheduled date and the same IRB chair will chair the meeting. For any study that was tabled in IRB-03, every attempt will be made to schedule the re-review of the tabled item at the next convened IRB-03 meeting. If there is not a returning member that attended the initial review, one will be asked to attend the meeting for review of the tabled item only to fulfill this requirement.
E. Expedited Review

The expedited review process may be used in accordance with federal regulations for applications that qualify for expedited or exempt review. UI IRB Chairs or their IRB member designees are responsible for these reviews. The criteria for approval using the expedited procedure are the same as those for review by a convened IRB. Approved studies are subject to at least annual review and this information is communicated to the principal investigator in the approval letter.

The HawkIRB system requires that the IRB Chair or his/her IRB member designee conducting an expedited review either concur with the investigator’s protocol-specific findings justifying determinations required by the regulations or document such findings themselves prior to approval. These include protocol-specific findings for:

- Waiver or alteration of the consent process
- Research involving pregnant women, human fetuses and neonates
- Research involving prisoners
- Research involving children

The Chair or his/her IRB member designee may approve projects as submitted or require modifications prior to approval. They are not empowered to disapprove projects reviewed through the expedited process; in such cases, the application must be submitted for full board review along with the comments and recommendations of the Chair or his/her IRB member designee. In cases where the full board concurs with the recommendation, the investigator may rebut the decision as provided below (Section X.G).

A listing of all protocols that have been reviewed and approved through the expedited process or determined to be exempt is e-mailed to all UI IRB members on a monthly basis. These reports include initial reviews, continuing reviews and reviews of modifications to previously approved research.

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:

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 the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml/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 routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncanulled saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by 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, electroencelphalography, 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.

The expedited review procedure for initial review of projects is not 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 reasonable and appropriate protections are implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal. The expedited review procedure is not used for classified research. With the exception of the studies described in Section IX.B, no studies involving prisoners may be reviewed under expedited procedures regardless of whether or not they meet the criteria described above.
Even when the above criteria are met, the Chair of the UI IRB or his/her IRB member designee retains the right to require full board review when warranted by the nature of the research where the Chair or his/her IRB member designee has concerns with regard to subject safety or welfare.

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 the definition of minor modification in Section XIX.

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

- 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. With the exception of the studies described in Section IX.B, no studies involving prisoners may be reviewed under expedited procedures regardless of whether or not they meet the criteria described above.
The IRB chair or his/her IRB member designee is responsible to determine that:

- Research undergoing initial or continuing review using the expedited procedure meet applicability criteria and represents one or more approvable categories of research.
- Modifications to previously approved research reviewed using the expedited procedures are minor.

Even when the above criteria are met, the Chair of the UI IRB or his/her IRB member designee retains the right to require full board review when warranted by the nature of the research where the Chair or his/her IRB member designee has concerns with regard to subject safety or welfare.

**F. Revisions Prior to Final Approval**

Revisions to human subjects applications may be required. Correspondence is sent to the investigator detailing requests for revisions, clarification, or additional information as well as information regarding continuing review. The investigator has a designated time period, not to exceed 60 days, in which to respond to the revisions requested. If the investigator does not respond in the designated time period, the application may be withdrawn and returned. If the investigator wishes to conduct a study that has been withdrawn, he/she must submit a new application, incorporating comments from the prior UI IRB review.

When specific changes are requested by the convened IRB in the protocol and/or consent document(s) (i.e. changes requiring no more than simple concurrence), these are reviewed for compliance by the Chair before final approval is given. In instances where extensive or substantive clarifications or modifications are requested during a full board review, the revised documents are returned to the full board for its review and approval. The application receives final approval when all required changes have been submitted and approved.

**G. Final Approval**

Upon receipt of final approval, HawkIRB automatically stamps approved Informed Consent Document(s) and other materials (e.g., letters to subjects, ads) with the UI IRB ID number, the date of approval, and the date of expiration. The system notifies the PI and designated members of the research team of the approval and allows access to currently approved documents. In addition, the investigator may access an electronic memo in HawkIRB indicating type of review, date of next continuing review, and a summary of investigator responsibilities. The 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.

**H. Rebuttal or Appeal of UI IRB Decisions**

Investigators may appeal the UI IRB requirement for specific changes in the protocol and/or consent document(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 UI IRB decides to require specific changes or to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision. An investigator may appeal any of the requested changes or the disapproval. Such appeals are submitted in writing via HawkIRB as a response to the meeting minutes. Such appeals must be reviewed at a full board meeting. If the appeal requires discussion or explanation beyond what can be 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 leaves prior to UI IRB discussion and vote on the issues.

In the case of a decision by the UI IRB to disapprove, suspend, or terminate a project, the decision may not be reversed by other parties as stated in Section IV.D.

I. Length of Approval

Except for studies determined to be exempt from IRB oversight (Section IV.C), all human subjects studies are subject to continuing review based on the level of risk as assessed by the board. This review takes place at a minimum annually, and may require more frequent review or reports as determined by the UI IRB. For projects receiving full board review, the length of approval is calculated from the date of the convened meeting at which the IRBs approve the protocol or approve the research with modifications. When a primary reviewer has been assigned, that reviewer is asked to provide a recommendation for the length of approval, not to be longer than annually. The appropriate length of approval is considered as a part of the full board discussion. Projects requiring review more frequently than annually may include:

1. Experimental therapies in which the clear potential for significant adverse experiences have been identified at the time of review;

2. Non-therapeutic projects based on risk information provided at the time of initial review;

3. 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;

4. Projects in which local or outside adverse experience reports create new concerns regarding the need for closer project scrutiny; or

5. Projects where the UI IRB has concerns with regard to previous or potential serious or continuing noncompliance.

In such cases, approvals may be granted for time periods less than one year, or a limited number of subjects over a period not to exceed one year, or additional monitoring may be required.

For projects approved via the expedited process, the Chair or his/her IRB member designee determines the length of approval, not to exceed one year. Investigators are notified in writing as to
when their projects are due for continuing review.
XI. Monitoring Approved Projects

A. Continuing Review

Except for studies determined to be exempt from IRB oversight (Section IV.C), all human subjects studies are subject to continuing review based on the level of risk as assessed by the board. The continuing review for these studies 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.

When a research project is due for continuing review, HawkIRB automatically e-mails the PI and specified members of the research team notifying them of the upcoming final submission date for review. The first e-mail is sent 30 days prior to the last day an application may be submitted to the HSO to allow time to review prior to expiration. Additional e-mails are sent at 14, 7 days and 1 day prior to this final submission date. On the final submission date, if no continuing review application has been received, notification is sent to the PI and all research team members indicating that UI 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.

A final notice is sent one day prior to the expiration date indicating all research activity must stop at the end of that day. This notice further indicates that the PI has 10 working days in which to submit the continuing review. If the form is not received in 10 days, the project is closed by the UI IRB. The final notice requires the investigator to submit immediately to the IRB Chair a list of research subjects for whom stopping research procedures would cause harm. Continuation of research interventions or interactions in already enrolled participants is allowed only when the IRB or IRB Chair determines that it is in the best interest of individual subjects to do so. For VA studies, this determination is made only in consultation with the VA Chief of Staff. The IRB notifies the sponsor of any VA studies for which the IRB does not grant continuing review.

Applications for continuing review and associated materials are submitted electronically via HawkIRB. The HSO staff conducts a preliminary review of applications for completeness. HSO staff assigns applications requiring full board review to the next available continuing review full board agenda (IRB-01) or the next regular full board meeting (IRB-02 and IRB-03.) Applications that appear to meet criteria for expedited review are forwarded to the Chair or his/her IRB member designee for review and determination as to full board review or expedited review. Research approved previously by expedited review is considered eligible for expedited review at the time of its regular continuing review, if, during the course of the study, the risks of the study have not increased. Projects that were initially reviewed by the full board continue to receive full board review unless the Chair or his/her IRB member designee determines that the study meets the specific criteria for expedited review as outlined in Section X.E.

All IRB members scheduled for a meeting receive the continuing review application form, the application form updated with changes, approved Informed Consent Document(s) and Assent Document(s) and newly proposed consent document(s) and Assent document(s), recruitment
materials (if there are changes), the number of participants accrued, other proposed correspondence with subjects (if applicable), a status report on the progress of the research and other materials as determined by the Chair. If the continuing review application is under IRB-03, this continuing review application requests the following to meet VA reporting requirements:

- the gender and minority status of those entered into the protocol
- the number of participants considered as members of specific vulnerable populations (as applicable)

In addition to these materials, all members receive a complete approved copy of materials plus laptops are available to all members to review the complete electronic project application which includes all currently active modifications reviewed by the UI IRB under expedited or full board review, and reports of unanticipated problems involving risks to subjects or others during the IRB meeting. All IRB members attending the meeting must review the materials in sufficient depth to discuss the information at the convened meeting.

The IRB or expedited reviewer reviews the consent document with the continuing review application particularly to ensure that the consent document remains accurate and complete. This is done by assessing the progress of the study and any changes to the risk/benefit ratio of the overall project and requiring changes to the consent document if the IRB determines that the change will provide more accurate or complete information to the study subject.

As part of the continuing review of research, the IRB or IRB chair may determine that a project needs verification from sources other than the investigators that no material changes have occurred since the previous IRB review. Projects requiring this verification may include:

- Complex projects involving unusual levels or types of risks to subjects, or
- Projects involving vulnerable populations, or
- Projects conducted by an investigator who previously failed to comply with IRB determinations, or
- Projects where the continuing review application or reports from other sources have indicated that changes may have occurred without IRB approval.

If the IRB or expedited reviewer determines that a project requires verification from other sources, they can send a UI IRB Monitor to review the study. The Monitoring & Education Compliance Program procedures are described in Section XI.D.

For projects undergoing continue review, the IRB may approve, approve pending required actions on the part of the investigator, table, or disapprove the protocol. Investigators are notified in writing of the decision of the UI IRB and any changes required. Final approval is not granted until all required changes have been made and submitted for review and approval (see Section X.F). When final approval will likely not be given prior to the expiration date, the minutes for full board reviews note the current expiration date and note that no further research may be conducted on or after that date. Likewise, for expedited review, when approval will not be given prior to the expiration date, the reviewing Chair or his/her IRB member designee notifies the PI of the current expiration date on or after which all research activity must be discontinued pending receipt of continuing review approval.
Upon receipt of final approval, HawkIRB automatically stamps approved Informed Consent Document(s) and other materials (e.g., letters to subjects, ads) with the UI IRB ID number, the date of approval, and the date of expiration. The system notifies the PI and designated members of the research team of the approval and allows access to currently approved documents. In addition, the investigator may access an electronic memo in HawkIRB indicating type of review, date of next continuing review, and a summary of investigator responsibilities. The 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.
B. Modifications

Investigators must report planned changes in the conduct of a study and receive approval from the UI IRB prior to implementing these changes, except when necessary to eliminate apparent immediate hazards to the subject. The investigator is required to promptly notify the IRB of these instances using the modification application on HawkIRB. The convened IRB reviews these modifications to determine if the modification made to eliminate apparent immediate hazards to the subject was consistent with ensuring the subject’s continued welfare.

The approval documentation sent to investigators of exempt, expedited, and full board studies notifies them of the need for submitting any changes in their research projects to the UI IRB for review and approval. Modifications include, but are not limited to, procedural changes to a protocol, adding or removing investigators, requesting additional subjects beyond the approved number, change in funding, and changes in recruitment materials and Informed Consent Document(s). Modifications are made via HawkIRB by making changes to the originally approved electronic application or associated electronic documents. Changes are documented in the system so that reviewers can view tracked changes versions of materials. Minor modifications may be expedited.

The principal investigator may request that a modification be considered as both a modification and a submission for continuing review. In requesting this action, submission materials must include all items required at time of continuing review as well as the details of the requested modification. Such applications are processed through the Continuing Review system. In these cases, the UI IRB may consider this as appropriate and “reset” the clock for continuing review.

All IRB members scheduled for the meeting receive the approved project application with the requested modifications identified, approved Informed Consent Document(s) and Assent Document(s) and newly proposed consent document(s) and Assent document(s), recruitment materials (if there are changes), other proposed correspondence with subjects (if applicable and the materials have changed), and other materials as determined by the Chair. In addition to these materials, the primary reviewer receives and reviews any changed protocols or Investigator Brochures. The primary reviewer conducts an in-depth review of all materials. All IRB members must review the materials in sufficient depth to discuss the information at the convened meeting.

Investigators are notified via e-mail through HawkIRB of the decision of the UI IRB and any changes required. Final approval is not granted until all required changes have been made and submitted for review and approval (see Section X.F). Upon receipt of final approval, HawkIRB automatically stamps approved Informed Consent Document(s) and other materials (e.g., letters to subjects, ads) with the UI IRB ID number, the date of approval, and the date of expiration. The system notifies the PI and designated members of the research team of the approval and allows access to currently approved documents. In addition, the investigator may access an electronic memo in HawkIRB indicating type of review, date of next continuing review, and a summary of investigator responsibilities. The 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.
C. Reporting Requirements for Investigators

Investigators are required to report to the appropriate UI IRB if any of the following items 1-6 occur in a study where IRB-01, IRB-02, or IRB-03 is the IRB of record. (For WIRB studies, items 1-6 are reportable directly to WIRB.

1. An unanticipated problem involving risks to subjects or others which occurs at UI or that impacts UI subjects or conduct of the UI study.

2. A serious adverse drug event (either expected or unexpected) occurring in a UI subject.

3. A serious adverse device effect (either anticipated or unanticipated) occurring in a UI subject.

4. An unanticipated serious adverse device effect occurring in a non-UI 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. An incident of noncompliance with federal regulations or the requirements or determinations of the IRB.

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

An unanticipated problem involving risks to subjects or others (see definition in XIX) is any event or problem that:

i. was not expected given the nature of the research, the population under study and the approved procedures or protocol for conduct of the study,

ii. 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

iii. is related to the research intervention, research procedures, and/or conduct of the research study.

These problems involve risk to subjects or others (for example research staff, family members, or others not directly involved in the research). The risks may impact the rights, safety, or welfare of subjects or others (including physical, financial, legal, social, emotional or psychological well being, privacy, or confidentiality.)

Examples of unanticipated problems involving risks to subjects or others include a breach of confidentiality, a subject complaint when the complaint indicates unexpected risks or cannot be resolved by 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 (see definitions in XIX.)
Investigators must report any unanticipated problem involving risk to subjects or others using the Reportable Event Form 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 UI subjects, and any planned changes or modifications to the project as a result of the event.

Investigators must submit these reports via HawkIRB within ten working days of the event or notification to the investigator of the event. These reports are reviewed by the UI IRB Chair and/or UI IRB according to the procedures described in Section IX.E.

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 UI IRB at the time of continuing review. In addition, reports of all such problems for all projects reviewed by the Chair or full board are provided by e-mail to all IRB members as appropriate on a monthly basis. These events are also reported to other entities as described in Section IX.F.

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

If a subject is enrolled by UI investigators, the investigator must report to the UI IRB either serious adverse drug events or unexpected adverse drug events (see definitions in XIX). 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. 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 subject are reviewed by a UI 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 subject are reviewed by the UI IRB Chair and/or UI IRB according to the procedures described in Section IX.E.

All reports of serious adverse drug events occurring in a UI subject are electronically filed with the appropriate research study. These reports are also reviewed by the UI 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 are provided by e-mail to all IRB-01 board members on a monthly basis. Any serious unexpected adverse drug event in a UI subject is reported to other entities as described in Section IX.F.
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 UI 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 subject.

If a subject is enrolled by UI investigators, the investigator must report either serious adverse device effects or unanticipated adverse device effects (see definitions in XIX). 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 subject to IRB-01 using the Reportable Event Form. 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 subject are reviewed by a UI IRB Chair to verify that the effect would be considered “anticipated” based on the information previously reviewed and approved by the UI 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 subject are reviewed by the UI IRB Chair and/or UI IRB according to the procedures described in Section IX.E.

All reports of serious adverse device effects occurring in a UI subject are electronically filed with the appropriate research study. These reports are also reviewed by the UI 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 are provided by e-mail to all IRB-01 board members on a monthly basis. Any serious unexpected adverse device effect in a UI subject is reported to other entities as described in Section IX.F.

4. Unanticipated serious adverse device effects occurring in a non-UI 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 (see definitions in XIX) to all reviewing IRBs and participating investigators. Any such reports are initially received by the UI investigator who is in turn responsible for reporting this information to the UI IRB-01. 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 subject to IRB-01 using the Reportable Event Form. 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. These reports are reviewed by the UI IRB Chair and/or UI IRB according to the procedures described in Section IX.E.

All reports of unanticipated serious adverse device effects occurring in a non-UI subject are electronically filed with the appropriate research study. These reports are also reviewed by the UI 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 board 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. 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 a UI 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, or IRB-03 use the Reportable Event Form. This form includes a description of the noncompliance and description of impact on the rights, safety, or welfare of subjects or others. (Others may report noncompliance as described in Section IX.D.) Reports from investigators to the IRB must be submitted via HawkIRB within ten working days of the event or notification to the investigator of the event. These reports are reviewed by the UI IRB Chair and/or UI IRB according to the procedures described in Section IX.D. Any serious or continuing noncompliance is reported to other entities as described in Section IX.F.
D. Other Monitoring Activities

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) IRB Education and Compliance Specialists

The Compliance Specialists select studies on a monthly basis from a database of open projects that have had at least one continuing review by the IRB. Priority for selection is given to studies:

- Involving unusual levels or types of risks to subjects
- Involving vulnerable populations
- Conducted by an investigator who previously failed to comply with IRB determinations
- Where a UI Investigator is the holder of the IND or IDE
- With a Principal Investigator who is new to the University of Iowa or who has not had monitoring of any research project(s)

b) An IRB Chair or Institutional Review Board

An IRB Chair or Institutional Review Board may request monitoring for projects in which HawkIRB submissions indicate that changes without IRB approval may have occurred. Monitoring may also be conducted to address subject complaints or concerns from other sources.

Notice of selection for monitoring is sent to the Principal Investigator and all Contact Persons on the research team via e-mail. The monitoring visit will be scheduled within approximately one month unless other arrangements are requested by the Principal Investigator. The Compliance Specialist
works with the Principal Investigator to select a meeting date and time. Monitoring visits are conducted in an office or conference room as arranged by the Principal Investigator or a research team member. This meeting space must be large enough to accommodate the number of people expected to attend the meeting. A computer or computer/projector combination must be available in the meeting space.

The Compliance Specialist meets with the Principal Investigator and research team members to conduct a two-part review process. The first part is an interview that will last approximately two hours. The Principal Investigator is required to attend this interview and may invite members of the research team to attend. The Principal Investigator is strongly encouraged to invite the person that prepares/submits HawkIRB applications and persons who conduct study procedures. The second part of the monitoring visit typically includes a review of signed Consent Documents or documentation of consent for enrolled subjects. This part may also include a tour of the research lab, and a review of sample storage, research records, and subject files.

The purpose of the monitoring visit is two-fold: 1) To review study oversight and procedures to ensure adherence with IRB policies and federal regulation, and 2) To provide education to Principal Investigators and research team members.

During the monitoring process the following will be reviewed and discussed:
- Roles and responsibilities of the Principal Investigator and members of the research team
- Staff training and communication procedures
- Recruitment procedures
- Screening procedures and the collection of screening data
- Consent process, documentation of consent, and tracking of optional agreements
- Study procedures and expected study end
- Current enrollment and tracking
- Reportable events
- Storage of study documents, data, and specimens or samples
- Privacy and confidentiality protections
- Data analysis
- Drug/Device accountability
- Subject payment
- Questions and concerns from Principal Investigators and research team members

The Principal Investigator and members of the research team who attend the monitoring visit will receive a written report of the visit within two to four weeks. This report will consist of a table of findings from the monitoring visit and corrective actions required of the Principal Investigator and/or research team by the IRB. The report is sent by e-mail, and a response is typically required from the Principal Investigator within two weeks.

If the monitoring visit was requested by the full board or if a finding requires full-board review, the report will be sent to the Principal Investigator and research team following the full-board meeting. The timeframe for reports referred to full board is subject to the IRB meeting schedule.

A written record of these activities is attached to the HawkIRB application for the project.
If any of the findings require full board review as designated in the UI IRB Monitoring Guidelines, the report is referred to the next available Executive IRB-01 meeting or regular full board meeting (IRB-02 or IRB-03) for review. If none of the items require full board review, the final approved report is e-mailed to the PI and research team and response is required within two weeks. If the PI does not respond in this timeframe, the PI is sent a letter by e-mail indicating they must respond within 2 weeks or the report may be sent to the full board for consideration of study suspension until the issue is resolved.

Following study initiation visits, the Compliance Specialist completes a checklist and notes any issues which need to be addressed by the research team. If the PI needs to respond to an item, the checklist first is reviewed by the Chair for approval. The checklist is e-mailed to the PI with copies to any research team member who met with the Compliance Specialist and the UI IRB Chair within two weeks of the visit. The PI is then given two weeks to respond to the required action. If the PI does not respond in this timeframe, the PI is sent a letter by e-mail indicating they must respond within 2 weeks or the report may be sent to the full board for consideration of study suspension until the issue is resolved.

Directed monitoring visits may include any of the items above or other specific investigation as requested by the UI IRB Chair or UI IRB. The Compliance Specialist generates a written report within two weeks following these visits based on the information requested. The Chair determines if any findings constitute noncompliance. If so, the procedures described in IX.D are followed. If the findings do not constitute noncompliance, the Chair resolves the issues directly with the research team when the issues involve no or minimal risk to subjects or others. If the issues involve more than minimal risk to subjects or others, the report is forwarded to the next Executive IRB-01 meeting or regular full board meeting (IRB-02 or IRB-03) for review.

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. Study Closure

The PI may close a study by submitting the appropriate electronic closure form via the HawkIRB system. Submission of this form electronically closes the UI IRB-approved project. The study may also be closed by the HSO/UI IRB as described in Section XI.A. In cases of externally funded projects, DSP or CTO is notified of the study closure by either the PI or HSO/UI IRB and makes an independent determination regarding the need to notify the sponsor.
XII. **Notifications Regarding IRB Review Activity**

Members and alternates of the UI IRBs receive via e-mail, minutes of regular full board meetings and monthly reports of UI IRB business for their respective board. Reports include listings of:

1. New projects approved (full board and expedited),
2. Projects determined to be exempt,
3. Continuing reviews (full board and expedited),
4. Modifications (full board and expedited),
5. Unanticipated problems involving risks to subjects or others
6. Serious adverse drug events and/or serious adverse device effects

Minutes and determinations made by the IRB-01 Executive Committee are distributed only to members of the IRB-01 Executive Committee.

In addition, the minutes of all full board meetings are distributed via e-mail to the UI IRB’s *ex officio* member representing the UI General Counsel’s Office, and to the Institutional Official from the Office of the Vice President for Research.

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XIII. Informed Consent and Documentation of Participation

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. For VA studies, if someone other than the investigator conducts the discussion and obtains consent, the investigator must first formally delegate this responsibility to a person who is a member of the research team and who has received appropriate training to conduct this process.

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.

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.

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 make an exception to this guideline in studies 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.

Signed informed consent is required on all human subjects research that is not exempt from IRB review (Section IV.C) except as provided in this section. In addition, for VA studies the following documentation is required in a progress note placed in the subject’s medical record:

- The name of the study.
- The person obtaining the subject’s consent.
- A statement that the subject or the subject’s legally authorized representative is capable of understanding the consent process.
- A statement that the study was explained to the subject.
- A statement that the subject was given the opportunity to ask questions.
The investigator must enter a progress note in the subject’s medical record when:
- The subject is entered into the study.
- The subject’s participation is terminated

The HSO has developed Informed Consent Document templates that provide investigators with guidance in developing this information. The templates are initially composed by the HawkIRB system based on information provided in the study application. The templates then provide prompts to the investigator to add details about the study, levels of risk, and other issues as indicated.

A. Content of the Informed Consent Document

The Informed Consent Document must include all of the following that are applicable to the particular study in question:

1. Title of project.
2. The name of the PI and a study contact person (may be the PI) and their degrees.
3. A statement that the study involves research.
4. An explanation of the purpose(s) of the research.
5. The expected duration of participation.
6. A description of the procedures/what will happen during the study and identification of any procedures that are experimental.
7. A description of any reasonably foreseeable risks or discomforts.
8. A description of any benefits to subjects or others that may reasonably be expected from the research only.
9. Appropriate alternative procedures or courses of treatment, if any.
10. Extent to which confidentiality of records identifying subjects will be maintained and a statement that notes those outside the research team who may have access to identified records including regulatory authorities (e.g. DHHS and FDA).
11. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatment is available if injury occurs, and if so, what they consist of and where further information may be obtained.
12. For VA studies, the following is included in the consent and regulations pertaining to the participation of veterans including requirements for indemnification in cases of research-related injury pertains to both veterans and non-veteran subjects enrolled in VA-approved research:
a. a statement that in the event of a research-related injury the VA has to provide necessary medical treatment to a subject injured by participation.

b. a statement that except in limited circumstances, the necessary care is provided in VA medical facilities.

   Exceptions include:
   - Situations where VA facilities are not capable of furnishing economical care.
   - Situations where VA facilities are not capable of furnishing the care or services required.
   - Situations involving a non-veteran subject.
   - An explanation of the VA’s authority to provide medical treatment to subjects injured by participation in a VA research project.
   - A statement that a veteran-subject will not be required to pay for care received as a subject in a VA research project except in accordance with Title 38 United States Code (U.S.C.) 1710(f) and 1710(g) certain veterans are required to pay co-payments for medical care and services provided by the VA.

13. Contact information for questions about the research project, and research subjects’ rights, and whom to contact in the event of research-related injury.

14. A statement that participation is voluntary and that refusal to participate or discontinuing participation at any time will involve no penalty or loss of benefits to which the subject is otherwise entitled.

15. The signature and signature date for subject and/or legally authorized representative.

16. Signature and date lines for person providing verbal explanation of study and obtaining consent (where study appropriate.)

17. For VA studies, the signature and date for a witness to the subject’s or legally authorized representative’s signature and a note placed under the witness’ signature line 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 needs to serve both purposes. In addition, a statement indicating that a copy of the signed and dated consent document is given to the person signing the consent document.

Based on the study design and in consideration of the subject’s safety and welfare, as well as the relevance of the information in allowing the prospective subject to make an informed decision about participation, the UI IRB may require additional information in the Informed Consent Document including:

1. A statement that the particular treatment or procedure may involve risks to the subject which are currently unforeseeable.

2. A statement that the particular treatment or procedure may involve risks to the embryo or fetus, if the subject is or may become pregnant, which are currently unforeseeable.

3. Anticipated circumstances under which participation may be terminated by the investigator.
4. Any additional costs to the subject that may result from participation in the research.

5. Consequences of the subject’s decision to withdraw from the research.

6. Procedures for orderly termination of participation by the subject.

7. A statement that significant new findings developed during the course of a study that may relate to the subject’s willingness to continue will be provided to the subject.

8. The approximate number of subjects involved.

Staff in the HSO reviews the Informed Consent Document to determine if all basic elements of consent are contained in the document and if additional elements should be required. The primary reviewer also considers the criteria for inclusion of the additional elements of consent. Consent document(s) that are determined to be clearly inappropriate (e.g., significant deficiencies, too complex) are returned to the investigator for re-writing prior to being scheduled for UI IRB review.

The investigator receives written notice of required changes in the Informed Consent Document prior to final UI IRB approval. Final approval is not granted until all required changes have been made and submitted for review and approval (see Section X.F.)

All pages of the approved Informed Consent Document (including the VA Form 10-1086) are stamped with the IRB ID number, the date of approval, and the date of expiration. If the consent document is modified during the protocol approval period, all pages of the Informed Consent Document (including the VA Form 10-1086) are stamped with the IRB ID number, the approval date of the modification, and the date of expiration.

B. Permission of Parents/Guardians and Assent by Children

An Assent process, either verbal or written, may also be required when the study involves children. The IRB determines and documents when assent is required for all children in the research, for some of the children involved in the research or that assent is not required for any of the children in the research. If the IRB determines that assent is not a requirement for some of the children in the research, the IRB documents which children are not required to assent.

In making the determination as to whether an assent process will be required, and how assent will be obtained, the UI IRB considers the age of the subjects, their maturity, and their ability to read and comprehend a written document given their mental and physical capacities and psychological state. If the IRB determines that some or all of the children are limited such that they could not be asked about participation, or if the intervention provided in the research holds out a prospect of direct benefit that is important to the health or well-being of the prospective subject and is available only in the context of the research, the IRB may determine that assent of the child is not required. In addition, even when the IRB determines that some or all children in the proposed research are capable of assenting, the IRB may waive assent when all of the waiver criteria described under
XIII.C below are met. The IRB documents which of the above conditions are applicable when making a determination that assent is not a requirement for some or all of the children in the research.

If the IRB determines that an assent process is required for some or all of the children in the research, the IRB must determine whether or not assent should be documented. If the IRB determines that assent should be documented, the IRB also determines the process to document the assent of the child. For children in the 7-12 year old age range or when enrolling subjects over the age of 12 whose decision-making capacity may be impaired, an assent document may be used to provide information and document assent. Any approved Assent Documents are stamped with the UI IRB ID number, the date of approval, and the date of expiration.

When children are enrolled in research, the IRB also determines the appropriate provisions for soliciting the permission of each child’s parents or guardians (unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child). (See Definitions, Chapter XIX). When the IRB determines that the research is no more than minimal risk for the child, or is more than minimal risk with the prospect of direct benefit to the child, and the IRB determines that permission must be obtained from the parent(s), the IRB will make a determination whether the permission of one or both parents shall be required.

If the research does not fall into one of these categories, and the IRB determines that permission must be obtained from the parents, then the permission of both parents is required unless one parent is deceased, unknown, incompetent, or not reasonably available, or if only one parent has legal responsibility for care and custody.

In addition, for children who are wards of the state or any other agency, institution, or entity, they may only be included in research involving greater than minimal risk and no prospect of direct benefit to individual subjects (45 CFR 46.406) or 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) only if:

1. The research relates to their status as a ward, or
2. The research is conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

If one of the above criteria are met and the research is approved, the IRB requires the appointment of an advocate for each child who is a ward to act on their behalf in addition to their guardian. One individual may serve as advocate for more than one child. The advocate shall be an individual who has 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 who is not otherwise associated in any way (except in the role as advocate or member of the IRB) with the research, researchers, or guardian organization.

The IRB may waive the requirement for parental permission when the criteria described in XIII.C below are met, or if the IRB determines that parental permission is not a reasonable requirement to
protect the child due to the conditions or population under research and the research is not subject to FDA regulations and the waiver is otherwise consistent with Federal, State or local law. When this waiver is enacted by the IRB, the IRB determines an appropriate mechanism for protecting the children dependent upon the nature and purpose of the research, the risks, potential benefits, and the children’s age, maturity, status, and condition.

C. Waiver of Consent or Elements of Consent

The UI IRB may approve a consent procedure, which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent, provided the UI IRB finds the research is not FDA-regulated and documents that:

1. the research or demonstration project is to be conducted by, or subject to the approval of, state or local government officials, and is 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 payment for benefits or services under those programs; and

2. the research could not practicably be carried out without the waiver or alteration.

The UI IRB may also approve a consent procedure, which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirement to obtain informed consent, provided the UI IRB finds the research is not FDA-regulated and documents that:

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

D. Waiver of Documentation of Consent

The UI IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects, if it finds either:

1. 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. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern (not applicable to FDA-regulated research); or

2. 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 of the research context.
In cases in which the documentation requirement is waived, the UI IRB will determine whether the investigator must provide subjects with a written statement regarding the research if the UI IRB believes providing such will protect the rights or welfare of potential participants.

E. Emergency Research Consent Waiver/Exception from Consent

For research that is not subject to VA regulations, the UI IRB may consider an "Emergency Research Consent Waiver/Exception from Consent" for a class of research consisting of activities, each of which have met the following strictly limited conditions detailed under either 1 or 2 below:

1. Research subject to FDA regulations (Exception from Informed Consent)

   The IRB responsible for the review, approval, and continuing review of the clinical investigation described in this section may approve that investigation without requiring that informed consent of all research subjects be obtained if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following:

   (1) The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

   (2) Obtaining informed consent is not feasible because:

      (i) The subjects will not be able to give their informed consent as a result of their medical condition;

      (ii) The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and

      (iii) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

   (3) Participation in the research holds out the prospect of direct benefit to the subjects because:

      (i) Subjects are facing a life-threatening situation that necessitates intervention;

      (ii) Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and

      (iii) Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

   (4) The clinical investigation could not practicably be carried out without the waiver.
(5) The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.

(6) The IRB has reviewed and approved informed consent procedures and an informed consent document. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with paragraph (a)(7)(v) below.

(7) Additional protections of the rights and welfare of the subjects will be provided, including, at least:

(i) Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;

(ii) Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;

(iii) Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;

(iv) Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and

(v) If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the
clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.

The IRB determinations and documentation required by these regulations will be retained by the IRB for at least 3 years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by FDA.

Protocols involving an exception to the informed consent requirement must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under this requirement may not be submitted as amendments.

If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided above or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRB's that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.

2. Research not subject to FDA regulations (Waiver of Informed Consent)

The IRB responsible for the review, approval, and continuing review of the research has approved both the research and a waiver of informed consent and has (1) found and documented that the research is not subject to FDA regulations and (2) found and documented and reported to OHRP that the following conditions have been met relative to the research:

a. The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

b. Obtaining informed consent is not feasible because the subjects will not be able to give their informed consent as a result of their medical condition, the intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible, and there is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research.

c. Participation in the research holds out the prospect of direct benefit to the subjects because subjects are facing a life-threatening situation that necessitates intervention, appropriate animal and other preclinical studies have been conducted and the information derived from
those studies and related evidence support the potential for the intervention to provide a
direct benefit to the individual subjects, and risks associated with the investigation are
reasonable in relation to what is known about the medical condition of the potential class of
subjects, the risks and benefits of standard therapy, if any, and what is known about the risks
and benefits of the proposed intervention or activity.

d. The research could not practicably be carried out without the waiver.

e. The proposed investigational plan defines the length of the potential therapeutic window
based on scientific evidence, and the investigator has committed to attempting to contact a
legally authorized representative for each subject within that window of time and, if feasible,
to asking the legally authorized representative contacted for consent within that window
rather than proceeding without consent. The investigator will summarize efforts made to
contact legally authorized representatives and make this information available to the IRB at
the time of continuing review.

f. The IRB has reviewed and approved informed consent procedures and an informed consent
document. These procedures and the informed consent document are to be used with
subjects or their legally authorized representatives in situations where use of such procedures
and documents is feasible.

g. Additional protections of the rights and welfare of the subjects will be provided, including:

(1) consultation (including, where appropriate, consultation carried out by the IRB) with
representatives of the communities in which the research will be conducted and from
which the subjects will be drawn;

(2) prior to initiation of the research, public disclosure to the communities in which the
research will be conducted and from which the subjects will be drawn;

(3) plans for the investigation and its risks and expected benefits;

(4) public disclosure of sufficient information following completion of the research to
apprise the community and researchers of the study, including the demographic
characteristics of the research population, and its results;

(5) establishment of an independent data monitoring committee to exercise oversight of the
research, and;

(6) if obtaining informed consent is not feasible and a legally authorized representative is not
reasonably available, the investigator has committed, if feasible, to attempting to contact
within the therapeutic window the subject's family member who is not a legally
authorized representative, and asking whether he or she objects to the subject's
participation in the research. The investigator will summarize efforts made to contact
family members and make this information available to the IRB at the time of continuing
review.

In addition, the UI IRB is responsible for ensuring that procedures are in place to inform, at the
earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally
authorized representative of the subject, or if such a representative is not reasonably available, a
family member, of the subject's inclusion in the research, the details of the research and other
information contained in the Informed Consent Document. The IRB shall also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the research and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into research with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the research is to be provided to the subject's legally authorized representative or family member, if feasible.
XIV. Research Using FDA Regulated Products

A. Determination of Significant Risk (SR) vs. Nonsignificant Risk (NSR) for Non-Exempt Medical Devices

For determination of the need for an IDE, the convened UI IRB will address the applicability of FDA regulations under 21CFR812.2 and, if necessary, make a significant risk determination.

A Significant Risk (SR) device study is 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.

A Nonsignificant Risk (NSR) device investigation is one that does not meet the definition for a SR study.

The risk determination is based on the proposed use of a device in an investigation, and not on the device alone. In deciding if a study poses an SR, the UI IRB considers the nature of the harm that may result from use of the device. Studies where the potential harm to subjects could be life-threatening, could result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure is considered SR. Also, if the subject must undergo a procedure as part of the investigational study, e.g., a surgical procedure, the UI IRB considers the potential harm that could be caused by the procedure in addition to the potential harm caused by the device.

FDA has the ultimate decision in determining if a device study is SR or NSR. If an investigator or a sponsor proposes the initiation of a claimed NSR investigation to an IRB, and if the UI 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.

To help in the determination of the risk status of the device, an investigator is asked to include the sponsor’s (including the investigator on investigator-initiated studies) assessment of whether or not a device study presents a significant or nonsignificant risk. The investigator must provide the UI IRB with a description of the device, reports of prior investigations with the device, the proposed investigational plan, a description of subject selection criteria, and monitoring procedures. The investigator must inform the UI IRB whether other IRBs have reviewed the proposed study and what determination was made. The investigator must inform the UI IRB of the FDA’s assessment of the device's risk if such an assessment has been made. The UI IRB may also consult with FDA for its opinion.

The UI IRB may agree or disagree with the investigator/sponsor's initial NSR assessment. If the UI 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 UI IRB disagrees, the sponsor should
notify FDA that an SR determination has been made and the initiation of the study must be delayed until FDA approval of an IDE application has been granted.

If the UI IRB decides the device/study is significant risk, it notifies the investigator and sponsor of this decision. The UI IRB must be provided with notice that an IDE has been granted, and the IDE number must appear on the investigator’s UI IRB application prior to final full board review.

Once the SR/NSR decision has been reached and proper documentation provided, the UI IRB considers whether the study should be approved or not. Full UI IRB review is required for the initial review of all studies involving investigational devices. Studies that are determined to include NSR devices and that include no other risks that are considered more than minimal risk may be determined by the board to meet the criteria for expedited continuing review. The criteria for deciding if SR and NSR studies are approved are the same as for any other study. Minutes of UI IRB meetings document the rationale for SR/NSR and subsequent approval or disapproval decisions for the clinical investigation.

**B. Determination of Need for an IND**

Studies that involve FDA-regulated products that are submitted without a valid IND number will be reviewed with respect to determining the need for an IND, based on the investigator’s response to questions contained in the New Project application form.

If the UI IRB determines that the study is exempt from an IND and approves the study, the study may begin without submission of an IND application to FDA. If the UI IRB determines that an IND is needed, the investigator/sponsor must submit an IND application to the FDA and provide documentation of the outcome of the FDA determination to the UI IRB before the UI IRB approves the study.

The UI IRB may consider a study using a drug product that is lawfully marketed in the United States to be exempt from the requirements for obtaining an IND if all the following apply: 
(i) The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug; 
(ii) If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product; 
(iii) The investigation does not involve a route of administration or dosage level or use in a patient 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) The investigation is conducted in compliance with the requirements for institutional review and with the requirements for informed consent; and 
(v) The investigation is conducted in compliance with the requirements with regard to promotion and charging for investigational drugs in 21CFR312.7

A clinical investigation involving an in vitro diagnostic biological product that is a blood grouping serum, reagent red blood cells, or anti-human globulin is exempt from the requirements for an IND if (a) it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure and (b) it is shipped in compliance with 21CFR312.160.
A drug intended solely for tests in vitro is exempt from the requirements of an IND if it is shipped in accordance with 21CFR312.160.

A clinical investigation involving use of a placebo is exempt from the requirements of an IND if the investigation does not otherwise require submission of an IND.
XV. Emergency Use of an Investigational Drug/Device

The FDA human subjects regulations allow for an investigational drug/device to be used in emergency situations without prior IRB approval. Emergency use is defined as a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval for the use. The investigator is still required to obtain informed consent under these circumstances unless the FDA requirements in 21 CFR 50.23(a)-(c) allowing an exception to the requirement for informed consent are met. Whenever feasible, investigators must notify the IRB of the proposed emergency use in advance either verbally or in writing. In all cases, the emergency use must be reported to the UI IRB in writing within 5 working days.

The IRB chair reviews advance reports of proposed emergency uses using a checklist. If the proposed use complies with FDA regulations, the investigator is informed of this finding verbally. If the proposed use does not comply with FDA regulations, the investigator is informed of this finding verbally and informed that conducting the use as described will be considered noncompliance.

The written report submitted to the UI IRB chair after emergency use must include a cover letter explaining the medical condition, reason for use, and date administered as well as a copy of the Informed Consent Document and protocol if available. The investigator must also include any manufacturer information available on the product (e.g., drug brochure). All emergency use reports are reviewed at a convened meeting of the IRB. Any findings of noncompliance related to the emergency use will be reported according to the procedures in Section IX.F.2.

Written informed consent must be obtained prior to administration or use unless the emergency situation makes it not feasible to obtain informed consent prior to using the test article. Exemption from the informed consent requirement is granted only when: (1) a life-threatening situation necessitates use of the test article; (2) the subject is unable to provide effective consent; (3) there is insufficient time in which to obtain consent from the subject's legal representative; and (4) there is no available alternative method of approved or generally recognized therapy of equal or greater likelihood of saving the subject's life.

The investigator must document the infeasibility of obtaining consent as follows: The investigator and a physician who is not participating in the clinical investigation must certify in writing the existence of all four conditions listed above before use of the test article. If in the investigator's opinion immediate use of the test article is necessary to save the life of the subject and there is insufficient time to obtain the independent determination before using the test article, the investigator is to make his or her own written determinations, then obtain the written review and independent evaluation of a physician who is not participating in the clinical investigation. The documentation of the infeasibility of obtaining informed consent must be submitted to the UI IRB within five working days after the use of the test article.

The investigator’s report is presented at the next UI IRB meeting. When the UI IRB receives a report by an investigator of an emergency use, the UI IRB examines the case to assure that the emergency use was justified. If the UI IRB determines that the emergency use was not justified, this is considered noncompliance and the noncompliance procedures described in Section IX.D are followed. Since prior IRB approval is not obtained, the patient may not be considered a research
subject under DHHS regulations 45 CFR 46, but is considered a human subject under FDA regulations 21 CFR 56.102.

Although this procedure is designed to permit only a single emergency use of a test article for the treatment of one patient by one physician within the University, it is not intended to limit the authority of a physician to provide emergency care in a life-threatening situation. Should a situation arise which would require the emergency use of the test article for a second patient, either by the same or a second physician, for the same test article, subsequent emergency use should not be withheld for the purpose of gaining IRB approval. If it appears probable that similar emergencies will require subsequent use of the test article at the University, every effort should be made either to sign on to the sponsor's protocol or to develop a protocol for future use of the article at the institution. Either of these protocols would need to be prospectively reviewed and approved by the UI IRB for future use of the test article.

The use of a test article in an investigation designed to be conducted under emergency conditions (e.g., emergency room research) usually does not qualify for the emergency use exemption (see Section XIII.D.)
XVI. Other Use of an Investigational Drug/Device

IRB-01 reviews the use of investigational drugs/devices under the treatment use regulations. In all cases, treatment use of an investigational drug/device requires prospective UI IRB approval as well as subject informed consent.

A. Treatment Use

In non-emergency situations, treatment use allows a physician to obtain access to an investigational drug upon receiving approval from the UI IRB. This approval is granted for the treatment of a single or multiple patients. When an investigator desires to obtain treatment use approval, the investigator follows all procedures for submission of a new project application. The treatment use may occur only after UI IRB approval is obtained.

B. Humanitarian Use

Humanitarian use of investigational devices is prospectively reviewed by the convened UI IRB. The investigator is required to submit a new application for review. Included in the application must be evidence that the investigator/sponsor has obtained a Humanitarian Device Exemption (HDE) from the FDA. These projects are subject to the same new and continuing review requirements for research projects as outlined in this document. However, informed consent is not required for humanitarian use unless the investigator indicates intent to also use the data for research purposes.
XVII. Record Retention Policy

The HSO maintains an electronic copy of the complete study file including all reviewed research proposals and their associated application and report materials and any pertinent correspondence between the IRB and the investigator. For a complete listing of items that are maintained in the electronic copy see section X.B of this SOP. Correspondence by e-mail, letter, etc. pertinent to the review between the IRB and the investigator is attached to the HawkIRB application. The HSO also maintains minutes of UI IRB meetings as described in Section X.D.6, records of continuing review activities, UI IRB rosters, written procedures and correspondence relevant to UI IRB operations. All records are retained for a minimum of 3 years for studies that do not involve protected health information, 5 years for VA studies, or six years for studies that involve protected health information. Records relating to research which is approved and either carried out or not carried out are maintained for a minimum of 3 years for studies that do not involve protected health information, 5 years for VA studies after completion of the research, or six years for studies that involve protected health information. IRB records are retained in accordance with VHA Records Control Schedule (RCS 10-1).

A record of all closed project files is maintained on microfiche (studies closed before 1997), on a secure website maintained by the Office of the Vice President for Research (studies closed since 1997), or through HawkIRB (studies approved beginning in September/October 2004). Access to these records is limited to HSO staff and UI IRB members. Microfiche records are stored in a locked area in the HSO. All other electronic records are backed up as part of OVPR or UI ITS standard procedures.
XVIII. Education and Training

The UI IRB and HSO provide services to inform the research community on issues related to use of human subjects in research and ethics in research, and to make researchers aware of applicable Federal regulations.

A. Educational Activities Aimed at the Research Community at Large

The UI HSO maintains an internet website that contains detailed information on the UI human subjects review process as well as links to federal regulations and regulatory agencies, the UI human subjects FWA on file with OHRP, the OHRP Institutional Review Board (IRB) Guidebook, the Belmont Report, and other guidance documents.

The HSO also maintains a small library of materials that includes the OHRP Institutional Review Board (IRB) Guidebook, the Belmont Report, and other books and videotapes discussing ethical and regulatory issues relating to human subjects research. These materials are available to the entire UI campus community.

Application materials are provided with appropriate guidance (e.g., templates) as a means of educating investigators regarding the proper process for conducting human subjects research.

The HSO schedules and advertises numerous educational workshops throughout the calendar year directed at investigators and their research associates. These workshops cover topics that include UI policies and procedures as well as federal regulatory requirements.

Effective January 1, 2002, all investigators involved in the conduct of human subject research must show evidence of completing University-approved education in human subjects protections.

Members of the UI IRB or HSO staff may present information at meetings in academic departments or give lectures in University classes, to emphasize selected aspects of human subject research, and to keep various constituencies abreast of activities of the UI IRB.

B. Educational Activities Aimed at Members of the UI IRB

At the time of induction of a new member, the IRB Administrator, Assistant Director, and/or the Director of the HSO review with the member all procedures of the UI IRB and the general regulatory framework from which procedures and policies are derived.

Instruction by the HSO includes reviewing the UI human subjects website that contains detailed information on the UI human subjects review process as well as links to federal regulations, the UI human subjects Federalwide Assurance document on file with OHRP, the OHRP Institutional Review Board (IRB) Guidebook, the Belmont Report, and other guidance documents. The new member is also instructed in the use of HawkIRB for review of applications.
The UI provides the opportunity for each Chair of a UI IRB to attend, at least annually, a conference or workshop on human subject issues in research. Upon return, these individuals provide relevant information to all board members and, as appropriate, the rest of the University community, either through written or electronic means or by scheduling a special administrative meeting of the UI IRB.

C. Educational Activities Aimed at Members of the University Administration

The UI provides the opportunity for at least one professional staff member of the HSO and one senior administrator from the Office of the Vice President for Research to attend, at least annually, a conference or workshop on human subject issues in research. Upon return, these individuals brief appropriate members of the University community on relevant information obtained. Staff members within the HSO are selected based on their knowledge, skills, and abilities with respective to the role that they play in the HRPP. Staff members responsible for review of protocols or administrative activities specific to regulatory requirements are required to obtain Certified IRB Professional (CIP) certification when eligible. Staff in supporting roles is encouraged to work toward CIP designation as they become eligible. All staff members are provided opportunity to attend regional and/or national educational events as well as participate in appropriate local educational opportunities specific to their daily work responsibilities. All new staff members are required to complete the activities designated in the Orientation and Competency Checklist for their specific position. All HSO staff are formally assessed and provided feedback on an annual basis by their immediate HSO supervisor as required by University Human Resources.

D. Information for Subjects, Potential Subjects, and the General Community

The HSO website has information aimed specifically at the public and research subjects. Links to this information are provided in every UI consent document. The HSO also distributes informational brochures about the human research protection program.
XIX. 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))

**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 –

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.

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, individually or in aggregate, when such interest involves:

(1) 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);

(2) 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);

(3) 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);

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

(5) 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.

For UI IRB members only, the following indicate a conflict of interest with a protocol under review:

- s/he serves as a co-investigator or other member of the research team or
- a member of his/her immediate family serves as a co-investigator or other member of the research team.
Immediate family means spouse or domestic partner, and dependent children.

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.

**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:
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.

[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:

1. Names;
2. all geographic subdivisions smaller than a state, except for the initial three digits of the ZIP code if the geographic unit formed by combining all ZIP codes with the same three initial digits contains more than 20,000 people;
3. all elements of dates except year, and all ages over 89 or elements indicative of such age;
4. telephone numbers;
5. fax numbers;
(6) email addresses;
(7) social security numbers;
(8) medical record numbers;
(9) health plan beneficiary numbers;
(10) account numbers;
(11) certificate or license numbers;
(12) vehicle identifiers and license plate numbers;
(13) device identifiers and serial numbers;
(14) URLs;
(15) IP addresses;
(16) biometric identifiers;
(17) full-face photographs and any comparable images;
(18) any other unique, identifying characteristic or code, except as permitted for re-identification in the Privacy Rule.

**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
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))

**VA Research** - Research performed at the VAMC and/or utilizing VAMC resources, or performed by VAMC employees or agents on VAMC time.
REVIEWED AND Approved BY: (Signed document on file in HSO)

UI IRB Chairs

IRB-01 & IRB-03

______________________________________ ______________________________________
J. Andrew Bertolatus, MD Date Jerry Suls, PhD Date

Martha F. Jones, MA, CIP Date Janet Williams, PhD Date

Herbert A. Berger, MD Date Martha F. Jones, MA, CIP Date

Catherine Woodman, MD Date

Institutional Official/Associate Vice President for Research: Regulatory Affairs

______________________________________
James C. Walker, Ph.D. Date