

~~2015~~2016

UI Human Subjects Office

UNIVERSITY OF IOWA IRB STANDARD OPERATING PROCEDURES (SOP) & RESEARCHER GUIDE

This document provides information on human subjects research policies, regulations, and guidance. Investigators, researchers, Institutional Review Board members, members of other University of Iowa committees, other University of Iowa administrators, or others who are involved with research that involves human participants should use this document throughout the human subjects research review process.

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Section I

Part 1: Introduction to the University of Iowa Human Research Protections Program

The University of Iowa operates a centralized program to review and approve all research involving human subjects through the Office of the Vice President for Research and Economic Development. The Institutional Review Board must review and approve a research project involving human subjects before it starts subject recruitment and/or data collection. The University of Iowa IRBs are responsible for protecting the rights and welfare of study participants; however, the Principal Investigator has primary responsibility for the conduct of the study.

1.A Institutional Authority

The Office of the Vice President for Research and Economic Development at the University of Iowa has established three internal IRBs and has agreements with external IRBs to review all human subjects research. The University of Iowa's IRB-01, IRB-02, IRB-03, the Western Institutional Review Board (Western Institutional Review Board), and other IRBs review projects in a wide range of medical, social, and behavioral fields. Institutional oversight of the internal IRBs and the Human Research Protection Program is the responsibility of the Associate Vice President for Research: Regulatory Affairs who is the University's Institutional Official.

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 University of Iowa, 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, any other person, or entity including the Associate Vice President for Research: Regulatory Affairs or any other agent of the institution, state, or federal government may not reverse the decision.

1.A.1 Undue Influence

Investigations of attempts to influence unduly any member of the University of Iowa 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. IRB members and Human Subjects Office staff can report attempts by others to influence them unduly in the following manner. When a Human Subjects Office staff member experiences undue influence, s/he should report such an occurrence to the Executive Director of the Human Subjects Office or to the IRB Administrator/Assistant Director. These reports of

undue influence go to the Associate Vice President for Research: Regulatory Affairs or the Iowa City VHCS Facility Director, as applicable. If the staff member feels that undue influence is coming from either the Executive Director of the Human Subjects Office or the IRB Administrator/Assistant Director, s/he reports the occurrence to the Associate Vice President for Research: Regulatory Affairs or the Iowa City VHCS Facility Director, as applicable. 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 University of Iowa Ombudsperson.

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 Executive Director of the Human Subjects Office or the IRB Administrator/Assistant Director. The report then goes to the Associate Vice President for Research: Regulatory Affairs or the Iowa City VHCS Facility Director, as applicable.. If the IRB member feels that the undue influence is coming from the IRB Chair, the Executive Director of the Human Subjects Office, or the IRB Administrator/Assistant Director, the IRB member reports directly to the Associate Vice President for Research: Regulatory Affairs or the Iowa City VHCS Facility Director, as applicable.. If the IRB member experiences undue influence from any of the above reporting chain, the IRB member can report the incident to the University of Iowa Ombudsperson.

Staff will evaluate the allegation and will determine a course of action to take. 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.

1.B Mission

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

The mission of the University of Iowa IRBs is to assure adequate protections of the rights and welfare of human subjects research. To achieve this, University of Iowa 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 University of Iowa IRBs also inform and assist the University of Iowa and its researchers on ethical and procedural issues related to the use of human subjects in research, facilitate compliance with relevant regulations of the United States Government and relevant state law, and provide a framework suitable for continued support by Government agencies, private foundations and the industry for research involving human subjects at the University of Iowa. Principal Investigators who conduct research have primary responsibility for protecting the rights and welfare of the individuals. Others engaged in the conduct of the research share this

responsibility. Faculty or staff who assign or supervise research conducted by students or other staff have an obligation to consider carefully whether those individuals are qualified to safeguard adequately the rights and welfare of subjects

1.C Principles

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) guide all human subjects research conducted at the University of Iowa. Principles specific to the suitability of research at the University of Iowa are located in the University of Iowa Operations Manual (Part II Chapter 27.1).

1.C.i Principles Governing Restricted Access Research

The university policy regarding restricted access research is available in the University of Iowa Operations Manual Part II Chapter 27.2.

1.D Accreditation

The University of Iowa is the first non-commercial IRB to receive accreditation by the Association for the Accreditation of Human Research Protections Programs, Inc., (AAHRPP). In 2003, the University of Iowa IRB achieved accreditation and continues to be accredited. For more information about AAHRPP accreditation refer to the AAHRPP website.

Part 2: Components of the Human Research Protections Program (HRPP)

University of Iowa IRBs coordinate reviews with other Human Research Protections Program components as described below. None of these entities are a formal part of the University of Iowa IRB structure, but there is communication between the entities regarding status of review and/or conditions of approval. Refer to the University of Iowa Human Research Protection Program Flowchart for visual representation of the following relationships.

2.A Division of Sponsored Programs

The University of Iowa Operations Manual specifies operating procedures with regard to University of Iowa research conducted with funding from external sponsors. In particular, proposals for sponsored research must be submitted under signature of the Principal Investigator and approved in turn by the appropriate departmental executives for the Principal Investigator, the Principal Investigator’s collegiate dean, and the Office of the Vice President for

Research and Economic Development prior to submission to the sponsoring agency (University of Iowa Operations Manual Part II Chapter 27.1.C). The Office of the Vice President for Research and Economic Development has responsibility for approval of all sponsored research applications including budgets, budget revisions, and final agreements. Both the DSP and CTO may act as liaisons in negotiating and managing agreement terms and conditions for sponsored research. Departments and/or individual investigators cannot enter into Corporate or industry contracts; the University of Iowa (University of Iowa Operations Manual 27.7.a) must enter into contracts. Sponsorship of research within the University of Iowa setting may be awarded as a grant, cooperative agreement, or contract.

The Division of Sponsored Programs processes all human research with external support that is funding from governmental or private sources. Staff in the Division of Sponsored Programs review and provide institutional sign-off for all research projects, including negotiation of contracts if applicable. In addition, this office notifies the Grant Accounting Office to establish research accounts.

There are two primary types of support sources:

2.A.i Grant processing - Reserved

2.A.ii Contract execution

For projects with corporate support:

Contact: dsp-contracts@uiowa.edu

Note: IRB approval is not released to investigators until the contract has been finalized.

2.A.iii 310 Form - Reserved

2.B Pharmacy and Therapeutics

This sub-committee exists to provide University of Iowa 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:

Promote evidence-based, best practice standards in the formulary decision-making process to assure clinical efficacy, patient safety, and cost-effective prescribing within University of Iowa Health Care.

Review policies and procedures related to proper medication administration to assure medications are administered safely and appropriately.

Facilitate education of healthcare providers and students regarding medication-related issues. Assure that medications are prescribed appropriately, safely, and effectively through medication use evaluation processes.

Assure compliance with Joint Commission on Accreditation of Healthcare Organizations, Food and Drug Administration, and other regulatory guidelines related to medication use. Review and support investigational medication studies to ensure patient safety and adherence to University of Iowa Health Care policies.

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.

Pharmacy and Therapeutics must review a research protocol if it involves the administration of off-label investigational new drugs or drugs. Additionally, if a study involves Food and Drug Administration-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 Pharmacy and Therapeutics. It is not a requirement that an investigator have Pharmacy and Therapeutics approval prior to University of Iowa IRB review. Before the University of Iowa IRB grants final approval, Pharmacy and Therapeutics must review research studies using drugs as described above.

The University of Iowa IRB allows concurrent review by the University of Iowa IRB and Pharmacy and Therapeutics and defers release of the study contingent upon receipt and review of Pharmacy and Therapeutics deliberations. If Pharmacy and Therapeutics review is complete after the University of Iowa IRB review, the University of Iowa IRB Chair reviews any Pharmacy and Therapeutics comments. If the Chair believes the suggested changes are appropriate and qualify as minor modifications, the University of Iowa IRB Chair reviews these through an expedited process. If changes exceed minor modifications, the University of Iowa IRB Chair refers the application back to the full board for review prior to final approval. Prior to review by Western Institutional Review Board protocols must have Pharmacy and Therapeutics approval.

Pharmacy and Therapeutics approval is not required prior to emergency use of an investigational drug. The IRB forwards a copy of the information submitted to the IRB to Pharmacy and Therapeutics for its review and records.

2.C Pharmacy and Therapeutics Investigational Drug Service

The Investigational Drug Service stores, dispenses, labels, and distributes study medications. All research involving inpatient medication studies and for outpatient medication studies that involve non-FDA approved medications must use the Investigational Drug Service. This review is occurs separately from the Pharmacy and Therapeutics Committee but will occur concurrent with IRB review.

2.D Medical Radiation Protection Committee

The charge of the Medical Radiation Protection Committee is to ascertain 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 University of Iowa 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 University of Iowa's Radioactive Drug Research Committee. The Medical Radiation Protection Committee has developed a checklist for investigators to use to determine whether a project needs MRPC review.

It is not a requirement that an investigator have Medical Radiation Protection Committee approval prior to University of Iowa IRB review. However, if a study requires Medical Radiation Protection Committee review, the Medical Radiation Protection Committee must review the study before the University of Iowa IRB grants final approval. The University of Iowa IRB allows concurrent review by the University of Iowa IRB and the Medical Radiation Protection Committee and defers release of the study contingent upon receipt and review of Medical Radiation Protection Committee determinations.

If the Medical Radiation Protection Committee completes their review after the University of Iowa IRB review, the University of Iowa IRB Chair reviews any Medical Radiation Protection Committee comments. If the Chair believes the suggested changes are appropriate and qualify as minor modifications, the University of Iowa IRB Chair reviews these through an expedited process. If changes exceed minor modifications, the University of Iowa IRB Chair refers the application back to the full board for review prior to final approval. Protocols that will be sent to Western Institutional Review Board must have prior Medical Radiation Protection Committee approval. No member of the Medical Radiation Protection Committee may vote on any protocols on which s/he is an investigator or co-investigator.

2.E Institutional Biosafety Committee

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 exempt from the NIH guidelines. Institutional Biosafety Committee must review and approve the registration document prior to the initiation of the research. The Institutional Biosafety Committee 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 Institutional Biosafety Committee notifies the University of Iowa IRB of its approval of projects using recombinant DNA, but the Institutional Biosafety Committee does not share its deliberations

with the University of Iowa IRB unless there are specific subject protection issues raised by the Institutional Biosafety Committee.

It is a requirement that an investigator have Institutional Biosafety Committee approval prior to University of Iowa IRB review. IRB-01 retains protocols requiring Institutional Biosafety Committee for review; they are not sent to Western Institutional Review Board regardless of industry sponsorship.

2.F Holden Comprehensive Cancer Center/Protocol Review and Monitoring Committee

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

The purpose of the Protocol Review and Monitoring Committee review is to:

Conduct a scientific review (oncologic science, pharmacy & therapeutic science, and biostatistical science) of all proposed and ongoing institutional cancer clinical research.
Monitor all clinical cancer research protocols for sufficient progress.
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 Protocol Review and Monitoring Committee approval prior to University of Iowa IRB or Western Institutional Review Board review. A Protocol Review and Monitoring Committee member who is an investigator or consultant on a protocol that the Protocol Review and Monitoring Committee reviews 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 Protocol Review and Monitoring Committee 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 Executive 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.

2.G Conflict of Interest in Research Committee

The Vice President for Research and Economic Development appoints the Conflict of Interest in Research Committee. The Conflict of Interest in Research Committee is made up of faculty and staff representing the diversity of academic and research disciplines of the University of Iowa. The Conflict of Interest in Research Committee reviews those cases in which an Investigator has

disclosed a significant financial conflict of interest (see Definitions in Chapter XIX). The Conflict of Interest in Research Committee recommends management strategies to the Vice President for Research and Economic Development.

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 University of Iowa IRB is contingent upon University of Iowa IRB receipt and review of the Conflict of Interest in Research Committee management strategy once it is accepted and the conflicted investigator signs it. The University of Iowa 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 halt enrollment voluntarily 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 goes to the next IRB meeting for consideration of suspension of study enrollment until the IRB reviews and approves a management plan. It is a requirement that an investigator have a signed Conflict of Interest in Research Committee management plan prior to Western Institutional Review Board review. No individual who holds a significant financial interest in a project may participate in the review of its management strategy.

2.H Veterans' Affairs Health Care System (VAHCS)

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

2.H.i VA Research & Development (VA R&D)

Research under the direction of the VAHCS, or research that involves VAHCS patients requires review and approval by IRB-03 and the VAHCS Research and Development Committee (R&D Committee). Completion of the University of Iowa IRB-03 review and associated IRB findings and actions is documented on a VA form 10-1223, an IRB approval letter, and IRB minutes for full board studies. This documentation is sent to the VAHCS research office and VA Principal Investigator.

The VAHCS R&D Committee does not share its deliberations 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 Principal Investigator 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 VAHCS R&D Committee have reviewed and approved the new research project, the Human Subjects Office releases the project to the Principal Investigator.

2.H.ii VA Privacy Officer (VA PO)

The VA Privacy Officer helps to ensure that researchers and the IRB implement the VA's privacy policies at the local level. The VA Privacy Officer reviews all IRB-03 submissions. For additional information about the role of Privacy Officers visit the US Department of Veterans Affairs Privacy Service website.

2.H.iii VA Information Security Officer (VA ISO)

The VA Information Security Officer must review all human use protocols to ensure compliance with information security standards as defined by the VA. For additional information about the role of the Information Security Officer visit the Office of Information Security's website

2.H.iv VA Research Compliance Officer (VA RCO)

The VA Research Compliance Officer is responsible for monitoring the research conduct and documentation of VA investigators.

2.I Joint Office for Compliance Research Billing (Research Billing)

University of Iowa Health Care, through the Joint Office for Compliance, has procedures for investigators related to billing for items and services within research studies. The procedures will streamline and centralize the research billing process, and address the risks associated with inappropriate billing to Medicare and other third party payers. Direct questions regarding the

policy and/or procedures to the Joint Office for Compliance at:
researchbilling@healthcare.uiowa.edu or via phone.

2.J Clinical Research Unit (CRU)

The Institute for Clinical and Translational Science Research Protocol Review Committee reviews all protocols that propose to use the Clinical Research Unit. Each protocol is evaluated for scientific merit and utilization of CRU resources. Two reviewers also critique the protocols. This committee does not share its deliberations with the University of Iowa IRB unless there are specific subject protection issues raised. 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 Principal Investigator 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 University of Iowa IRB. The CRU Program Executive Director or the Associate/Assistant Program Executive Director may not Chair the CRU. 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 participate in are being discussed.

2.K Nursing Research Committee (NRC)

The Nursing Research Committee must give its approval for research within the Department of Nursing or that utilizes nurses or nursing resources at University of Iowa Health Care. This committee assures the protection of the rights and welfare of patients and nursing personnel. 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 Nursing Research Committee does not share its deliberations with the University of Iowa 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 Chair in writing following its deliberations. If the Chair agrees that the issue(s) are related to subject protection, the Chair will require the Principal Investigator to submit a modification to address the identified issue(s).

Part 3: Other related entities, programs, or committees involved with Human Subjects Research

The University of Iowa Institutional Review Boards coordinate reviews with other institutional committees. None of these committees are a formal part of the University of Iowa IRB

structure, but there is communication between the committees regarding status of review and/or conditions of approval.

3.A 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. To contact the Cooperating Schools Program, visit their website.

3.B University of Iowa Registrar's Office

The University of Iowa Registrar's Office provides the university faculty, staff, students, and public with official academic records. The Registrar's Office also coordinates and provides services related to the student records: course catalog, registration, fees, records, transcripts, data warehouse, institutional research, reporting, maintenance, and security for student records data, grading process, graduation and diploma services. Final student course grades and other student-related grade or personal information needed for research should be obtained from the Registrar's Office.

3.B.i Family Educational Rights and Privacy Act (FERPA)

All student records acquired for research must be used in accordance with protections afforded under the Family Educational Rights and Privacy Act. The Office of the Registrar provides information about FERPA and university policies related to FERPA on the office's website.

3.C Joint Office for Compliance

University of Iowa Health Care through the Joint Office for Compliance has procedures for investigators related to billing for items and services within research studies. The procedures streamline and centralize the research billing process, and address the risks associated with inappropriate billing to Medicare and other third party payers. Information about the compliance billing process is located here. This office houses the university's Privacy Officer.

3.C.i Health Insurance Portability and Accountability Act (HIPAA)

Research involving protected health information (PHI) must adhere to the privacy protections outlined in the Health Insurance Portability and Accountability Act. Frequently asked questions

and answers about the use of protected health information for research is available in the HIPAA FAQ.

3.C.i.a Privacy Officer

The Assistant Vice President for Compliance, Accreditation, and University of Iowa Privacy Officer monitors HIPAA compliance under the Joint Office for Compliance at University of Iowa Health Care.

3.C.i.b Business Associate Agreements

A Business Associate Agreement may be needed for data transactions of protected health information. The Joint Office for Compliance oversees these agreements. Information about data that may require an agreement can be found via the Information Security and Policy Office. Additional information about Business Associate Agreements may be obtained from the Joint Office for Compliance.

3.D Accounts Payable

The Accounts Payable (AP) department is responsible for the auditing and processing of invoices and payments for The University of Iowa including those paid to human subjects and for human subjects research purposes. Accounts Payable supports the systems for these transactions. Consult the Accounts Payable website for additional information about the Accounts Payable electronic submission systems (i.e. eVoucher, ProTrav, etc.).

3.D.i Cash Handling

All university researchers who plan to pay research subjects with cash or cash equivalents (as defined by the university) must have a cash handling policy in place prior to submitting an IRB application. Directions about how to prepare and obtain approval for cash handling is available from the University of Iowa Accounts Payable Office.

3.E Grant Accounting

The Grant Accounting Office is a central administrative department within Finance and Operations that reports to the University Controller. The Grant Accounting Office helps researchers with the following:

- 1) Establishing new accounts to allow spending
- 2) Maintaining grant information systems

- 3) Collecting funds from sponsors
- 4) Processing invoices to pay sub-awardees
- 5) Monitoring and advising on sponsor regulations and fiscal allowability
- 6) Preparing and submitting financial reports for sponsors
- 7) Distributing monthly financial statements
- 8) Providing training on post-award administration
- 9) Responding to external audit requests
- 10) Coordinating effort certification

The Grant Accounting website contains additional information about Grant Accounting services and requirements.

3.E.i Substitute W-9 requirement

For payments to research subjects that exceed \$75.00, the Purchasing and Accounts Payable Office requires a Substitute W-9. This form allows the university to collect necessary information for income tax reporting about people to whom it makes payments. This form should only be filled out for single payments of \$75.01 or greater, or for persons expected to exceed \$600 of payments in a calendar year. This form is available online; the Accounts Payable Office maintains it and can answer questions related to its use.

3.F IRB Advisory Committee

The Advisory Committee is composed of faculty who serve as "Communication Liaisons" between faculty, staff, and students in their respective colleges who conduct human subjects research and the Institutional Review Boards/Human Subjects Office (IRB/HSO) that review, approve, and monitor such research. The Office of the Vice President for Research and Economic Development website contains additional Information about the IRB Advisory Committee, its purpose, and its responsibilities.

Part 4: University of Iowa Institutional Review Board (IRB)

The Office of the Vice President for Research at the University of Iowa (UI) has established three internal IRBs and has agreements with external IRBs to review all human subjects research. These boards, the UI's IRB-01, IRB-02, IRB-03, the Western Institutional Review Board (WIRB), and others 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 who is the Institutional Official for the University of Iowa.

4.A What is an Institutional Review Board (IRB)?

An Institutional Review Board is a group of individuals charged with reviewing proposed research involving human subjects to ensure the protection of those subjects and compliance with federal human subjects regulations. The University of Iowa has three such review boards, each consisting of faculty, staff, and representatives from the university and the Iowa City community.

4.B Scope of IRB Review at the University of Iowa

The IRB must review and approve all human subjects research carried out at the University or under its auspices prior to the start of the research. The IRBs are guided by the principles of The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research's Ethical Principles and Guidelines for the Protection of Human Subjects of Research (known as the Belmont Report) and the Federal Policy for the Protection of Human Subjects (known as 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 at 45 CFR 46. Authority for IRB oversight of all research with products regulated by the Food and Drug Administration is provided in 21 CFR 50. In addition, the University of Iowa 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 Human Subjects Office 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 University of Iowa IRB.

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 Office for Human Research Protections guidance of October 16, 2008
- 5) the research involves the use of this institution's non-public information to identify or contact human subjects.

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 and continuing approval;
- 3) approve new research projects and the continuation of previously approved projects;
- 4) disapprove the initiation of new research projects;
- 5) monitor the activities in approved projects including regularly scheduled continuing review at least every twelve months
- 6) verification of compliance with approved research protocols and informed consent procedures,
- 7) observe or have a third party observe the consent process;
- 8) develop mechanisms for prompt reporting to the IRB of any planned changes in approved projects prior to the implementation of those changes;
- 9) 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;
- 10) suspend or terminate a previously approved project;
- 11) restrict aspects of a research study for the purpose of subject protection;
- 12) review and monitor the use of test articles (investigational drugs, biologicals and devices) for the purpose of treatment of serious or life-threatening illnesses.

The University of Iowa IRB Chair may, at his/her discretion, refer the review of a research project to another University of Iowa IRB if s/he 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 Food and Drug Administration-regulated research or that include physical or physiologic interventions involving more than minimal risk may not be referred to IRB-02, and projects involving VAHCS must be reviewed by IRB-03.

Before a research project involving human subjects starts subject recruitment and/or data collection, it must be reviewed and approved by a University of Iowa Institutional Review Board (IRB).

4.B.i IRB-01

All research projects involving human subjects which do not meet the criteria for review by Western Institutional Review Board are reviewed by IRB-01 (identified as IRB-01-NR by Department of Health and Human Services, indicating no restriction) when any of the following conditions apply:

The study is conducted in or involves patients or staff of University of Iowa Health Care.

The Principal Investigator is from the College of Dentistry, Medicine, Pharmacy, Public Health, or the Department of Communication Sciences and Disorders in the College of Liberal Arts. The Principal Investigator is from the College of Nursing and the project involves physical or physiological interventions exceeding minimal risk.

The study involves the use or creation of Protected Health Information (PHI) as defined by the federal Health Insurance Portability and Accountability Act (HIPAA).
The study is not a VA study

4.B.i.a IRB-01 Executive Committee

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.

4.B.ii 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 Department of Health and Human Services, indicating no membership expertise in the medical sciences) when any of the following conditions apply:

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

the Principal Investigator is from the Colleges of Public Health or Nursing (if the study does not involve a physical or physiological intervention that is greater than minimal risk and does not involves access to or creation of any protected health information about the subject that is maintained in a health care provider's records.)

IRB-02 does not review VA Studies or Food and Drug Administration-regulated research. Policy issues and reports of noncompliance are reviewed during regular full board meetings.

4.B.iii IRB-03

IRB-03 provides IRB review for the Iowa City VAHCS pursuant to its Memorandum of Understanding. 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 a Food and Drug Administration-regulated article.

Research projects involving human participants and the Iowa City VAHCS, which includes VA patients, records, is funded by the VA, or occurs on VAHCS premises, are reviewed by IRB-03. Any research projects that occur at both the Iowa City VAHCS and the University of Iowa locations are reviewed under IRB-03. Policy issues and reports of noncompliance are reviewed during regularly scheduled IRB-03 full board meetings. The use of advertisements for Non VA, federally-funded research at the VA may be allowed if approved by the VA research Office prior to use. This includes, posting or distributing recruitment documents, flyers, or advertisements for research related to Veterans. Posting or distributing may include announcing, distributing, publishing, or advertising the study either electronically, by hard copy, or other means to anyone, including Veterans, clinicians, or other staff. If a research study that does not otherwise involve the VA, but intends to post advertisements at the VA, the study may be reviewed under IRB -01 if the research team provides approval of the from the VA Research Office at the time of submission.

Part 5: Use of an External IRB Model

5.A. Reliance/Deferment Process

Discussion of how to assure the rights and welfare of human subjects in research at each entity involved in the research usually begins with an evaluation of whether or not each entity is “engaged” in human subjects research (refer to the section on Cooperative Research). If a determination is made that the outside institution is engaged in human subjects research and the outside institution is receiving federal funds through a subcontract with the UI, the UI Division of Sponsored Programs requires documentation that the outside institution holds an FWA through the subcontract process. If the outside institution does not hold its own FWA, the UI requires that they obtain one prior to finalization of the subcontract.

If this is the case, and the other institution obtains its own FWA, there are a few methods of IRB oversight that the UI IRB would consider acceptable based on the circumstances of the project and the role of the other institution. The UI IRB may accept the other institution’s IRB as the IRB of record for the project. This would be in cases where the UI determines that the outside institution’s IRB review will provide more appropriate expertise, oversight, and/or knowledge of local context for the UI role in the study. This agreement is formalized using an IRB Authorization Agreement or other equivalent agreement. The outside IRB is then added to the UI FWA. Research projects utilizing the VAMC are not eligible to receive this type of deferred judgment.

5.B Relationship with Western Institutional Review Board

Western Institutional Review Board provides IRB review and oversight for research that meet all of the following conditions:

- 1) The study is sponsored or funded by the Department of the Navy
- 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 University of Iowa investigator has not previously submitted the study to another University of Iowa IRB.

No transfers of projects already submitted to IRB-01 are allowed.

The project cannot involve any of the following:

- 1) Xenotransplantation
- 2) Embryonic stem cells
- 3) Review and approval by the University of Iowa 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 VAHCS and/or utilizing VAHCS resources, or performed by VAHCS employees or agents on VAHCS time.

Western Institutional Review Board 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 University of Iowa coordinates application materials and coordinates other University of Iowa committee review prior to submission to Western Institutional Review Board for review. By contract, Western Institutional Review Board notifies the University of Iowa Human Subjects Office of any Western Institutional Review Board 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 University of Iowa's compliance with applicable regulations and laws governing human subjects research.

The University of Iowa has the contractual right to withhold any protocol from Western Institutional Review Board review and keep it for review and oversight by IRB-01. The University of Iowa may decide to retain a study if the protocol has significant local context issues such as a unique vulnerable population, involves an investigative team that has had previous serious and/or continuing noncompliance issues, or if the research design or intervention adds unusual risk for the subjects. If investigators have questions about whether or not the protocol should be submitted to Western Institutional Review Board, please call the Human Subjects Office.

5.C National Cancer Institute Central Institutional Review Board Initiative (CIRB)

The University of Iowa anticipates working with CIRB in 2014. Additional details regarding submitting protocols to CIRB via the University of Iowa will be added to the University of Iowa Human Subjects Office website as they become available.

5.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 regulations. Federal regulations from Department of Health and Human Services and Food and Drug Administration (45 CFR 46.114 and 21 CFR 56.114) allow for cooperative research projects which involve more than one institution. To avoid duplication of review efforts by IRBs, the University of Iowa can choose to conduct joint reviews, rely upon the review of another qualified IRB, or make other arrangements to establish oversight responsibilities. The University of Iowa makes a determination about whether or not a cooperating outside institution is also engaged in human subjects research in collaboration with the university. This determination is made by a University of Iowa IRB Chair based on the outside institution's role and whether that role meets any of the criteria for "engaged in research" as defined in Office for Human Research Protections guidance of October 16, 2008.

When the outside institution is engaged and is receiving federal funds through a subcontract with the University of Iowa, the University of Iowa Division of Sponsored programs requires documentation that the outside institution holds a Federalwide Assurance through the subcontract process. If the outside institution does not hold its own Federalwide Assurance, the University of Iowa requires that they obtain one prior to finalization of the subcontract. Under limited circumstances, when the University of Iowa 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, University of Iowa may choose to extend its Federalwide Assurance to cover the outside institution's role in a single project.

When the outside institution is engaged, but is not receiving federal funding for this study through a subcontract with the University of Iowa, the University of Iowa IRB requires that the research be conducted under either another entity's IRB oversight or the University of Iowa IRB takes on oversight of the research. In the former instance, the University of Iowa IRB will require documentation that the outside IRB will provide this oversight. In the latter instance, this agreement is documented through a formal agreement. The University of Iowa IRB will oversee research for an outside institution only when the University of Iowa 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.

When the outside institution is engaged as described above, and the University of Iowa determines that the outside institution's IRB review will provide more appropriate expertise, oversight, and/or knowledge of local context, the University of Iowa 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 University of Iowa Federalwide Assurance. The final determination to enter into any agreements is made by the Institutional Official.

5.E IRBshare

The IRBshare System is a shared IRB review model for multi-site studies. Participating institutions such as the University of Iowa share documents and the review process for IRB submissions. For additional information about how and when to use the IRBshare system, contact the HSO Assistant Director via irb@uiowa.edu or via the Human Subjects Office main phone line at 319-335-6564.

5.F Quorum

The University of Iowa anticipates working with Quorum IRB in 2014. Additional details regarding submitting protocols to Quorum via the University of Iowa will be added to the University of Iowa Human Subjects Office website as they become available.

5.G Other Models - Reserved

Part 6: Foundation of Human Subjects Protection

The foundation for modern human subjects protections and those at the University of Iowa are based on The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research's report Ethical Principles and Guidelines for the Protection of Human Subjects of Research. The report, disseminated in April 1979, is commonly referred to as the Belmont Report. The Belmont Report outlines three guiding concepts for the protection of human subjects.

6.A Respect for Persons

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

6.A.i Information

The Belmont Report suggests that "the extent and nature of information should be such that persons, knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether they wish to participate in the furthering of knowledge." Federal regulations now provide detail about the information to share with human subjects in order for the subject to make an informed choice to participate in research.

6.A.ii Comprehension

Investigators should adapt their presentation of information to the subject's level of understanding in order to conduct the informed consent process. When a subject's comprehension is limited due to immaturity or mental disability, respect for persons requires that the individual be given the opportunity to choose whether or not to participate to the extent they are able. Permission from a third party who understands the subject's situation and can act in the subject's best interest further protects the subject from harm.

6.A.iii Voluntariness

Finally, in order to be voluntary, consent must be given under conditions that are free of coercion and undue influence. Consent is valid only if the agreement to participate in the research is given voluntarily.

6.B Beneficence

The principle of beneficence requires that the investigator not only protect individuals from harm, but make efforts to secure their well-being. Beneficence goes beyond the idea of "do no harm" and requires investigators to "maximize possible benefits and minimize possible harms".

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

6.C Justice

The principle of justice means that the benefits and burdens of the research are fairly distributed. It is a violation of the principle of justice to select a class of subjects (e.g., welfare patients, an ethnic minority, institutionalized persons) simply because of easy availability rather

than for reasons directly related to the topic under study. The principle of justice requires fair procedures and outcomes in the selection of research subjects.

Part 7: Regulatory Requirements for IRB Review

The Department of Health and Human Services via the Office for Human Research Protections and the Food and Drug Administration among others provide the regulatory framework for the conduct of human subjects research and human subjects research protections. The department's respective regulations were modified in 1981 to be compatible; the Federal Policy for the Protection of Human Subjects or the "Common Rule" was published in 1991.

7.A Office for Human Research Protections and the Common Rule

The Office for Human Research Protections (formerly the Office for Protection from Research Risks) is an agency of the Department of Health and Human Services. The office "provides leadership in the protection of the rights, welfare, and wellbeing of subjects involved in research conducted or supported by the U.S. Department of Health and Human Services (HHS). OHRP helps ensure this by providing clarification and guidance, developing educational programs and materials, maintaining regulatory oversight, and providing advice on ethical and regulatory issues in biomedical and social-behavioral research. (Citation) "

7.A.i Maintaining a Federalwide Assurance

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

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

The Iowa City Veterans Affairs Health Care System (VAHCS) has its own Federalwide Assurance. The University of Iowa provides IRB review for human subjects research conducted at the Iowa

City VAHCS under a Memorandum of Understanding (MOU). The MOU states IRB-03 is the IRB of record for the Iowa City VAHCS.

The Human Subjects Office maintains the Federalwide Assurance and IRB registrations for IRB-01 and IRB-02 and notifies Office for Human Research Protections of any changes in the Federalwide Assurance or IRB membership as they occur. IRB staff maintains a list (known as a “roster”) of the IRB members for each IRB. University of Iowa researchers may request a copy of the current roster via e-mail from irb@uiowa.edu.

7.B Food and Drug Administration

In studies involving products regulated by the Food and Drug Administration regulations, the University of Iowa 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.

Clinical investigations involving human participants are subject to IRB review under Food and Drug Administration regulations with some exceptions as provided in 21 CFR 56.104.

7.C Guidelines for Good Clinical Practice (ICH E6 (R1)-GCP)

The University of Iowa IRB reviews human subjects research studies in accordance with the International Conference On Harmonisation (ICH)’s Harmonised Tripartite Guideline, Guideline for Good Clinical Practice (ICH E6 (R1)-GCP) at the request of Principal Investigators on a per study basis. To have a study reviewed under these guidelines select “Regular Review in Compliance with ICH-GCP” in Section IV, question 1 of the HawkIRB New Project Application.

7.D National Institutes of Health (NIH)

Human subjects research studies that have National Institutes of Health funding or support must follow regulations, requirements, and additional policies and guidance as mandated by the National Institutes of Health’s Office of Extramural Research.

7.E VHA Handbook 1200.05

In addition to HHS and FDA regulations, IRB-03 and studies conducted at the VAHCS must follow VHA regulations outlined in the VHA Handbook 1200.05.

7.F Department of Defense (DoD)

The IRB reviews studies funded or supported by the Department of Defense under the regulations set forth by the Department of Defense in DoD Directive 3216.2: Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research. Depending on the specific source of support, regulations from the Departments of the Army, Navy, Air Force, or Marines may apply additionally to the research. The University of Iowa does not provide oversight for studies that have Department of Defense funding and are transnational.

7.G National Science Foundation (NSF)

The IRB reviews studies funded or supported by the National Science Foundation under the regulations contained in 45 CFR 46 Part 690.

7.H Department of Justice (DOJ)\National Institutes of Justice (NIJ)

The IRB reviews studies funded or supported by the Department of Justice/National Institute of Justice under the regulations contained in 28 CFR Part 46.

For National Institute of Justice-funded research:

- 1) The confidentiality statement on the consent form must state that confidentiality can only be broken if the participant reports immediate harm to participants or others.
- 2) Under a privacy certificate, researchers and research staff do not have to report child abuse unless the participant signs another consent form to allow child abuse reporting.
- 3) For research conducted within the Bureau of Prisons required elements of disclosure include:
 - a. Identification of the researchers
 - b. Anticipated uses of the results of the research
 - c. A statement that participation is completely voluntary and that the participant may withdraw consent and end participation in the project at any time without penalty or prejudice (the inmate will be returned to regular assignment or activity by staff as soon as practicable)
 - d. A statement regarding the confidentiality of the research information and exceptions to any guarantees of confidentiality required by federal or state law
 - i. For example, a researcher may not guarantee confidentiality when the participant indicates intent to commit future criminal conduct or harm himself or herself or someone else, or, if the participant is an inmate, indicates intent to leave the facility without authorization.
- 4) A statement that participation in the research project will have no effect on the inmate participant's release date or parole eligibility

7.I Department of Education (DOEd)

The IRB reviews studies funded or supported by the Department of Education under the regulations contained in 34 CFR Part 97.

7.J Department of Energy (DOE)

See the DoE policy located [here](#).

Part 8: Legal Requirements for IRB Review

In addition to federal regulations, the University of Iowa IRBs must also be aware of and follow as applicable laws specific to the state of Iowa which may affect human subjects research.

8.A State of Iowa Laws that May Indirectly Affect Research with Human Participants

Neither Federal nor State law specifically addresses mandatory reporting requirements for those engaged in research. However, this does not mean that a researcher does not have an ethical obligation, as outlined in the Belmont Report, to make efforts to secure the well-being of subjects. Researchers have an ethical obligation to report suspected maltreatment. In addition, providing subjects with referrals to services which can respond to their situations is a minimum standard for conducting research with subject populations who are at risk of violence. Regardless of mandatory reporting requirements, assistance should be provided to these subjects.

8.A.i Iowa State Law Provisions on Mandatory Reporting (Iowa Code Chapters 235 B, 232.69)

Iowa law provides for the mandatory reporting to the Department of Health and Human Services (DHHS) of child abuse and neglect as well as dependent adult abuse.

8.A.ii Current Abuse of a Dependent Adult (Iowa Code Chapter 235 B)

"Dependent adult" is defined in as 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.

8.A.iii Current Child Abuse (Iowa Code Chapter 232.69)

The State of Iowa has defined mandatory reporters regarding children in Iowa Code §232.69. An important distinction contained in subsection 1 of Iowa Code §232.69 is in regard to children under the age of twelve. Mandatory reporters must make a report if abuse is suspected in a

child under the age of twelve. They may make a report if the child is over the age of twelve, unless the suspected abuse is being perpetrated by the child's caretaker. In this case, it must be reported for a child of any age.

8.A.iv Wounds or "other serious bodily injury"

The general licensing provisions for a number of health care professions 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 (Iowa Code Chapter 147.111).

8.A.v Reportable Diseases

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 University of Iowa. 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. (Iowa Code Chapter 641.1.1-1.3 (139A))

8.A.vi Iowa State Law Prohibition on Human Cloning (707C)

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

8.A.vii Intent to hurt one's self or others

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

8.B State of Iowa Definitions that Affect Research with Human Participants

The following definitions are provided in the Iowa Code and may affect investigators conducting research in the State of Iowa. Investigators are expected to comply with all federal and state laws applicable to the conduct of human subjects research.

8.B.i Minor (also referred to as “Child”) (Iowa Code Definitions 600A.2 (13))

"Minor" means an unmarried person who is under the age of eighteen years.

"Child" means a son or daughter of a parent, whether by birth or adoption.

8.B.i.a Pregnancy in a Minor Subject Population

8.C Applicability of the laws of other states

In cases of human subjects research under the authority of the University of Iowa IRB(s) but conducted outside of the state of Iowa, the University of Iowa IRB confers with the University of Iowa 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 University of Iowa IRB will apply the law of the state in which the research is 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 Department of Health and Human Services and Food and Drug Administration definition of “children” at that site.

Part 9: Institutional Requirements for IRB Review

In addition to federal regulations, guidance, state and local laws, the University of Iowa IRB is required to adhere to policies as outlined in the University of Iowa Operations Manual.

9.A University of Iowa Policy on Mandatory Reporting of Physical and Sexual Abuse of Children

In accordance with Iowa Code 232.67, the University of Iowa Operations Manual Part II, Chapter 15 outlines the university’s policies with regard to mandatory reporting of child abuse.

9.B IRB authority as a Privacy Board

The University of Iowa 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 as described in this act.

IRB-03 operates as a Privacy Board for the Iowa City VAHCS under the authority of a Memorandum of Understanding with the Iowa City VAHCS outlining IRB responsibilities. The

request for a full or partial waiver of HIPAA authorization opens in the application based on the PI's response to either Section IV or Section VII, Question D.1 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. Documentation of IRB approval is captured as part of the IRB meeting minutes, when applicable, and the final IRB approval is issued via an authorization memo documenting criteria have been satisfied under partial or full waiver of HIPAA Authorization per 45 CFR 46.164.512.

9.B.i Privacy Board Responsibilities

The National Institutes of Health offers specific information about the role and responsibilities of Privacy Boards on their website under the section "What Is a Privacy Board and What is its Role under the Privacy Rule?"

9.B.ii Activities not covered by this authority

The National Institutes of Health offers specific information about the limitations of the IRBs role under the privacy rule on their website under the section "IRB Role under the Privacy Rule".

9.C 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:

Following an IRB determination of suspension or termination of research, noncompliance investigations, and UPIRTSOs), a full board Human Subjects Office staff member in collaboration with the IRB Chair prepares a letter for signature by the IRB Chair(s) that contains the following information:

- 1) The nature of the event (whether or not the event was an unanticipated problem involving risks to subjects or others, serious or continuing non-compliance, or a suspension or termination of approval of research or a combination of these events),
- 2) The name of the institution conducting the research,
- 3) The title of the research project and/or grant proposal in which the problem occurred,
- 4) The name of the Principal Investigator on the protocol,
- 5) The IRB number assigned to the research project and the number of any applicable federal award(s) such as grants, contracts, or cooperative agreements,
- 6) A short summary of the project,

- 7) A detailed description of the problem including the findings of the organization and the reasons for the IRB's decision,
- 8) Actions the institution is taking or plans to take to address the problem (e.g. revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, increase IRB monitoring of the project, etc.),
- 9) Plans, if any, for any follow-up action

A full board Human Subjects Office staff member sends a copy of this letter no more than one month following the review and final determination by the convened IRB to:

- 1) The University of Iowa Institutional Official (Office of the Vice President for Research and Economic Development),
- 2) Principal Investigator,
- 3) Division of Sponsored Programs (if applicable)
- 4) Departmental Executive Officer (Departmental Executive Officer) of the Principal Investigator,
- 5) Dean of the College of the Principal Investigator,
- 6) Research Integrity Officer (RIO) if the event involved research misconduct

The letter is also sent to the following federal agencies (as applicable):

- 1) Office for Human Research Protections, if the study is subject to Department of Health and Human Services regulations or subject to a Department of Health and Human Services Federalwide assurance,
- 2) Food and Drug Administration, if the study is subject to Food and Drug Administration regulations (21 CFR 50 and 56)
- 3) If the study is conducted or funded by any Federal Agency other than Department of Health and Human Services that is subject to "The Common Rule", the report is sent to Office for Human Research Protections or the head of the agency as required by the agency.

~~3)4)~~ The Department of Defense Human Research Protections Official, if the finding occurs in Department of Defense funded research

For VA Studies reports are also sent to the Iowa City VA Research Office who will ensure the report is sent to the following:

- 1) Office of Research and Development
- 2) Regional VA Office of Research Oversight
- 3) VA Privacy Officer, when the report involves unauthorized use, loss, or disclosure of individually identifiable private information
- 4) 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 Human Subjects Office Assistant Director can provide copies to others as deemed appropriate by the Institutional Official.

For studies reviewed by Western Institutional Review Board, events of serious or continuing noncompliance are reported directly to Western Institutional Review Board and reporting is the responsibility of Western Institutional Review Board. Reporting of suspensions or terminations made by Western Institutional Review Board are the responsibility of Western Institutional Review Board. For studies reviewed by Western Institutional Review Board, unanticipated problems involving risks to subjects or others are reported directly to Western Institutional Review Board and reporting is the responsibility of Western Institutional Review Board. For studies reviewed by Western Institutional Review Board, unanticipated problems involving risks to subjects or others are reported directly to Western Institutional Review Board and reporting is the responsibility of Western Institutional Review Board.

In addition to the above notices, when the institution is notified by any federal department or agency or national organization that any part of its Human Protections Program is under investigation for cause involving a Department of Defense supported research protocol, the appropriate Department of Defense Human Research Protections official will be notified.

9.C.i Suspension or Termination of IRB approval

The University of Iowa IRB has the authority to suspend or terminate approval of human subjects research that is not being conducted in accordance with the University of Iowa IRB's requirements or that has been associated with unexpected serious harm to subjects. The University of Iowa IRB also has the authority to suspend or terminate research being conducted under the oversight of Western Institutional Review Board. 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 Departmental Executive Officer, 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 Western Institutional Review Board-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):

- 1) Considers actions to protect the rights and welfare of currently enrolled participants.
- 2) Considers whether procedures for withdrawal of enrolled participants considered their rights and welfare.

- 3) Considers whether participants should be informed of the termination or suspension.
- 4) Requires any adverse events or outcomes to be reported to the IRB.

9.C.ii Noncompliance Investigations and Actions

In the federal regulations, non-compliance refers to failure to comply with the regulations, or the requirements or determinations of the IRB. For VA studies, this includes failure to follow the requirements of VHA Handbook 1200.5.

An allegation of noncompliance occurs when information or suspected noncompliance comes to the attention of the IRB or an IRB Chair. After further investigation, the IRB Chair or full board makes a noncompliance determination. Noncompliance can be serious, continuing, serious and continuing, or neither serious nor continuing

Serious noncompliance is 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 carried out without IRB review and approval or without appropriate informed consent.
Substantive modifications to IRB-approved research without IRB approval.

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

9.C.ii.a Allegations of Noncompliance

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

When information comes to the attention of the IRB outside of a full-board meeting, the Chair of the appropriate IRB reviews the allegations of noncompliance. The Chair makes a determination as to whether the alleged practices appear to (1) cause injury or any other unanticipated problems involving risks to subjects or others, or (2) constitute serious or continuing noncompliance with IRB determinations or federal regulations. In such cases, the

Chair may choose to suspend the study procedures, taking into consideration the welfare of currently enrolled subjects, pending an investigation and review by the full IRB. If an IRB Chair requests the research team suspend study procedures on a federally funded study, reporting to OHRP and the FDA (where applicable) may be required. The suspension of study procedures may be lifted either by the IRB Chair or the full IRB once a determination has been made based on the information gathered as a result of the investigation. If the Chair determines that the potential noncompliance did not involve any risk to subjects or others, and did not constitute serious or continuing noncompliance, the Chair may resolve the issue directly with the Principal Investigator and research team.

When potential noncompliance is first identified during a full board review, the full board rather than the IRB Chair makes the decisions described above.

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

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

- 1) When made aware of an allegation of noncompliance, HSO staff immediately notifies the UI IRB Chair for the IRB of record and works with the Chair to compile any required background file information.
- 2) If the alleged noncompliance involves a WIRB or other external IRB study, the allegation is reported to an IRB-01 Chair who in turn immediately notifies the appropriate IRB of record.
- 3) The UI IRB Chair makes a determination as to whether to pursue the matter with the Principal Investigator via telephone call, e-mail, paper memo, or in person based on the nature and seriousness of the alleged noncompliance.
- 4) The Chair may also choose to send an IRB Compliance Specialist to meet with research team members and review study materials as appropriate. The purpose of such contact is fact-finding, i.e. to determine if indeed there is noncompliance.
- 5) For WIRB studies, the UI IRB Chair coordinates the UI investigation with the IRB of record. Investigations are initiated within 5 working days of initial notification.
- 6) The UI Chair and/or Compliance Specialist document the outcome of any and all pertinent communications and discussions in writing, by either e-mail or paper memo with a copy to the IRB files. Such documentation should be factual and objective, and include timelines for resolution (e.g. meeting dates, response deadlines).
- 7) The UI Chair makes a decision based on the information gathered as to whether the allegation is credible.

If the UI Chair believes the allegation is credible, the UI Chair determines whether the noncompliance could possibly meet the definition of serious or continuing noncompliance.

In making this decision, the Chair may bring the issue to the appropriate Chairs' meeting for discussion.

If the IRB Chair decides that the noncompliance is not serious or continuing, then the Principal Investigator typically submits a Reportable Event Form or a Modification form to document the outcome in writing and address any Chair concerns.

If the IRB Chair decides that the noncompliance may be serious and/or continuing, the allegation is reviewed at a full board meeting.

Prior to the IRB-01 Executive Committee Meeting or IRB-02(03) Full Board Meeting, the IRB Chair contacts the Principal Investigator (PI) and grant-holder (if different from the PI) via e-mail to inform them of the issue of possible noncompliance and the required reporting for serious and / or continuing noncompliance. Investigators may attend the meeting if they choose or if the IRB Chair decided that the investigator should attend.

During the IRB Executive Committee Meeting:

- 1) Initial discussion of the allegation and issues of possible noncompliance occurs without the PI present.
- 2) The PI attends the meeting to allow the opportunity to describe the issue of possible noncompliance.
- 3) The IRB Executive members ask the PI questions, and give the PI an opportunity to provide any new information that was not previously presented to the Board.
- 4) PI is provided an opportunity for final comment before being asked to leave the meeting.
- 5) The IRB Executive members have a final discussion and vote.
- 6) The possible actions, include but are not limited to, that could be taken by the IRB include:
- 7) Suspension or termination of IRB approval of protocols that are found to be noncompliant with institutional policies and procedures, state laws, and/or federal laws or regulations, taking into consideration the welfare of currently enrolled subjects,
- 8) Compliance monitoring,
- 9) Letters of reprimand,
- 10) Restrictions on serving as an investigator on human subjects protocols,
- 11) Notification of currently enrolled subjects,
- 12) Providing additional information to past subjects,
- 13) Modification to research protocols,
- 14) More frequent continuing review or monitoring,
- 15) Changes in consent process or documents,
- 16) Requirement that currently enrolled subjects re-consent to participation,
- 17) Request more information prior to making a final decision,
- 18) Referral of the issue to other organizational entities such as UI legal counsel, risk management, or the research integrity officer, or

19) Other actions as appropriate.

The IRB determines which sanctions and/or requirements must be met for the study to proceed. If the investigator can meet these sanctions/requirements with simple concurrence, the IRB Chair determines when these are met and gives approval for the study to continue or recommence. If sanctions or requirements require more than simple concurrence, the issue is returned to the full board for consideration before resumption of the research project.

The IRB determines whether the noncompliance meets the definition of serious or continuing noncompliance.

After the IRB Executive Committee Meeting:

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

Appeal Process for Determinations of Serious and/or Continuing Noncompliance:

The PI may appeal IRB determinations of serious and/or continuing noncompliance. Such an appeal must be submitted in writing to the Chair of Record listed on the Monitoring Report. The basis for the appeal must be new information that was not previously available or considered by the IRB during the meeting in which the determination was made. The investigator must provide a rationale for the appeal and any other relevant supporting documentation.

Appeals containing new information will be scheduled for review by IRB Executive Committee. If the appeal requires discussion or explanation beyond what is provided to the board in written format, the PI may be invited to attend the meeting to answer questions. The IRB will notify the PI in writing via the meeting minutes of the discussion and vote on the appeal.

The notification process for determinations of Serious and/or Continuing Noncompliance follows the procedures outlined in the section IRB Determinations Requiring Reporting.

9.C.iii Review of Unanticipated Problems Involving Risk to Subjects of Others

Refer to the section on Review of Reportable Events.

If an unanticipated problem involving risks to subjects or others is related to serious and/or continuing noncompliance as determined by the full board, the IRB will follow procedures for reporting to the appropriate regulatory agencies and institutional officials. Refer to Allegations of Noncompliance.

Part 10: Operations of the University of Iowa IRBs

10.A IRB Records and Confidentiality

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

Copies of all research records for studies that do not involve protected health information must be kept for at least three years after the close of the study.

Copies of all research records for studies that involve protected health information must be kept for at least six years after the close of the study. HIPAA regulations provide individuals the right to receive an accounting of certain disclosures of protected health information made by a covered entity. This accounting must include disclosures of protected health information that occurred during the six years prior to the individual's request for an accounting and must include specified information regarding each disclosure.

Copies of all research records for VAHCS studies must be kept indefinitely after the close of the study. IRB records are retained in accordance with VHA Records Control Schedule (RCS 10-1).

Studies that involve drugs or devices seeking FDA approval must be kept for two years after the FDA has taken final action on the marketing application. Sponsors may require a longer retention rate.

Ultimately, it is the Principal Investigator's responsibility to maintain accurate files of IRB correspondence, approvals, and research records during the life of the study and after completion of the research. All correspondence and IRB documentation related to the project is available electronically through the HawkIRB application.

All research records should remain confidential and be stored in a manner such that confidentiality can be maintained even after the research study is complete.

10.B IRB Chairs & Members

10.B.i Appointments of Members

The Associate Vice President for Research: Regulatory Affairs (Institutional Official) appoints all University of Iowa IRB-01 and IRB-02 Chair(s) and members. The length of appointment is at

the discretion of the Associate Vice President for Research: Regulatory Affairs. The IRB-03 Chair(s) are appointed by the VA Medical Center Executive Director for a term of three years and may be re-appointed indefinitely.

10.B.i.a IRB Chairs

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 University of Iowa IRB. 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 Human Subjects Office administration and through periodic reports of University of Iowa IRB application activity.

Responsibilities of the Chairs include:

- 1) determining the type of review for initial, continuing review, and modification applications (exempt, expedited, full board) based on regulatory criteria,
- 2) conducting expedited reviews and approvals,
- 3) assigning primary reviewers for and running full board meetings,
- 4) reviewing minutes,
- 5) reviewing specific revisions to protocols/consent documents that are required as conditions of approval,
- 6) signing the application form certifying project approval,
- 7) reviewing reports of unanticipated problems involving risks to subjects or others,
- 8) suspension of research procedures,
- 9) referral to convened IRB for consideration of termination of research procedures.
- 10) Review and reporting 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
- 11) In addition, the Chairs serve as resources for investigators and University of Iowa IRB members regarding issues related to University and federal policies

10.B.i.b Primary members

Each University of Iowa 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. University of Iowa IRB members are selected with varying backgrounds of expertise, experience, and diversity to promote complete and adequate review of research activities. Each University of Iowa 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. 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/Assistant Director and reviewed on an ongoing basis by the University of Iowa IRB Chairs and Human Subjects Office Executive 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/Assistant Director conducts directed recruitment of individuals with the needed expertise or experience. Recommendations may come from the University of Iowa IRB Chairs, other University of Iowa IRB members, academic unit Deans, Directors, or Officers. Recommendations are reviewed with the Institutional Official who makes the final offer of membership.

10.B.i.c Alternate members

Alternate IRB members 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. 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.

10.B.i.d IRB Chair Designee(s)

Whenever a Chair is not available to conduct University of Iowa 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.

10.B.i.e 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 University of Iowa. The presence of these members at the meetings of the University of Iowa IRBs 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 at the meetings. University of Iowa IRB meeting minutes reflect the presence of non-voting members.

10.B.ii Responsibilities of members

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 all meeting materials.

University of Iowa 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 University of Iowa IRB Chair may be asked to step down from University of Iowa IRB membership by the Associate Vice President for Research: Regulatory Affairs.

10.B.ii.a Criteria for Approval

The University of Iowa IRBs approves all studies using the Criteria for IRB Approval of Research, the full text of which is listed in 45 CFR 46.111.

In order to approve research involving human subjects, the IRB must determine at every review that:

- 1) Risks to subjects are minimized
- 2) 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.
- 3) Selection of subjects is equitable.
- 4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116.
- 5) Informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117.
- 6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- 7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- 8) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or

economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

10.B.ii.b Suspension or Termination of IRB Approval

“Suspension” means the convened IRB or an IRB Chair has required 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” means the convened IRB has required a permanent halt to some or all research activities in a previously approved IRB project.

Federal regulations (45 CFR 46.113) grant the IRB the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval must include a statement of the reasons for the IRB's action and must be reported promptly to the investigator, the appropriate institutional officials, and the department or agency head.

10.B.ii.c Determinations of Noncompliance

The IRB Chair and members are responsible for reviewing allegations of noncompliance and making determinations of noncompliance and serious and/or continuing noncompliance. IRB determinations of serious and/or continuing noncompliance require reporting to appropriate institutional entities and regulatory agencies. Refer to the section on Noncompliance Investigations and Actions and IRB Determinations Requiring Reporting.

10.B.ii.d Review of Reportable Events

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

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

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

are reportable directly to WIRB. [For IRB-03 studies, reporting must occur within five working days. When IRB-03 is the IRB of record, all VHA reporting actions are in accordance with the requirements of the VHA Handbook 1058.01 "Research Compliance Reporting Requirements found here.](#)

Field Code Changed

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

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

Examples of unanticipated problems involving risks to subjects or others include, but are not limited to:

- 1) a breach of confidentiality
- 2) a subject complaint when the complaint indicates unexpected risks or cannot be resolved by the investigators,
- 3) a research team member experiences harm in the conduct of the study,
- 4) 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.

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

- 1) death
- 2) life-threatening adverse drug experience
- 3) inpatient hospitalization or prolongation of existing hospitalization
- 4) a persistent or significant disability/incapacity
- 5) a congenital anomaly/birth defect
- 6) important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug event when, based upon

appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed above.

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

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.

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

If a subject is enrolled by UI\VAHCS investigators, the investigator must report either serious adverse device effects or unanticipated adverse device effects. FDA regulations require the sponsor to report the results of any evaluation of an unanticipated serious adverse device effect to all reviewing IRBs and participating investigators. Any such reports are initially received by the investigator who is in turn responsible for reporting this information to the IRB-01 or IRB-03. By definition, these effects must be associated with the use of the device.

Investigators must also report any 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 also self-report noncompliance. Noncompliance is a failure to follow the federal regulations with respect to protection of human subjects in research or failure to follow the determinations of the IRB with respect to conduct of the research as approved by the IRB.

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

Research Involving Recombinant DNA Molecules (NIH Guidelines). Gene therapy investigators must submit annual reports to OBA as set forth in Appendix M-I-C-3 of the NIH Guidelines.

Investigators must report any of the above issues using the Reportable Event Form (REF) in the HawkIRB system. This form includes a description of the event, the date of occurrence, whether it is a local or outside report, how the event affected the rights, safety or welfare of the subject or others, current status of subjects, and any planned changes or modifications to the project as a result of the event. Reports from the investigator to the IRB must be submitted via HawkIRB within ten working days of the event or within 10 working days of the PI becoming aware of the event.

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

All reportable events are electronically filed with the appropriate research study. These reports are also reviewed by the IRB at the time of continuing review.

[Reports of all such problems for all projects reviewed by the Chair or convened IRB are provided by e-mail to all IRB-01 and IRB-02 members as appropriate on a monthly basis. For IRB-03, they are reviewed by the full board at regular monthly IRB meetings.](#)

~~[Reports of all such problems for all projects reviewed by the Chair or convened IRB are provided by e-mail to all IRB-01, IRB-02, or IRB-03 members as appropriate on a monthly basis.](#)~~

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 will vote on the recommended actions.

The IRB or IRB Chair may take any of the following actions or other actions as appropriate:

- 1) Modification of the protocol,

- 2) Modification of the consent document,
- 3) Providing additional information to current subjects – this is done whenever the information relates to the subject’s willingness to continue participation,
- 4) Providing additional information to past subjects,
- 5) Requiring current subjects to re-consent to participation,
- 6) More frequent continuing review or monitoring (this can include observation of the research or consent process),
- 7) Requiring additional training of the investigator,
- 8) Notification of investigators at other sites,
- 9) Suspension or termination of the research
- 10) Obtain additional information

10.B.iii Compensation of Members

The Office of the Vice President for Research and Economic Development provides no compensation to members of the University of Iowa IRBs with the exception of parking vouchers provided to community members to cover the cost of parking during meetings of the University of Iowa IRB. The departments of physician members and of IRB Chairs receive compensation for their time commitment to the University of Iowa IRBs.

10.B.iv Role of Consultants

The University of Iowa IRBs may invite scientists or non-scientists from within or outside the University of Iowa, 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 University of Iowa IRB relevant to the specific project under review, may participate in the deliberations and make recommendations on the project, but may not vote. At the time of preliminary review of a project application, the University of Iowa IRB Chair or Primary Reviewer may decide that the study requires further review by a consultant with expertise outside of the current University of Iowa 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 or other reasons.

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. A signed confidentiality agreement will be required from the consultant prior to completing the review process. 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. The consultant’s written response to

these questions will be provided to the full University of Iowa 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, complete a primary reviewer checklist, and attend the full board meeting during the review of that particular study. The consultant will leave prior to the final vote by the University of Iowa IRB. Documentation of the discussion with the consultant will be included in the meeting minutes.

10.B.v Conflict of Interest of IRB Members

No University of Iowa 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 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 University of Iowa IRB; however, he/she cannot participate in the review and approval process for any project in which he/she has a conflict of interest. The 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 University of Iowa 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 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.

10.B.vi IRB Member Liability

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

Part 11: Human Subjects Office

11.A What is the Human Subjects Office?

The Human Subjects Office is the administrative office that supports the Institutional Review Boards at the University of Iowa. The department is a unit of the Office of the Vice President for Research and Economic Development.

11.A.i Structure of the Human Subjects Office

The staff of the Human Subjects Office report to the Executive Director of the Human Subjects Office. The Associate Vice President for Research, Regulatory Affairs oversees all staff of the Human Subjects Office. A chart depicting the organizational structure of the office is on the Human Subjects Office website.

11.A.ii Scope and role of the Human Subjects Office

The mission of the University of Iowa Institutional Review Boards is to assure that the rights and welfare of human subjects are protected adequately in research.

Staff of the Human Subjects Office maintains:

- 1) files on all human subjects research (including copies of all correspondence between the IRB and investigators) that takes place at the University of Iowa;
- 2) databases for tracking studies;
- 3) files of minutes of full board meetings;
- 4) the institution's Federalwide Assurance, the IRB membership rosters, and a resume for each IRB member;
- 5) information on federal regulations relating to human subjects research;
- 6) a human subjects research monitoring program;
- 7) all correspondence between the IRB and the R&D Committee.

Staff of the Human Subjects Office assists:

- 1) the University of Iowa IRBs in preparing for and monitoring IRB meetings;
- 2) with preparation of meeting minutes;

In addition, staff:

- 1) screens research applications for completeness prior to initiating the IRB review process;
- 2) acts as a resource for investigators on general regulatory information, guidance with forms, and assistance in preparing an application for IRB review;
- 3) provides staff support to the IRBs for all written correspondence;
- 4) sends notices of approval, study closure (other than closure of the study by the investigator) for externally sponsored projects to the University of Iowa DSP or the CTO;

- 5) generates and sends reminder notices to investigators of upcoming continuing reviews;
- 6) provides education regarding the IRB process and regulations to the University community;
- 7) coordinates submission of application materials required by Western Institutional Review Board;
- 8) checks the short form consent process for compliance with regulatory requirements

11.B Electronic Research Application – HawkIRB

HawkIRB is the electronic application system for the University of Iowa IRB. University of Iowa faculty, staff, and student investigators must submit IRB applications via HawkIRB. The Human Subjects Office does not accept paper-based IRB applications. Additional information about HawkIRB is on the HSO website.

11.B.i Access to HawkIRB

Access to the HawkIRB system is available only to University of Iowa faculty, staff, and student researchers and research administration staff via HawkID authentication. Additional information about HawkIDs is available from Information Technology Services.

11.B.ii Inbox Settings

The inbox page is the HawkIRB equivalent of a personal homepage. By default, the page is set to show any studies for which the employee is the Principal Investigator. An employee may view others studies for which s/he is a research team member by changing the filter. To see projects other than those that are currently open, change the project status at the far right side of the filter.

11.B.iii Setting up a Profile

The first time an employee logs into the HawkIRB system, the employee will be required to update his/her profile on a screen that will automatically appear directly after log in. The IRB uses this information to contact the employee about his/her studies and to provide the investigator's degree information for the Informed Consent Document. As such, it is very important that this profile contain accurate information. An employee can only make changes to his/her profile using the Personalize menu in HawkIRB.

11.B.iv Delegate Permissions

A Principal Investigator may designate another person to act on his or her behalf in the HawkIRB system. This person is a delegate and has the same permissions within HawkIRB as the Principal Investigator. Instructions for HawkIRB's Delegate Permissions system, including visual depiction of the delegation process is available on the HawkIRB Delegate Permissions Page of the Human Subjects Office website.

11.B.v Version updates

Due to changes in university policies, regulatory guidance, or other reasons, technical support for the Human Subjects Office will make periodic updates to the HawkIRB application. The current version number of the HawkIRB application is shown in the lower left hand corner of the Inbox page. When possible, the Human Subjects Office will announce any periods of "downtime" in advance on the Human Subjects Office webpage under the heading Announcements.

11.B.vi Compliance

HawkIRB is compliant with Food and Drug Administration guidance about electronic records and signatures as outlined in 21 CFR Part 11 often referred to as "Part 11 compliance".

11.C HawkIRB Application Processing/Workflow

HawkIRB is the electronic application system for IRB review at the University of Iowa. All application processing occurs via the electronic system. Due to the volume for IRB-01, and the bi-monthly meetings for IRB-02, investigators should allow a minimum of three to four weeks for an application to be scheduled for review at a convened meeting. IRB-03 investigators should allow a minimum of four weeks for an application to be scheduled for review based on the IRB-03 meeting monthly schedule.

Once an investigator submits an application to the IRB, Human Subjects Office staff review the application prior to its review the IRB. Human Subjects Office staff and IRB Chairs communicate with investigators via the HawkIRB workflow system. Instruction about how to use the workflow system is located in the "What to Expect During the IRB Review Process" FAQ.

Staff Review is an initial check of the application to make sure that it is completed with expected attachments, and all questions answered, and a cursory look at responses for compliance with HSO policy.

Senior Staff Review is a higher level of review that involves analysis of responses for compliance with federal regulations, current guidance, and other applicable policies.

The IRB Coordinator schedules IRB members to meetings ensuring a quorum is available, and ensures that materials for review are presented to members.

11.C.i Staff Review

All HawkIRB applications receive an initial administrative review or staff review by the HSO. Staff members conduct a thorough review of the entire HawkIRB form and only return the application to the investigator for the following reasons:

- 1) The incorrect IRB (IRB-01, IRB-02, or IRB-03) was selected. The board that reviews the application depends on the department in which the research is conducted.
- 2) The full grant application for each funding source is not attached to the application.
- 3) The incorrect Consent and/or Assent Documents are attached or the documents are not attached in the correct format (Rich Text Format) with a valid IRB approval stamp placeholder in the upper right hand corner.

The attached Assurance Document does not include all of the required signatures (the Principal Investigator, Department Executive Officer (DEO or Dean) and Faculty Advisor (if the investigator is a student)).

The staff reviewer will also note any other issues or concerns and route the application to the senior staff reviewer.

11.C.ii Senior Staff Review

The HSO has groups of staff dedicated to the review of applications for biomedical research or social/behavioral research (for more information, refer to the section on the Scope of IRB Review at the University of Iowa). Senior staff reviewers attend IRB meetings and are familiar with the concerns that are typically raised by the IRB. During this level of staff review or application analysis, reviewers make requests or suggestions for revisions for the following reasons:

- 1) To provide the IRB Chair or the full board with a thorough description of the study
- 2) To address issues that are common concerns for the IRB Chair or the full board
- 3) To ensure that the HawkIRB application fully addresses the regulatory criteria for approval

Senior staff review the application to ensure the following

- 1) There are thorough, detailed answers to the HawkIRB questions
- 2) The answers provide the information requested in each section of the application
- 3) The Informed Consent Document includes all of the required elements of consent

- 4) A complete description of subjects' eligibility criteria
- 5) All recruitment and consent methods/materials are described and attached
- 6) All potential risks to subjects and efforts to minimize those risks are described
- 7) Consistency between the responses and the attached documents
- 8) All study procedures comply with federal regulations and UI policies and procedures

11.C.iii IRB Coordinator Responsibilities

Each IRB has a meeting coordinator who is responsible for polling the availability and scheduling of board members to attend meetings. The coordinator makes sure there are board members with the necessary expertise to review each study and a member will be present whose background and training is in a nonscientific field. The coordinator is also responsible for ensuring that there will be quorum for each item on the meeting agenda before preparing and distributing meeting materials to board members.

11.C.iii.a Scheduling of Meetings and Applications for Full Board Review

IRB-01 is scheduled to meet once or twice each week. In addition, on an every-other-week basis, an additional meeting is held. 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 fourth week of the month. IRB-03 meetings are scheduled once per month.

Human Subjects Office 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, Human Subjects Office 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 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.

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

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

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

11.C.iii.a.i Western Institutional Review Board application processing

If a research study goes to Western Institutional Review Board for review, there are some requirements of the University of Iowa prior to submission. First, the Division of Sponsored Programs must have a copy of the contract and protocol for the project. Second, if the project requires review by any University of Iowa committees, investigators must have the approvals of the applicable committee prior to Western Institutional Review Board review. Finally, investigators will need to send all of Western Institutional Review Board submission materials to the University of Iowa Human Subjects Office so that the Western Institutional Review Board coordinator can check for other committee approvals and the required University of Iowa consent language. At this point, the University of Iowa Human Subjects Office will provide the investigator with an approval memo for submitting new project materials to Western Institutional Review Board for review. The Human Subjects Office charges a \$2000 one-time fee for this administrative review. The Human Subjects Office website contains a detailed description of the University of Iowa process for submission to Western Institutional Review Board and required forms.

Once the new project has been sent to Western Institutional Review Board for review, Western Institutional Review Board is the IRB of record for the project. At that point, all investigator correspondence regarding the project will be with Western Institutional Review Board. In addition, after Western Institutional Review Board approval of the project, the investigator is responsible for submitting all modifications, continuing reviews, serious and/or unexpected adverse experiences, major protocol violations that result in additional risks to subjects, and project closure notice to Western Institutional Review Board using Western Institutional Review Board procedures. The University of Iowa Human Subjects Office will not coordinate any of these submissions after the approval of the new project by Western Institutional Review Board. For more information on Western Institutional Review Board procedures, review the Western IRB website.

11.C.iii.b Review of Closure Forms

Once a Project Closure Form is submitted the IRB, it cannot be withdrawn. The forms are reviewed by human subjects office staff prior to being filed. Investigators may receive questions related to closure forms if the form contains any information that is unclear or that is not in agreement with the existing information about the project in HawkIRB.

11.C.iv Full Board Review Responsibilities

If the project requires full board review, the date of the full board review will be listed under the heading "Agenda Date" on the Project Summary page in HawkIRB. The HSO will notify the investigator if s/he is requested to attend the meeting. The HSO distributes copies of the Application Form, Informed Consent Document, and other supporting materials to members attending the meeting about a week in advance. The Principal Investigator should review the workflow in HawkIRB to track the project progress. Email notifications are not sent for the stages of meeting preparation.

In HawkIRB, when the project is ready to be scheduled to a full board meeting, it shows in workflow as "Pre- Meeting Prep." At this stage, the application and materials are being prepared for a full board meeting. When the application moves in workflow to "Scheduled," it has been scheduled to a meeting.

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

11.C.iv.a IRB Meeting Procedures

The University of Iowa 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. A senior Human Subjects Office Full Board staff member or the University of Iowa IRB Chair monitors the quorum throughout the meeting.

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 University of Iowa 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; informed consent will be appropriately documented or waived; 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 University of Iowa IRB and any changes required.

11.C.iv.b Documentation of Meeting Minutes and Board Determinations

IRB Full Board staff write minutes that contain the following information:

- 1) which IRB (IRB-01, IRB-02, or IRB-03) reviewed the project;
- 2) attendance at each meeting including those members or alternate members who participated through videoconference or teleconference,
- 3) documentation that those members not physically present received all pertinent materials prior to the meeting and were able to participate in all discussions.
- 4) 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;
- 5) the vote on actions taken by the IRB including the number, for, against and abstaining;
- 6) Separate deliberations for each action, where applicable;
- 7) 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;
- 8) justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in the Department of Health and Human Services-approved sample informed consent document;
- 9) the basis for requiring changes in or disapproving research;
- 10) the length of time of an approval;
- 11) a written summary of the discussion of controverted issues and their resolution;
- 12) specific comments relevant to inclusion of certain populations;
- 13) whenever a significant risk/non-significant risk determination is made, the rationale for significant risk/non-significant risk device determinations.
- 14) 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. After approval by the IRB, the minutes cannot be altered by anyone including a higher authority.

11.C.iv.c Revisions Prior to Final Approval

Revisions to human subjects applications may be required after IRB review. The IRB sends correspondence 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 University of Iowa IRB review.

When specific changes are requested by the convened IRB in the protocol and/or consent document(s) that require no more than simple concurrence, the Chair reviews these for compliance 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.

11.C.v Expedited Review

Federal regulations recognize certain kinds of research that may be reviewed and approved by an IRB Chair (or designee) rather than by the full board. Expedited review does not mean that the review occurs more quickly than full board review.

The expedited review procedure cannot be used for projects where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless the investigator has documented that reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

The IRB Chair or designee is responsible for determining whether the research meets the expedited criteria, based on review and approval of the investigator's application to the IRB. However, it is at the IRB Chair's or designee's discretion to require full board review, even when the project appears to meet the criteria for expedited review.

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 University of Iowa IRB members on a monthly basis. These reports include initial reviews, continuing reviews and reviews of modifications to previously approved research.

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

The expedited review process may be used for the initial review of projects involving no more than minimal risk, and only those procedures listed in one or more of the following categories. The activities listed are not deemed to be of minimal risk simply because they are included on the list. Inclusion on the list means that the activity is eligible for expedited review when the specific circumstances of the proposed research involve no more than minimal risk to human subjects. If the research project as a whole involves more than minimal risk, it is reviewed by the full board, even if the activities are limited to those listed.

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.

The continuing review of research may be expedited in certain instances as designated by federal regulations:

- 1) 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).
- 2) 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 (e.g. research is within those categories and experience confirms the research to be of no greater than minimal risk)
- 3) If continuing review of the research was previously approved by the convened IRB and 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
- 4) no subjects have been enrolled and no additional risks have been identified; or
- 5) the remaining research activities are limited to data analysis.
- 6) If continuing review of the research was previously approved by the convened IRB and
- 7) the research is not conducted under an investigational new drug application or an investigational device exemption, and
- 8) the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk, and
- 9) 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 as described above.

Studies involving prisoners may not be reviewed under expedited procedures regardless of whether they meet the criteria above except for (1) new studies limited in scope to retrospective review of prisoners' records and (2) minor modifications to already approved research. In the case of these exceptions, approval of the research can only be granted after review of and comment on the protocol by the prisoner advocate member of the IRB.

11.D Education

The Education and Compliance Program staff in the Human Subjects Office provides a variety of educational opportunities for the IRB members, Human Subjects Office staff, the research community at the University of Iowa, and at public events.

11.D.i Responsibilities of Education and Compliance Program Manager

The Education and Compliance Manager provides administrative oversight and guidance to all Education and Compliance Specialists and the Education and Compliance Program student employee. Additionally, the Education and Compliance Manager investigates complaints and concerns, oversees program development and project management, and assigns monitoring and other responsibilities to the Education and Compliance Program staff.

11.D.ii Responsibilities of Senior Education and Compliance Specialists

Senior Education and Compliance Specialists monitor ongoing research, investigate allegations of noncompliance and complaints and concerns. In addition, the Sr. Specialists assist in program development for monitoring and education, conduct monitoring visits, lead educational programs, promote and conduct outreach activities, write and maintain educational materials, and provide guidance to non-senior Specialists and student workers.

11.D.iii Responsibilities of Education and Compliance Specialists

Education and Compliance Specialists who are not senior level employees conduct monitoring visits, assist in scheduling and promoting educational programs, assist in writing and maintaining educational materials, and provide guidance to student workers.

11.D.iv Scope of Education

The Institutional Review Board (IRB) Education and Compliance Program is charged with addressing the needs of investigators and research team members as well as that of the

institution to ensure research is conducted according to UI policy and federal regulations for the protection of human subjects.

To assist investigators, IRB members, and Human Subjects Office staff in complying with federal regulations, IRB and university policies for the protection of human subjects, the IRB Education and Compliance program offers a variety of educational resources.

11.D.vi Researchers

The Education and Compliance Staff offer educational sessions for university researchers each semester, and throughout the year.

11.D.vi.a HawkIRB Training Sessions

HawkIRB is the web-based IRB application and review system. HawkIRB training sessions provide basic information about technical aspects of the HawkIRB system and guidance about content for specific sections and questions in the HawkIRB application. These sessions are for anyone preparing to submit a HawkIRB application for the first time and for those who would like guidance about completing HawkIRB forms.

These sessions are intended to teach investigators, delegates, and research team members how to prepare HawkIRB applications to facilitate the IRB review process. There is a two-part HawkIRB training series:

11.D.vi.b How to Complete a New Project Application

Attendance at the New Project session is recommended before attending the second session on Investigator Responsibilities after IRB Approval. Individuals interested in attending a HawkIRB training session are encouraged to pre-register for the session on the HSO website. Presentations on Research-Related Topics

The IRB Education and Compliance Program offers hour-long presentations on a variety of topics related to human subjects research. These presentations are designed to provide information on topics of interest to Principal Investigators, Study Coordinators, research team members, and members of the University of Iowa research community. Individuals interested in attending a presentation can review the semester schedule and pre-register to attend on the HSO website. IRB Education and Compliance Program staff welcome suggestions via email or phone on topics of interest by the UI research community.

11.D.vi.c Classroom Presentations

The IRB Education and Compliance Program staff deliver classroom presentations on a variety of research-related topics. We consult with course instructors to create presentations that meet the needs of the students, on topics such as:

- 1) Requirements for course-related student projects
- 2) When and why IRB approval is required
- 3) How to ask whether IRB approval is necessary using the Human Subjects Research Determination (HSRD) form
- 4) What to expect from the IRB review process
- 5) Ethical conduct of human subjects research
- 6) Flexibility in the federal regulations regarding IRB review and informed consent
- 7) Ethical conduct of human subjects research

Faculty members or class instructors interested in requesting a classroom presentation may contact the IRB Education and Compliance Staff by phone or email.

11.D.vi.d IRB Connection Newsletter

The monthly IRB newsletter is shared with UI investigators and research team members involved in the conduct of human subjects research who are interested in learning more about:

- 1) UI IRB policies, federal regulations and guidance
- 2) Human subjects research in the news
- 3) Helpful advice from front line IRB application reviewers
- 4) Answers to frequently asked questions

The newsletter is posted on the HSO web site and distributed to people on the IRB LISTSERV. Sign up for the LISTSERV on the HSO website.

11.D.vi.e Office Hours

IRB Office Hours are for all UI faculty, staff, and student Principal Investigators, HawkIRB delegates, and research team members involved with Human Subjects research.

Office Hours Objectives:

- 1) Answer questions about conducting human subjects research.
- 2) Provide guidance and answer questions about the electronic application forms in the HawkIRB system.
- 3) Provide suggestions and guidance about study procedures that are in compliance with federal regulations and the UI IRB policies.

- 4) Provide guidance and answer questions about the submission of industry-initiated and industry-sponsored research projects to Western IRB (WIRB).

11.D.vi.f *ICON Courses for Researchers*

The HSO offers web-based education on the HawkIRB application system as well as topical issues on human subjects research. Courses are available via Iowa Courses Online (ICON). Many in-person presentations and training sessions provided by the IRB Education and Compliance program are recorded and available for viewing on ICON.

University of Iowa faculty, staff, students, and non-University of Iowa investigators engaged in Community-Based Research can access ICON courses by going to the HSO website.

Faculty members or courses instructors who are interested in using IRB ICON courses as a class or group requirement may contact the IRB Education and Compliance Program staff by phone or email.

IRB members and Human Subjects Office staff Education and Compliance Program Staff are also responsible for providing education to IRB members, Human Subjects Office staff, and university departmental liaisons.

Continuing Education is provided on a monthly or twice a month basis. The education consists of written modules about topics relevant to IRB review and human subjects research protections. Each month's education includes a quiz to document staff and member compliance with the education requirement. Completion rates of continuing education activities are reviewed annually by the HSO Director. An annual notice of this review is provided to the Institutional Official, VA Research Office and the IRB member.

11.E Compliance monitoring

11.E.i *Scope of monitoring*

The IRB Education and Compliance Specialists are full-time Human Subjects Office staff members who conduct pre- and post-approval monitoring of human subjects research under the purview of the University of Iowa IRB and Western Institutional Review Board. The program also provides educational resources, training sessions, and other programming to University of Iowa faculty, staff and students.

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/Human Subjects Office 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.

11.E.ii Types of Compliance Monitoring

11.E.ii.a Post-Approval Responsibilities Review

PARR is an educational session that takes place after a study is approved by the IRB. During the session, the IRB Education and Compliance Specialist will review post-approval responsibilities of the investigator and research team members based on university policies and federal regulations such as reporting requirements regarding recruitment, consent, and conduct of the study.

Post-approval responsibilities for the following topics will be reviewed:

- 1) Recruitment Process
- 2) Consent Process
- 3) Study Enrollment
- 4) Continuing Review
- 5) Modifications
- 6) Unanticipated Problems Involving Risks
- 7) Record-Keeping
- 8) HawkIRB System

Goal of PARR Visit. The goal of a PARR visit is to educate investigators and research team members about their responsibilities after IRB approval of the research study and to highlight available resources.

11.E.ii.b Post-Approval Monitoring and Education Visit

PAM and Ed encompasses all monitoring and follow-up education activities of open, IRB-approved human subject research studies conducted by University of Iowa faculty, staff or students.

During the PAM and Ed process, the IRB Education and Compliance Specialist reviews current study procedures (compared with IRB-approved study procedures) and may also review research records including:

- 1) Screening records and logs
- 2) Enrollment logs
- 3) Signed consent documents
- 4) Research subject files
- 5) Sample storage
- 6) Study data records and transmission procedures

Goals of PAM and Ed Visit. The goals of a PAM and Ed visit are to ensure that (1) the research is conducted in accordance with federal regulations and University of Iowa Standard Operating Procedures for the conduct of human subjects research; (2) to facilitate communication between the IRB and researchers at the University of Iowa, (3) to provide individualized education regarding the conduct of human subject research.

11.E.ii.c Directed Monitoring

Directed monitoring is any monitoring that is done at the request of the IRB. This monitoring can be mandated as a result of information from outside sources such as subjects or research team members, etc. or information that comes to light during the review of an application or another study by the IRB. Directed monitoring could also include observing the informed consent process.

Directed monitoring provides the IRB with additional information to substantiate or refute allegations of noncompliance on the part of the researchers. Information reviewed during a Directed visit will vary based on the nature of the visit.

Goal of Directed Visit. The main goal of Directed monitoring is to investigate possible non-compliance of researchers. In addition, action plans and additional education will be employed to remedy noncompliance or potential noncompliance.

11.E.ii.d Department of Defense (DoD) Sponsored Research Monitoring

Research conducted or supported by the DoD, including its separate components (i.e., the Army, Navy, Air Force and Marine Corps), requires compliance with additional federal regulations, directives and instructions. The Principal Investigator (PI), IRB and institution involved in DoD research must be knowledgeable about these obligations in order to adhere to them. UI investigators conducting DoD sponsored research should expect to meet with an IRB Education and Compliance Specialist at least once to discuss and document DoD compliance. Additional monitoring activities to deliver education and document compliance may be

conducted via email. Investigators are encouraged to work closely with their DoD component contact to insure all the necessary information and documentation is obtained for the UI IRB review process.

Goal of DoD-Sponsored Research Monitoring. The goal of a DOD-sponsored research monitoring visit is to deliver investigator education on additional DoD regulatory requirements and to document PI and IRB compliance with DoD and DoD component (Army, Navy, Air Force and Marine Corps) regulations, directives and instructions.

11.E.ii.e Student Principal Investigator/Faculty Advisor Oversight and Assurances Review

The SPI-FA Oversight and Assurances Review starts with an online Qualtrics surveys sent to the student PI and their Faculty Advisor. The surveys provide information about and documents acknowledgment of PI and Faculty Advisor responsibilities regarding the conduct of human subjects research. If both surveys are completed and submitted to the IRB Education and Compliance Program and there are no issues or concerns noted in the survey responses, or the PI/Faculty Advisor do not request an in-person meeting, the review will conclude with a memo signed by the IRB Chair.

Goals of SPI-FA Oversight and Assurances Review. The goals of a SPI-FA review are (1) to offer individual education and assistance to student investigators and their Faculty Advisors; (2) answer questions about the IRB and/or the review process; (3) address potential concerns or problems before they occur; (4) provide guidance on PI and Faculty Advisor responsibilities; (5) establish long term connections with faculty members advising student investigators.

11.E.iii Compliance Monitoring Process

Notification. Once a study has been selected for compliance monitoring, an IRB Education and Compliance Specialist sends an e-mail notice to the Principal Investigator (PI) and contact persons for the study. The e-mail notice requests that the PI arrange two meetings; one meeting is for the review of Informed Consent Documents (ICDs), and the other is for the study review meeting.

If the Education and Compliance Specialist does not hear back from the research team within two business days, s/he will either send a second notification via e-mail, or call the PI and/or research study contact person(s) until contact is made.

Notification and Review of SPI-FA Oversight and Assurances Review. Once a student PI and their Faculty Advisor are selected for review, the IRB Education and Compliance Specialist sends separate e-mail notices to the PI and their Faculty Advisor. The e-mail notice includes a unique survey link for the PI and Faculty Advisor to follow. Responses should be provided in each

survey and the attached educational materials should be reviewed before the survey is submitted by the PI and Faculty Advisor.

If the Education and Compliance Specialist does not hear back from the PI and/or the Faculty Advisor within the 2-week deadline to submit the survey, a reminder notification will be sent via e-mail. If both surveys are not submitted within 2 business days, the IRB Education and Compliance Specialist will send a follow-up email to the PI and Faculty Advisor notifying both that an in-person compliance monitoring visit will be required within the next 2 weeks.

Number of Visits and Length. The compliance monitoring process is made up of two in-person meetings. The length of the first meeting (referred to as the 'Consent Document Review') varies based on the number of ICDs to be reviewed. The IRB Education and Compliance Specialist will inform the team of the approximate time needed for review when scheduling the meeting. The PI is not required to attend this meeting; however, at least one member of the research team who conducts the informed consent process should be available to answer questions if needed. The IRB Education and Compliance Specialist will discuss specifics about the accommodations needed when scheduling the visit.

The second visit is the study review meeting. The PI is required to attend this meeting. S/he may invite any members of the research team to the meeting that s/he wants or thinks would benefit from attendance. Those in attendance typically include the Principal Investigator, the study coordinator, and persons who conduct the recruitment and consents process, or study procedures. The length of the second visit is approximately two hours. However, the length may vary based on complexity of study and the amount of discussion that occurs with the research team during the visit.

Both visits should occur within one month of the investigator's receipt of the monitoring notice. Exceptions may be granted with appropriate justification.

Reporting and Response Process. After both meetings have been held, the IRB Education and Compliance Specialist will write a report of the monitoring process. This monitoring report will include required actions for the research team, a summary of the information discussed throughout the process, additional educational information, and regulations and guidance that pertain to the conduct of research involving human subjects.

Monitoring reports are reviewed by the IRB Chair of Record for the study. During the monitoring process, the IRB Education and Compliance Specialist will tell the research team the name of the Chair of Record for the study so that s/he may be contacted if the team has any questions or concerns that cannot be addressed by the IRB Education and Compliance Specialist.

Monitoring reports are provided to the Chair for review within two weeks after the date of the last compliance monitoring visit. If you have not received a final report within three weeks of

the visit and have not had any interim contact, please contact the IRB Education and Compliance Specialist that conducted the monitoring process.

Monitoring reports will be released to the PI via HawkIRB. The PI will receive an e-mail notice when the report is available for review. If applicable, a Modification form to submit any changes required as a result of the monitoring process will be created in the PI's Draft Forms section of his/her HawkIRB inbox. Additionally, the PI may be required to provide information via e-mail to the IRB Education and Compliance Specialist or the Chair of Record.

Response Review Process. Typically, the PI's response to the monitoring report requires the submission and review of a HawkIRB Modification form. However, in instances where the Chair of Record decides that the report findings may constitute serious and/or continuing noncompliance, reports will be referred to the IRB Full Board for review.

11.F Community Based Research

The Institutional Review Board/Human Subjects Office established the University of Iowa Community-Based Research (CBR) Program to address the needs of UI researchers involved in research collaborations or affiliations with non-UI organizations or independent individuals.

11.F.i Scope of Review

The CBR Program helps researchers to navigate the process of translational research. Information specific to community-based research including eligibility criteria and contact information is available [here](#).

11.G Quality Improvement

The HSO conducts a variety of quality improvement activities on an ongoing basis in order to provide the UI research community with timely IRB review of applications, educational resources and assistance in obtaining IRB approval, and ensuring compliance with federal regulations and UI policies for the protection of human subjects.

11.G.i Metrics Reporting

The University of Iowa IRB tracks metrics about the IRB review process including length of review, number of submissions per board, and other information as need arises. The Human Subjects Office updates these metrics periodically; they are available on the Human Subjects Office website under "UI IRB Metrics".

Part 12: University of Iowa Projects Involving Human Subjects or Their Data

When both Department of Health and Human Services and Food and Drug Administration regulations apply to research involving human subjects, the University of Iowa IRB applies the more rigorous regulations from each to the research being conducted to ensure the protections of the rights and welfare of the human participants.

12.A What is Research?

Department of Health and Human Services and the Food and Drug Administration define research as it relates to human subjects in 45 CFR 46.102 (d) and 45 CFR 56.102 (c) respectively. Unless otherwise noted, the university uses these definitions of research in determining whether IRB review is required.

12.B Who is a Human Subject?

Department of Health and Human Services and the Food and Drug Administration define the term human subject in 45 CFR 46.102 (f) and 45 CFR 56.102 (e) respectively. Unless otherwise noted, the university uses these definitions of human subject in determining whether IRB review is required.

12.C How do I know if my project is research involving human subjects?

If in doubt as to whether a project requires review by the IRB, prior to submitting a full New Project Application for IRB review, faculty and staff of the university should review information regarding obtaining a Human Subjects Research Determination.

If in doubt as to whether a project requires review by the IRB, prior to submitting a full New Project Application for IRB review, university students should review information regarding the Course-Related Student Project Policy, the Course-Related Student Policy Checklist, and the Human Subject Research Determination Form.

12.D Course-Related Student Projects and Human Subjects Research

The Course-Related Student Project Policy applies to all human subjects research activity conducted for purposes of teaching research methods at the University of Iowa. All activities meeting the federal definitions of human subjects research that are carried out at the University of Iowa or under its auspices must be reviewed and approved by an Institutional Review Board (IRB) prior to the start of the research. This policy document applies to undergraduate and/or graduate students at the University of Iowa and faculty members or instructors who supervise course-related student projects. This policy explains when students

should submit a human subjects research application for IRB review. The full text of the policy is located in the (in progress) policy e-book here.

12.D.i Course Related Student Project Policy checklist

The Human Subjects Office provides a checklist for students and their instructors/advisors to assist in the decision of whether or not a student project is subject to IRB review. This form is for use by the student and his /her advisor only; do not submit this checklist to the IRB. Access the checklist here.

12.E Human Subjects Research Determination

The University of Iowa IRB Chairs or Human Subjects Office staff provides guidance and determination with regard to when an activity meets either the Department of Health and Human Services definitions for human subjects research or Food and Drug Administration definitions for clinical investigation with human subjects. Submit requests for determinations via the HawkIRB application by completing a Human Subjects Research Determination form (HSRD). This short form is reviewed typically within 48 hours of submission by the IRB Chair or their designee.

A formal memo documents whether submissions meet the regulatory definition of Human Subjects Research. For those studies that meet the regulatory definition of Human Subjects Research, a new project application is automatically initiated on the Principal Investigator's behalf based on responses provided in the HSRD form. The remaining application will need to be completed and submitted for IRB review and approval prior to initiation of the research. For those studies that do not meet the regulatory definition of Human Subjects Research, the IRB does not require additional action on the part of the investigator.

12.E.i HSRD Booklet

The Human Subjects Office provides additional information regarding Human Subjects Research Determinations, and how to determine whether Quality Assessment\Quality Improvement projects and Case Reports require IRB review in a convenient pamphlet.

12.F Quality Assessment/Quality Improvement

Quality improvement projects (also referred to as quality assurance or quality improvement programs) are generally not considered research unless there is a clear intent to contribute to generalizable knowledge and use the data derived from the project to improve or alter the quality of care or the efficiency of an institutional practice. Any individual who is unsure whether or not a proposed quality improvement project should be classified as research should

contact the IRB for guidance. If the data are re-examined or re-analyzed and new information surfaces that would contribute to generalizable knowledge, an application must be submitted to the IRB.

12.G Case Reports

A case history, case report or case study which are published and/or presented at national or regional meetings are not considered research if the case is limited to a description of the clinical features and/or outcome of a three or fewer patients and do not contribute to generalizable knowledge.

Investigators should contact the IRB if they are uncertain as to whether or not they are contributing to generalizable knowledge.

Part 13: Exempt Human Subjects Research

University of Iowa policy requires all human subjects research proposals to be submitted for IRB review. However, certain types of human subjects research may be classified as exempt from the federal regulations. The IRB Chairs or designee are the sole authority for determining whether the research meets the exempt criteria, based on review and approval of the investigator's New Project application to the IRB. In making this determination the IRB Chair or designee considers any ethical issues. Exempt research projects have no requirement for continuing review.

Exemptions under the Department of Health and Human Services regulations are limited to research activities in which the only involvement of human subjects will be in one or more on the following categories. The exemption criteria listed below do not apply to research involving prisoners (45 CFR 46, Subpart C). There are six categories of exemptions (full text of the regulations is located at 45 CFR 46.101):

13.A

Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as

- 1) research on regular and special education instructional strategies, or
- 2) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

13.B

Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:

information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

13.C

Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if:

- 1) the human subjects are elected or appointed public officials or candidates for public office; or
- 2) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

13.D

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.

13.E

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:

- 1) Public benefit or service programs;
- 2) procedures for obtaining benefits or services under those programs;
- 3) possible changes in or alternatives to those programs or procedures; or
- 4) possible changes in methods or levels of payment for benefits or services under those programs.

13.F

Taste and food quality evaluation 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.

13.G Exempt research under the FDA regulations

Clinical investigations involving human participants are subject to IRB review under FDA regulations unless one of the following criteria applies:

- 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, 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.
- 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.

Part 14: Expedited Review

University of Iowa policy requires all human subjects research proposals to be submitted for IRB review. However, certain types of human subjects research may be reviewed under expedited procedures rather than reviewed by the full board. The IRB Chairs or designee are the sole authority for determining whether the research meets the expedited criteria, based on review and approval of the investigator's New Project application to the IRB. In making this determination the IRB Chair or designee considers any ethical issues. Expedited research projects must submit Continuing Review applications at least annually. In order to receive expedited review, research studies must meet federal regulatory requirements as described in 45 CFR 46.110 of the Department of Health and Human Services regulations. For any studies under IRB-03 review, a VA Supplemental Checklist documenting VA specific findings will be completed, when necessary, by the IRB Chair or their designee prior to final IRB approval.

A list of expedited review categories is posted in the Federal Register. The full text of these categories and how to apply them is available for review via the Department of Health and Human Services. A summary is provided below.

14.A

Clinical studies of drugs and medical devices only when condition (a) or (b) is met:

14.A.i

Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

14.A.ii

Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

14.B

Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

- 1) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
- 2) from other adults and children², considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than 2 times per week.

14.C Prospective collection of biological specimens for research purposes by noninvasive means.

Examples:

- 1) hair and nail clippings in a nondisfiguring manner;

- 2) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
- 3) permanent teeth if routine patient care indicates a need for extraction;
- 4) excreta and external secretions (including sweat);
- 5) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue;
- 6) placenta removed at delivery;
- 7) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
- 8) 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;
- 9) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
- 10) sputum collected after saline mist nebulization.

14.D Collection of data through noninvasive procedures

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:

- 1) 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;
- 2) weighing or testing sensory acuity;
- 3) magnetic resonance imaging;
- 4) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;
- 5) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

14.E Research involving materials

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).

(NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

14.F Collection of data from voice, video, digital, or image recordings made for research purposes.

Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

14.G Continuing review of research previously approved by the convened IRB as follows where:

- 1) the research is permanently closed to the enrollment of new subjects;
- 2) all subjects have completed all research-related interventions; and
- 3) the research remains active only for long-term follow-up of subjects; or
- 4) where no subjects have been enrolled and no additional risks have been identified; or
- 5) where the remaining research activities are limited to data analysis.

14.H Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

Part 15: Overall Approval

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

Overall approval is given via the expedited review procedure. Projects which have received only overall approval may not enroll human subjects. To obtain approval for the individual projects described in the training grant, center grant, or program project grant, the principal investigator of each individual project should submit a New Project Application in HawkIRB for each project that involves human subjects. When completing the application form for each

individual project in HawkIRB, the investigator should indicate the funding source as the funding agency that provided the overall award.

Part 16: Concept Approval

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

Human subjects may not be enrolled in a project given Concept approval. Concept approval is given via the expedited review procedure. Refer to the section on submitting modifications to the HawkIRB application to learn more about changing a project from Concept to Regular approval once the investigator is ready to enroll human subjects.

Part 17: Umbrella Project Approval

Umbrella project approval is an administrative term to describe a research study in which a single investigator submits an IRB application that will cover multiple projects which have a common hypothesis, set of investigators, or data set and for which details of the study procedures will only change minimally, if at all. This project, termed the "umbrella", allows for simple modification of research teams, study aims, or procedures at the discretion of the lead investigator, and approved by the IRB. For additional information and guidance about submitting an umbrella project, contact irb@uiowa.edu.

Part 18: Full Board Review

Studies that do not qualify for Exempt or Expedite review are assigned to review by full board at a convened meeting. All projects involving the use of investigational drugs, devices, or biologics for which an IND/IDE is required receive full board review.

18.A What it is?

A research study undergoes full board review after the Chair or his/her IRB member designee reviews the entire application and makes a determination that the project constitutes human subjects research which is more than minimal risk. The IRB reviews studies that are more than minimal risk studies at a convened IRB meeting that achieves quorum and meets federal

regulatory requirements for who is required to attend a convened IRB meeting in order for review to take place.

18.B How it's conducted

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

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

The primary reviewer makes a recommendation to the convened IRB to:

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

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

18.C Notification of Meetings and Distribution of Materials

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.

The agenda and application materials are distributed to all University of Iowa IRB members scheduled to attend a meeting, the University of Iowa general counsel (ex-officio member of IRB-01 and IRB-02), and identified consultants, if applicable. The materials are distributed 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, attending University of Iowa IRB members, the University of Iowa general counsel, and identified consultants, review electronically 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 additionally reviews other documents such as the full protocol and investigator's brochure, if applicable. In addition, all University of Iowa IRB members and the University of Iowa 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.

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 as defined in this document 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.

18.D Urgent Review of Applications

Urgent review procedures may be invoked only under unusual circumstances. Urgent review procedures are not invoked for 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 University of Iowa 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.

18.E IRB Determinations

After review by an IRB Chair or at a full board meeting, the IRB can make the following determinations with regard to a research study:

18.E.i The study can be Approved

Approval means that the IRB Chair or full board has approved your application with no required changes. You can start your research as soon as the approval memo is released to you

18.E.ii The study can be Approved Pending with changes

Approved Pending with changes means that the IRB full board has approved your application, pending the completion of specified required actions. You will receive notification of and access to the meeting minutes in HawkIRB, which will state the required actions. The IRB Chair can approve the project once the required actions have been completed successfully.

18.E.iii The study can be Tabled

Tabled means that the IRB full board has declined to make a determination about the study at this time and that your application and has specified required actions. Following completion of the required actions, the full board must review your application at another meeting.

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. 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 Human Subjects Office 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, the IRB Chair designates one of the members as the voting member, 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.

18.E.iv The study can be Disapproved.

Disapproved means that the IRB full board has not and will not approve the current research application. You must start a new project application if you wish to pursue this application further. Applications can only be disapproved by the full board, not by an IRB Chair.

The study can be withdrawn. Withdrawn means that the application has been removed from the review process, either at the request of the PI, or by the IRB if the PI failed to respond in a timely manner to requests for more information. Once an application is withdrawn, it cannot be reviewed further. For the study to be reviewed at a later time, a new application must be submitted.

18.E.v Length of Approval

Except for studies determined to be exempt from IRB oversight, 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 University of Iowa 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 University of Iowa 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.

18.F Meeting Minutes

Reserved

Part 19: Notification of 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 University of Iowa IRB ID number, the date of approval, and the date of expiration. The system notifies the Principal Investigator 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.

Part 20: Documentation of IRB Approval

Documentation of IRB approval is available for all approved studies. This documentation is available electronically via the HawkIRB system study-specific Approval tab, and is accessible to the research team as soon as the approved project is released.

20.A Link to DSP 310 Form

Reserved

Part 21: Appeal of IRB Decision

Investigators may appeal the University of Iowa 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 University of Iowa 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

board invites the investigator for the purpose of answering questions and participating in discourse with board members. The investigator leaves prior to University of Iowa IRB discussion and vote on the issues. In the case of a decision by the University of Iowa IRB to disapprove, suspend, or terminate a project, other parties may not reverse the decision.

Part 22: Post Approval Survey

Reserved

Part 23: 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 monthly reports and minutes of all full board meetings are distributed via e-mail to the UI IRB's ex officio members representing the UI General Counsel's Office and to the Institutional Official from the Office of the Vice President for Research. For IRB-03, the monthly reports and minutes of all full board meetings are distributed via email to the VA Research Office Director, VA ACOS, VA RCO, and VA Liaison for distribution to the VA Research and Development Committee.

Section II

Part 1: Human Subjects Research Application Process

Investigators are required to submit an application for IRB review prior to initiating a research project. The Human Subjects Office requires all new project applications be submitted using HawkIRB. HawkIRB is an online application submission tool that uses "smart form" technology to guide investigators through the application process. Instructions for completing the new

project application are contained within each section of the HawkIRB system. Many educational sessions are held when new aspects of the system are introduced. HSO staff are available for consultation and help using the system. Please refer to the list on our HawkIRB FAQ page.

1.A Beginning the IRB New Project Application

HawkIRB requires the investigator to respond to all applicable items on the New Project Application in order to submit the project to the HSO. The most common problem with New Project applications is that not enough detail is provided for the IRB Chair or members to evaluate the study's purpose and/or procedures.

In particular, investigators are required to provide detailed information regarding how potential subjects are initially identified, and how consent is obtained. The Principal Investigator must accurately and completely describe the study procedures in the HawkIRB application. The more complete the initial description is, the less likely that time will be spent with correspondence back and forth between the investigator and Human Subjects Office staff and/or IRB chairs to fill in the details. The New Project application in HawkIRB will indicate what is required with regard to supporting documentation.

In general, a complete submission for IRB review includes the following items as applicable:

- 1) HawkIRB application
- 2) Separate, written protocol (an existing written protocol)
- 3) Informed Consent Document(s) (or other applicable consenting materials):
- 4) Assent Document
- 5) Letter or information sheet containing the elements of consent
- 6) Exempt Information sheet
- 7) Record of Consent (for studies in which the UIHC Record of Consent policy applies)
- 8) Short Form Consent (for non-English speaking subjects)
- 9) Letters of Agreement (when either of the following applies):
- 10) Study activities will be conducted off-campus at an agency, school or other non-UI site
- 11) Data will be obtained from an outside agency or organization
- 12) Sample Informed Consent Document(s) (for example, the DHHS or other sponsor sample consent, if available).
- 13) Recruitment materials
- 14) Posters, flyers, brochures
- 15) E-mail messages
- 16) Scripts and/or presentation materials
- 17) Letters
- 18) Data collection instruments
- 19) Surveys or questionnaires
- 20) Written assessments

- 21) Interview questions
- 22) Grant application, statement of work, or other materials used to acquire support/funding
- 23) Investigator's Brochure (Clinical Investigator's Brochure)
- 24) Other materials specific to the proposed study (e.g. sponsor correspondence with a regulatory agency such as the FDA regarding test article risk, etc.)

There are detailed instructions within the HawkIRB application regarding how to attach supporting documentation. HSO staff are available to respond to questions by e-mail or phone. Staff members are also available to consult individually with investigators on how to use HawkIRB. Investigators are encouraged to contact the Human Subjects Office with their questions.

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

All investigators conducting human subjects research at the University of Iowa or the Iowa City Veteran Affairs Health Care System (VAHCS) are required to complete an education program and become "certified" in human subject protections. This educational requirement applies to: All members of the research team, including the principal investigator and all other individuals (faculty, staff, or student) who have contact or interactions with research subjects or with their private, identifiable information; Faculty supervisors of student researchers or principal investigators; Investigators who are not affiliated with the UI; who are engaged in a UI research study and whose IRB of record will be IRB-01 or, IRB-02, ~~or IRB-03~~ as designated by a formal written agreement

The option available for becoming certified is by completing the UI or VAHCS modules of the on-line tutorial called the Collaborative Institutional Training Initiative program (CITI). Instructions can be found on the HSO Website on how to complete CITI training. For IRB-03 VAHCS researchers, in addition to completion of all applicable human subjects certification(s), VA credentialing is also required. If credentialing has not been completed, individuals cannot be added as research team members to the research project.

1.C eCOI disclosure requirements prior to submission

Federal regulations place the responsibility for determining the existence of a financial conflict of interest in research on the institution. Researchers must disclose all financial interests in outside entities in the eCOI Disclosure System. The Conflict of Interest in Research Office (COIR) reviews the disclosures in the context of all routing forms and IRB applications. For more information, refer to the University of Iowa's Conflict of Interest in Research policy and the Conflict of Interest in Research website.

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

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

The HawkIRB interfaces with the eCOI disclosure system and will automatically update once a financial disclosure has been completed by an investigator. The HawkIRB application automatically designates the Principal Investigator and all faculty members listed on the research team as “key personnel.” The Principal Investigator, or their delegate, will be responsible for indicating whether or not all remaining research team members should be designated as “key personnel.” Any designated key personnel will be required to complete a COI training module and annual financial conflict of interest disclosures. HawkIRB will not allow any form type (new, modification, continuing review, or modification + continuing review) to be submitted until this annual financial disclosure requirement is met.

1.D Assurances and Responsibilities

1.D.i Principal Investigator

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

- 1) S/he is ultimately responsible for the conduct of the study
- 2) S/he agrees to comply with all applicable UI policies and procedures, and applicable federal, state and local laws
- 3) The application is consistent with proposal(s) submitted to external funding agencies
- 4) The research will only be performed by qualified personnel
- 5) all persons assisting with the research are adequately informed about the protocol and their research-related duties and functions
- 6) S/he will not implement any changes in the approved IRB application, study protocol, or informed consent process without prior IRB approval (except in an emergency, if necessary to safeguard the well-being of a human participant)

- 7) If unavailable to conduct this research personally, as when on developmental leave, or permanently leaves the institution s/he will arrange for another investigator to assume direct responsibility for the study
- 8) S/he will obtain Continuing Review approval prior to 12:01AM on the date the approval for the study expires. S/he understands if s/he fails to apply for continuing review, approval for the study will automatically expire, and all study activity must cease until IRB approval is granted
- 9) If protected health information is used or created as part of this research project, the research team agrees NOT to reuse or disclose the information to any other person or entity (beyond the named research team) except as required by law, for authorized oversight of the research project, or unless subsequent IRB approval is obtained for such reuse or disclosure.
- 10) If members of the research team access protected health information from a covered component in order to seek consent/authorization for research, such access is necessary for the research, is solely for that purpose, and the information will not be removed from the covered component.
- 11) Neither the principal investigator nor any member of the research team has entered into a financial arrangement with a sponsor of this study whereby the value of the compensation to the principal investigator or any member of the research team for conducting the study could be influenced by the outcome of the study. See the Conflict of Interest in Research policy here
- 12) S/he further assures that the proposed research is not currently being conducted and will not begin until IRB approval has been obtained

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

1.D.i.a Student PI

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

1.D.ii Faculty Advisor

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

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

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

1.D.iii Department Chair

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

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

1.D.iv Research Team Members

Research team members include all UI faculty, staff or students and VAMC employees who have direct contact (by phone or in person) with research subjects or access subjects' private identifiable information collected for research purposes. Research team members must have the appropriate experience and expertise to conduct the study. For example, if your project involves medical procedures or interventions, the research team should include a member who is qualified to conduct the procedures.

Part 2: HawkIRB Section I Project Introduction

In Section I of the HawkIRB New Project Application, investigators:

- 1) Select the IRB the project will be reviewed by (IRB-01, IRB-02, IRB-03)
- 2) Provide the project title that will also appear on the Consent Document
- 3) Provide an optional short title for the project. If provided, the short title is used in the automated e-mail messages sent from HawkIRB
- 4) Provide an overview of the study
- 5) Provide the research questions, study aims, or hypotheses
- 6) Provide background information for the research and the scientific rationale for the proposed study
- 7) Provide a list of the top 10-20 most relevant literature citations

2.A Research Purpose, Aims, & Hypothesis

The IRB reviews the research purpose, study aims, and hypothesis of each project. This information must be provided in Section I of the HawkIRB application.

Part 3: HawkIRB Section II Research Team

3.A CITI Certifications

For UI team members, the investigator will be asked to provide the person's HawkID and whether or not the individual will be a contact person for the project. If the person has completed human subjects protections training and is entered into the HSO database, his/her certification date will show up automatically in HawkIRB. Investigators will not be able to submit their application until all members of the research team have met this requirement. Information about how to obtain the required human subjects protections training can be found on the HSO website. All team members must have an active faculty, staff, or student appointment at the University of Iowa to be considered UI research team members.

3.B UI Team Members

As part of the New Project Application, investigators are asked to list all members of the research team for the project. The HawkIRB application should list all individuals who have contact or interactions with research subjects or their private, identifiable information as research team members.

HawkIRB will reflect a deactivated status if no formal appointment with the University is in place.

3.C Non UI Team Members

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

3.D Status of PI

Section II of the HawkIRB application asks for the status of the Principal Investigator. The Principal Investigator may be identified in HawkIRB as one of the following:

- 1) Faculty
- 2) Staff
- 3) Resident
- 4) Fellow
- 5) Graduate student
- 6) Undergraduate student
- 7) Other

When options 3-6 are selected, the name of the investigator's mentor or Faculty Advisor must be provided and that individual must be listed on the research team. The mentor or Faculty Advisor also signs the Assurance Document (refer to the section on Assurances and Responsibilities).

If "Other" is selected, the Principal Investigator's status or position within the UI or VAHCS must be provided.

Trainees or students are **not** permitted to be listed as PI on IRB 03 (VA) research applications. The PI for these applications must be conducting the research as a faculty or staff member.

Part 4: HawkIRB Section III Funding/Support

All original sources of funds that will be used to support the study must be listed in Section III of the HawkIRB application. This includes "pass-through" funding, in which the Principal

Investigator of the study and identified in the HawkIRB application, is not the Principal Investigator of the funding grant.

4.A Federal Funding Sources

Federal funding sources include all funds received from a federal agency (such as the National Institutes of Health (NIH) or the National Science Foundation (NSF)). Federal funding sources include those that are passed through another institution, organization, or individual. Investigators who are recipients of federal funding are expected to comply with all applicable federal regulations.

4.A.i Just in Time Funding

“Just in time” funding status refers to the stage in federally funded projects which have received a favorable score and the Principal Investigator has been notified to complete just in time procedures (such as obtaining IRB approval).

4.A.ii Department of Defense Funding

Department of Defense (DoD) supported research involving human subjects for which the DoD is providing at least some of the resources. Resources may include but are not limited to funding, facilities, equipment, personnel (investigators or other personnel performing tasks identified in the research protocol), access to or information about DoD personnel for recruitment, or identifiable data or specimens from living individuals. It includes both DoD-conducted research involving human subjects (intramural research) and research conducted by a non-DoD institution.

Research conducted or supported by the DoD, including its separate components (i.e., the Army, Navy, Air Force and Marine Corps), requires compliance with additional federal regulations, directives and instructions. The DoD has adopted 32 CFR 219, a version of the Common Rule that mirrors 45 CFR 46. The Department of Defense Instruction 3216.02 (DoDI 3216.02) establishes policy and assigns responsibilities for protection human subjects in DoD-supported research. The Principal Investigator, IRB and institution involved in DoD research must be knowledgeable about these obligations in order to adhere to them.

4.A.iii National Institutes of Justice Funding

The National Institute of Justice (NIJ) is the research, development and evaluation agency of the U.S. Department of Justice. To ensure that human subjects are adequately protected in

research, NIH and recipients of its funds are required to comply with Department of Justice regulations at 28 CFR Part 46

4.A.iv National Science Foundation Funding

The IRB reviews studies funded or supported by the National Science Foundation under the regulations contained in [45 CFR 46 Part 690](#).

4.B Corporate or Industry Funded sources

Investigators conducting research supported by corporate or industry sources must list each source in Section III of the HawkIRB application and the Consent Document.

4.C Departmental Funding

Investigators conducting research supported by funds for their academic departments must indicate the use of departmental funding in Section III of the HawkIRB application.

4.D VA Cooperative Funding Group

Reserved

4.E Pass Through Funding

Pass-through funding is funding in which the Principal Investigator of the study and identified in the HawkIRB application is not the Principal Investigator named on the funding grant.

Part 5 HawkIRB Section IV Project Type

5.A Refer to sections on Exempt, Expedited, Full Board, Overall, Concept, & WIRB

5.B ICH-GCP

This option to receive IRB review in compliance with ICH-GCP requirements may only be selected if the sponsor will not accept contract language that states the University of Iowa will “comply with ICH-GCP requirements as adopted by FDA.” The investigator should select “Regular review” when the contract contains this language. Principal Investigators who select

ICH-GCP review are required to sign an additional assurance for adherence to ICH-GCP guidelines.

5.B.i What does this mean?

Additional standards are required under full ICH-GCP compliance. Specific information on those standards can be found here.

5.B.ii Expectations

When the option for ICH-GCP review is selected, the Principal Investigator is held solely responsible for ensuring all study procedures meet ICH-GCP standards.

5.B.iii Process

Reserved

5.B.iv CVs included as an attachment

ICH-GCP requires the IRB review the Principal Investigator's CV. The CV should be attached to the HawkIRB application at the time of submission

5.C Waiver of Informed Consent

Federal regulations (45 CFR 46.116(d)) allow for the IRB to grant a waiver of consent in some cases. This waiver allows the investigator to collect and use data without obtaining the information consent of subjects. Subjects do not provide consent for participation and are not given the opportunity to decide whether or not their information will be used for research purposes. A waiver of consent is approved by the IRB if the investigator requests the waiver and provides justification for the use of the waiver in the HawkIRB application. The IRB chair may waive informed consent if research is minimal risk, the rights and welfare of the subjects are not adversely affected, the research could not practicably be carried out without the waiver, and, when appropriate, subjects are provided with pertinent information after participation.

5.C.i Waiver of Consent Process for Public Demonstration Projects

The research is conducted by or subject to the approval of state or local government officials.
The research or demonstration protocol is designed to study, evaluate, or otherwise examine:

- 1) Public benefit or service programs
- 2) Procedures for obtaining benefits or services under those programs
- 3) Possible changes in or alternatives to those programs or procedures
- 4) Possible changes in methods or levels of payment for benefits or services under those programs.
- 5) The research cannot practicably be carried out without the waiver or alteration
- 6) The research is not FDA-regulated

5.C.i.a Waiver of Parental Permission – Public Demonstration Project

The research is conducted by or subject to the approval of state or local government officials.
The research or demonstration protocol is designed to study, evaluate, or otherwise examine:

- 1) Public benefit or service programs
- 2) Procedures for obtaining benefits or services under those programs
- 3) Possible changes in or alternatives to those programs or procedures
- 4) Possible changes in methods or levels of payment for benefits or services under those programs
- 5) The research cannot practicably be carried out without the waiver or alteration
- 6) The research is not FDA-regulated

5.C.i.b Waiver of Consent Process – Permission is not a reasonable requirement

The research is designed for conditions or for a participant population for which parental or guardian permission is not a reasonable requirement to protect the participants

An appropriate mechanism for protecting the children who will participate as participants in the research is substituted

The research is not FDA-regulated

5.C.ii Criteria

The waiver is commonly granted when there will be no contact with subjects, for example a secondary data analysis or use of data that has already been collected as of the date of the HawkIRB application (such as a retrospective medical record review). Secondary analysis of already aggregated data sets (e.g., meta-analysis) does not require IRB review, since the investigator does not obtain individual human subject information.

If the data the investigator wishes to use does not currently exist (such as in a medical record) or it will be collected prospectively for the purpose of the study, consent is typically required.

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

5.C.iii VAHCS requirements to access CPRS, VISTA, or other national VAHCS-maintained record systems

Reserved

5.D HIPAA

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

Protected Health Information (PHI) is health information that:

- 1) is transmitted or maintained in any form (electronic, oral, paper) by a covered entity
- 2) identifies the individual or could reasonably be used to identify the individual
- 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 health care to an individual.

5.D.i Link to Privacy Board

Reserved

5.D.i.a Hybrid Covered Entity

The University of Iowa is a “hybrid entity”. A hybrid entity is a single legal component with both covered (e.g. UI Health Care, student health, College of Dentistry) and non-covered functions (e.g. College of Law). The hybrid entity designation limits the HIPAA liability for the institution. The covered components may use or disclose PHI for treatment, payment, or operations. As

research is not treatment, payment or operations, the covered components may not use or disclose PHI for research except as permitted in the regulations (i.e. obtained written authorization from the patient or obtaining a waiver of authorization from the IRB).

A covered entity is any of the following:

- 1) a health plan
- 2) a health care clearinghouse (electronic billing service), or
- 3) a health care provider (doctor, clinic, pharmacy, etc.) that transmits health information electronically (over the Internet). These transactions include claims, benefit eligibility inquiries, referral authorization requests, or other transactions for which HIPAA applies

5.D.ii HIPAA Identifiers

Any of the following information for the individual, relative, employer, or household member of the individual are examples of the 18 HIPAA identifiers:

- 1) Names
- 2) All geographic subdivisions smaller than a state, including street address, city, county, precinct, ZIP Code, and their equivalent geographical codes, except for the initial three digits of a ZIP Code if, according to the current publicly available data from the Bureau of the Census:
 - 3) The geographic unit formed by combining all ZIP Codes with the same three initial digits contains more than 20,000 people
 - 4) The initial three digits of a ZIP Code for all such geographic units containing 20,000 or fewer people are changed to 000
- 5) All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older
- 6) Telephone numbers
- 7) Facsimile numbers
- 8) Electronic mail addresses
- 9) Social security numbers
- 10) Medical record numbers
- 11) Health plan beneficiary numbers
- 12) Account numbers
- 13) Certificate/license numbers
- 14) Vehicle identifiers and serial numbers, including license plate numbers
- 15) Device identifiers and serial numbers
- 16) Web universal resource locators (URLs)
- 17) Internet protocol (IP) addresses numbers
- 18) Biometric identifiers, including fingerprints and voiceprints

- 19) Full-face photographic images and any comparable images
- 20) Any other unique identifying number, characteristic, or code, unless otherwise permitted by the Privacy Rule for re-identification

5.E Full Waiver of Authorization

Federal regulations permit the use of Protected Health Information (PHI) for research under two conditions:

- 1) the investigator obtains a signed authorization from the patient, or
- 2) the investigator obtains a waiver of authorization from the IRB

A waiver of HIPAA authorization is a regulatory determination that is made by the board. Federal regulations allow the IRB of a covered entity to waive in full or in part the individual authorization required by HIPAA for use and disclosure of PHI for research purposes. At the University of Iowa, the authorization to use PHI is combined with the research informed consent document. The informed consent document template includes a section called “Will My Health Information be Used During this Study?” and provides the authorization language. If the investigator plans to look at, use, or create PHI for research purposes, a signed informed consent document that includes the “HIPAA” section authorizes the covered entity to disclose the PHI to the research team.

The waiver of authorization to use PHI for research purposes is different from the waiver of elements of consent allowed under Department of Health and Human Services (DHHS) regulations at 45 CFR 46. Similar to the DHHS waiver however, the waiver of authorization to use PHI for research must be approved by the IRB.

An example of research that might be eligible for a waiver of HIPAA authorization includes a retrospective chart reviews. The New Project Application in HawkIRB includes questions to help the IRB decide whether or not the regulatory criteria for a waiver have been met for a given research project.

These criteria include:

- 1) The research could not practicably be conducted without the waiver AND
- 2) The research could not practicably be conducted without access to and use of the PHI.
- 3) The use or disclosure of the PHI involves no more than minimal risk to the privacy of individuals based on, at least, the presence of the following elements:
- 4) The PI has an adequate plan to protect identifiers from improper use/disclosure
- 5) The PI has an adequate plan to destroy identifiers at the earliest opportunity
- 6) The PI gives adequate written assurance that the PHI will not be disclosed to others.
- 7) Investigators or members of the research team may look at, use, or create PHI in the following situations:

- 8) Look at a clinic schedule, a medical chart, or an electronic record, to schedule subjects for a study visit or identify a diagnosis for subjects
- 9) Conduct research with an inpatient population
- 10) Conduct medical testing
- 11) Conduct research on the Clinical Research Unit (CRU)
- 12) Conduct a retrospective or prospective chart review
- 13) Create or add information to an in-house database or registry for research use
- 14) Provide treatment through a research protocol
- 15) Collect medical records from an outside institution
- 16) Look at or use data from a Quality Assurances/Quality Improvement (QA/QI) database
- 17) Compare information collected on a survey to information in the medical record

For more information about the HIPAA Privacy Rule, review the HIPAA page on the HSO website or the following links:

- 1) HIPAA Privacy Rule Office of Civil Rights
- 2) NIH Information for Researchers on the HIPAA Privacy Rule
- 3) Privacy Rule Complete Regulation (45 CFR 160 and 164)
- 4) Privacy Rule Summary

For more information, refer to the section on the Partial Waiver in Section VII.D.

5.E.i Link to Partial Waiver Section VII.D.

Reserved

5.F Letter of Agreement granting permission to access data

Investigators planning to use a restricted data set need to obtain documented permission. The UI IRB requires documentation of approval to access and use the data from the owner. This permission should be provided in a letter on letterhead or an e-mail signed by an individual with authorization to grant permission for the use of the data for research purposes.

5.F.i Ownership of data/medical record system to be accessed

If collaborating with an outside agency, company or clinic and that non-UI entity is giving the investigator access to its clients, files, or premises, a letter of agreement from that agency will need to be attached to the HawkIRB application. This letter should confirm knowledge of the project's purpose and permission for the investigator to conduct the study there.

5.F.ii Who can provide authorization

Authorization for access to and use of data for research purposes must be provided by the owner or administrator of the data set or medical record system. Authorization should be documented in a letter on letterhead or an e-mail and signed by an individual who has the authority to grant the permission.

Part 6: HawkIRB Section V Other HRPP Committee Review

Part 7: HawkIRB Section VI Subject Enrollment

Section VI of the HawkIRB application asks the investigator to provide the number of adult and minor subjects that will be enrolled in the study. The number provided in the response is the maximum number of subject that can be enrolled without submitting a modification to increase the enrollment number. This number cannot be exceeded without prior IRB approval for an increase in the approved number of subjects. Investigators should consider the potential for screening failures or dropouts and be sure to request an appropriate number of subjects.

7.A Who is a Subject?

DHHS regulations (45 CFR 46.102(f)) define a human subject as a living individual about whom an investigator (whether professional or student) conducting research obtains either: data through intervention or interaction with the individual, OR identifiable private information

FDA regulations (21 CFR 50.3(g)) define a human subject as an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient. For research involving medical devices, a human subject is also an individual on whose specimen an investigational device is used.

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

Intervention (45 CFR 46.102(f)) includes both physical procedures by which data are gathered (e.g., drawing blood) and manipulations of the subject or the subject's environment that are performed for research purposes.

An example of an intervention occurring in the conduct of biomedical research includes randomly providing pamphlets to some patient-subjects that provide tips for sticking to medication regimens while not providing that information to a set of other patient-subjects with the intent of testing the effectiveness of such a program on increasing compliance with

medication schedules. This type of project involves human subjects because there is an intervention (handing out educational pamphlets) with living individuals.

An example of an intervention occurring in the conduct of social/behavioral research includes administering a paper-and-pencil survey to a group of elementary school student-subjects before and after the research investigator teaches a novel lesson to analyze their ideas and beliefs on a particular topic. This type of project involves human subjects because there is an intervention (a lesson plan the children would not otherwise receive) with living individuals.

Interactions (45 CFR 46.102(f)) include communication or interpersonal contact between an investigator and subject.

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

An example of an interaction with a human subject occurring in the conduct of social/behavioral research includes administering surveys, conducting interviews or focus groups for research purposes. In this case, there is an interaction with a living individual that is being done to collect private information.

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (e.g., medical record information).

Private information must be individually identifiable (i.e. the identity of the subject is or may readily be ascertained (easily discovered) by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

Obtaining a person's private information means receiving or accessing identifiable private information or identifiable specimens for research purposes. "Obtain" includes an investigator's use, study, or analysis for research purposes of identifiable private information or identifiable specimens already in the possession of the investigator. In general, private information or specimens are individually identifiable when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

"Coded" means that:

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

thereof (i.e., the code); AND a key to decipher the code exists, linking the identifying information to the private information or specimens

7.B Subject Enrollment Requirements

An enrolled subject is anyone who has signed an Informed Consent Document, whether or not that individual actually completes the study. Thus, someone who signs a consent document but is determined during screening to be ineligible, or chooses not to continue, must still be counted as an enrolled subject. For studies granted a waiver of documentation of consent, a subject is considered enrolled when they have returned information to the research team or have indicated agreement to participate.

7.B.i Inclusion Criteria

All inclusion criteria for each subject population must be described in Section VI of the HawkIRB application. Potential subjects must also be told why they are being asked to participate in the study in the Informed Consent Document.

For all IRB-03 studies enrolling non veterans as a study population, the Principal Investigator must present a compelling argument to the IRB in Section VI for the inclusion of non-Veterans (e.g., insufficient number of Veterans; survey of VA employees; study of active duty military; study involving Veterans' family members), and the research is relevant to the care of Veterans or active duty military personnel."

7.B.ii Exclusion Criteria

All exclusion criteria for each subject population must be described in Section VI of the HawkIRB application. Exclusion criteria which may endanger subject health or safety should also be clearly described in the Informed Consent Document.

7.C Vulnerable Population(s) Considerations

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

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:

- 1) Only incompetent persons or persons with impaired decision making capacity are suitable as participants.
- 2) Competent persons are not suitable for the proposed research.
- 3) 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.
- 4) Incompetent persons or persons with impaired decision-making capacity are not being proposed as participants simply because they are readily available.
- 5) 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.
- 6) 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.
- 7) 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:

(1) The IRB determines that the proposed research entails: (a) No greater than minimal risk to the subject; or

(b) Presents a greater probability of direct benefit to the subject than harm to the subject; or

(c) Greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition that is of vital importance for the understanding or amelioration of the subject's disorder or condition.

(2) In addition to satisfying the conditions above, the IRB determines that:

(a) The research cannot be performed solely with persons who possess decision-making capacity and the focus of the research is the disorder leading to the subjects' lack of decision-making capacity, whether or not the lack of decision-making itself is being evaluated (e.g., an individual who lacks decision-making capacity as the result of a stroke can participate in a study of cardiovascular effects of a stroke); or

(b) The subject of the research is not directly related to the subjects' lack of decision-making capacity but the VA investigator has presented a compelling argument for including such subjects (e.g., transmission of methicillin-resistant staphylococcus aureus infections in a nursing home where both individuals with and without decision-making capacity are affected).

In addition:

- 1) 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.
- 2) 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.
- 3) 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:

- 1) Research involving fetuses cannot be approved.
- 2) Research involving in vitro fertilization cannot be approved.
- 3) Research involving prisoners as subjects cannot be approved unless a waiver has been granted by the Chief Research and Development Officer (CRADO).

3/4) _____.

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Research involving children as subjects cannot be approved unless:

- 1) The VA medical facility Director must approve participation in the proposed research that includes children. A waiver is granted by the Chief Research and Development Officer.
- 2) The study presents no greater than minimal risk.
- 3) The study meets all requirements of Subpart D of the DHHS or FDA regulations.
- 4) The Medical Center Director certifies that the facility is able to respond to pediatric emergencies.
- 5) If a contractor or a non-VA employee conducts the research, the individual or entity performing the research has appropriate liability insurance.

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Research on women who are known to be pregnant and/or their fetuses may be involved in research if all of the requirements of 45 CFR 46.204 are met including informed consent requirements and the following ethical and scientific criteria:

(1) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

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(2) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or fetus. If there is no such prospect of benefit, then the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means;

(3) Any risk is the least possible for achieving the objectives of the research; and

(4) The VA medical facility Director certifies that the medical facility has sufficient expertise in women's health to conduct the proposed research

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Research involving pregnant women as subjects cannot be approved unless:

- 1) The research includes adequate provisions to monitor the risks to the subject and the fetus
- 2) Adequate consideration is given to the manner in which prospective subjects are going to be selected.
- 3) Adequate provision is made to monitor the actual consent process by procedures such as:
 - a. Overseeing the process by which individual consents are secured either by:
 - b. Approving enrollment of each individual.
 - c. Verifying, perhaps through sampling, that approved procedures for enrollment of individuals into the activity were being followed
 - d. 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.

Where relevant, the IRB must document why it considers an individual or population to be vulnerable, and that adequate safeguards have been included in the study to protect the rights and welfare of participants who are likely to be vulnerable.

Individuals or populations that might be temporarily or permanently vulnerable include, but are not limited to, those who:

- 1) Are susceptible to coercion or undue influence (e.g., the homeless, prisoners, students, patients with limited or no treatment options, socially and economically disadvantaged)
- 2) Lack comprehension of the research and its risks (e.g., educationally disadvantaged, dementia, schizophrenia, or depression)
- 3) Have increased susceptibility to harm from the procedures of the specific study under review (e.g., individuals who would have to answer study survey questions about their sexual assault)
- 4) Are at risk for economic, social, or legal consequences from the study (e.g., individuals who would have to answer study survey questions about their drug use or HIV status)

For adults unable to consent:

When researchers are likely to approach adults who lack decision-making capacity, the IRB evaluates whether:

- 1) The proposed plan for the assessment of the capacity to consent is adequate
- 2) Assent of the participants is a requirement, and if so, whether the plan for assent is adequate
- 3) A re-consenting process might be necessary for participants with fluctuating decision-making capacity or those with decreasing capacity to give consent

7.D Children

By regulatory definition, a child is a person who has not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted (45 CFR 46.402(a)). By FDA definition, a child is a person who has not attained the legal age for consent to treatments or procedures involved in clinical investigations, under the applicable law of the jurisdiction in which the clinical investigation will be conducted. For purposes of research conducted in the state of Iowa, the term “child” as used in both the DHHS and FDA definitions is analogous to “minor” under Iowa Code and is viewed as “an unmarried person under the age of eighteen years.” (Iowa Code 600A.2(13))

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. 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.

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

- 1) Research that does not involve greater than minimal risk may be approved if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians. The IRB may determine that permission of one parent or guardian is sufficient.
- 2) Research involving greater than minimal risk, but presenting the prospect of direct benefit to an individual subject, or a monitoring procedure that is likely to contribute to the subject's well-being, may be approved if the IRB finds that:
 - a. the risk is justified by the anticipated benefit to the subject;
 - b. the relationship of anticipated benefit to risk is at least as favorable as that presented by available alternative approaches; and
 - c. adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.
- 3) Research involving greater than minimal risk with no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition, may be approved if the IRB finds that:
 - a. the risk represents a minor increase over minimal risk;
 - b. the intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
 - c. the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the subject's disorder or condition; and
 - d. adequate provisions are made for soliciting assent of the children and permission of their parents or guardians.
- 4) Research that is not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children may be approved if the IRB and the Secretary of DHHS, after consultation with a panel of experts in pertinent disciplines and following an opportunity for public review and comment, find that:
 - a. the research satisfies one of the above three conditions; or
 - b. the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;

- c. the research will be conducted in accordance with sound ethical principles; and adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.

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

Federal regulations (45 CFR 46.409(b)) also indicate that children who are wards of the state, or any other agency, institution, or entity can only be included in research in this category if the research is related to their status as wards or conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards. If one of these criteria is met and the research is approved, the IRB must require appointment of an advocate for each child who is a ward in addition to the person acting as guardian or in loco parentis. One person may serve as the advocate for multiple wards, however this advocate must have the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and cannot be associated in any way (except as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

Research involving children is only permitted at the VA with the approval of the Facilities Director. This approval must be attached to any research proposals at the VA which propose to involve children. The research participation of children must be no greater than minimal risk.

7.E Pregnant Women, Human Fetuses and Neonates

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

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

- 1) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
- 2) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means;
- 3) Any risk is the least possible for achieving the objectives of the research;

- 4) If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, the woman's consent is obtained OR
- 5) If the research holds out the prospect of direct benefit solely to the fetus, then the consent of the pregnant woman and the father is obtained except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest;
- 6) Each individual providing consent under (d) or (e) is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
- 7) For children who are pregnant, assent and permission are obtained in accord with the regulations for children in research (45 CFR 46, Subpart D);
- 8) No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- 9) Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
- 10) Individuals engaged in the research will have no part in determining the viability of the neonate.

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

Research involving women known to be pregnant is only permitted at the VA with the approval of the Facilities Director. This approval must be attached to any research proposals at the VA which propose to involve women known to be pregnant.

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

- 1) Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;
- 2) Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate;
- 3) Individuals engaged in the research will have no part in determining the viability of the neonate;

- 4) The requirements regarding neonates of uncertain viability (see below) or nonviable neonates (see below) have been met as applicable.

VA Research involving neonates is only permitted for observational or retrospective studies. Interventional research on neonates is prohibited.

7.F Neonates of uncertain viability

Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research unless the IRB determines that the following additional conditions have been met:

- 1) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective; OR
- 2) The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; AND
- 3) The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained (except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest).

7.G Nonviable neonates

After delivery, nonviable neonates may not be involved in research unless all of the following additional conditions are met:

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

7.H Viable neonates

A neonate, after delivery, that has been determined to be viable may be included in the research only to the extent permitted by and in accord with the requirements for children involved in research.

- 1) Research not otherwise approvable will only be allowed in this vulnerable population if:
 - a. The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates; AND
 - b. The Secretary of DHHS, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following an opportunity for public review and comment, including a public meeting announced in the Federal Register has determined that the research may take place.
- 2) Research involving human fetal tissue (placenta, or tissue from a spontaneous or induced abortion or from a stillbirth) is evaluated as tissue specimen research, using the guidelines for research involving specimens.

Studies using human fetal tissue for transplantation research and studies of human embryos involve very explicit regulations concerning consent and study procedures. Investigators wishing to conduct transplantation research with human fetal tissue should contact the Human Subjects Office well in advance of IRB application submission to discuss applicable regulations.

7.I Non-English speaking Subjects

See the Short Form Consent policy outlined on the HSO Website found [here](#).

7. J Students in Research

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. Refer to the section on Coercion and Undue Influence.

7.K Students as Subjects

Consistent with an overall concern that no research subject should be coerced, researchers should take particular precautions to avoid the unintentional or subliminal coercion that may occur when a potential research subject is also a student. For this reason, researchers should avoid using their own students as research subjects. Researchers who wish to use their own

students should be able to provide a good scientific reason, rather than convenience, for selecting those students as research subjects. The research project should be relevant to the topic of the class, and participation should be part of the learning experience for the students.

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

7.K.i Extra Credit

The IRB may approve projects that give extra credit to students who participate in a research project only when alternative means of obtaining equivalent extra credit with equivalent effort is made available to students who do not wish to volunteer as research subjects. The IRB carefully reviews the alternatives to ensure that students are not being coerced into participating.

For example, if volunteering for a survey project takes 30 minutes and the student's output is not evaluated for its quality to determine whether extra credit is given, the alternative should involve 30 minutes of effort and the output should not be evaluated (beyond assurance that a good faith effort was made).

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

7.K.ii Faculty Use of Class Assignments as Research Data

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

7.K.iii Departmental Subject Pools

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

7.L UI Staff or research team members as subjects

Potential subjects must be able to decide whether or not to participate in a study free from coercion or undue influence. Individuals who are subordinates of the PI or a research team member may not feel entirely free to decline or refuse participation because of their relationship with the PI or research team member. The recruitment of UI staff as research subjects should be undertaken with caution. It is important that supervisors in research settings refrain from recruiting or enrolling their own employees and staff to participate in their research. There can be inherent coercion in these situations and so should be avoided.

There are limited instances when it may be appropriate to enroll persons who are subordinates of the PI or research team member. These are primarily treatment studies for which the exclusion of these persons might restrict them from receiving medical treatments that would otherwise be unavailable to them.

In other cases it may be acceptable to enroll subordinates of the PI or a research team member if someone other than the supervisor conducts the recruitment and consent processes and/or if the supervisor is blinded to whether or not the subordinate participates in the study. The enrollment of subordinates should be approved by the IRB and precautions should be described in the HawkIRB application.

7.M Cognitively Impaired Persons

Individuals in a wide variety of situations may have impaired decision-making capacity. For example, impairment may occur at times of great stress. Impaired capacity is not limited to individuals with neurologic, psychiatric, or substance abuse problems; conversely, individuals with neurologic, psychiatric, or substance abuse problems should not be presumed to be decisionally impaired. Some research questions may be answered only by research that involves persons with impaired decision making capacity; precluding this research would contribute to needless suffering. The most severely impaired individuals have the greatest

need for the benefits of research on etiology and treatment. While this area is controversial, limiting research to the least impaired individuals would hamper research on the underlying causes and potential therapies of many disorders. Not all research will directly benefit the individual participant but may offer future benefits to others who have or will develop the condition or disorder. For example, genetic studies, biochemical measures, or other non-therapeutic approaches may benefit subsequent generations.

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

The National Institutes of Health (NIH) offers Points to Consider for research involving individuals with questionable capacity to consent.

The IRB will consider the following to ensure the protection of the rights and welfare of research subjects who, due to impairments in their capacity to give informed consent, may be vulnerable to coercion or undue influence:

7.M.i Conflicting Roles and Potential Conflicts of Interest

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

7.M.ii Assessing Capacity to Consent

Individual's capacities, impairments, and needs must be taken into account in order to develop practical and ethical approaches to enable them to participate in research. A clear understanding of the implications of various cognitive impairments, along with a careful consideration of proposed clinical research methodology, is required. A key factor in participants' decision making is their appreciation of how the risks, benefits, and alternatives to participation in the study apply to them personally.

Limited decision making capacity covers a broad spectrum. Researchers should be sensitive to the differing levels of capacity and use assessment methods tailored to the specific situation. Further, researchers should carefully consider the timing of assessment to avoid periods of

heightened vulnerability when individuals may not be able to provide valid informed consent.

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

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

Investigators may use a questionnaire to assess an individual's capacity to provide consent. The HSO offers one option, Evaluation to Sign an Informed Consent Document for Research, on the HSO website.

7.M.iii Comprehension

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

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

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

7.M.iv Voluntary Agreement

Closely related to the determination of the ability to comprehend the nature of the study is the importance of ensuring that subjects' participation is completely voluntary. Some knowledge and assessment of the subject's competence is relevant to a determination of whether

voluntary participation is evidenced by a written consent, or in the case of persons lacking legal capacity to consent, their assent. Research should not be conducted against the wishes of the subject, and making certain that the written documents are indeed a reflection of reality is the function of the individual researcher and the IRB.

7.M.v Second Signature on the Consent Document

There are many situations in which a subject should be encouraged to authorize the involvement of family members. However, the permission of another party will be required only when the subject is determined to lack the legal ability to provide an informed consent. This would include children (when research is conducted in the state of Iowa, unmarried persons under the age of 18) and persons legally determined incompetent. This also includes persons who are not capable of understanding the nature of their illness or the risks, benefits, and natural consequences of participation.

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

7.N Prisoners

Because incarceration could affect a person's ability to make a truly voluntary and uncoerced decision whether or not to participate in a research project, the federal regulations provide additional safeguards for the protection of prisoners (45 CFR 46, Subpart C). A prisoner is defined as any individual involuntarily confined or detained in a penal institution. This definition includes individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

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

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

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

- 1) The research under review represents one of the categories of research permissible under 45 CFR 46.306(a)(2);
- 2) Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;
- 3) The risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers;
- 4) Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;
- 5) The information is presented in language which is understandable to the subject population;
- 6) Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and
- 7) Where the Board finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

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

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

- 2) Studies of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
- 3) Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere); and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults; or
- 4) Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject.

The Informed Consent Document must include additional information for potential subjects regarding the fact that participation or non-participation will have no effect on the duration of incarceration or terms of parole. For the review of research involving prisoners, a majority of the IRB members (exclusive of prisoner members) has no association with the prison involved, apart from their membership on the IRB.

7.0 Veterans diagnosed with PTSD

Any VAHCS study that involves PTSD undergoes additional review to ensure all safety measures are met for this population. The IRB-03 Supplemental Primary Reviewer Checklist is completed by the Primary Reviewer in the Full Board review of the research protocol.

Part 8: HawkIRB Section VII.A. Collaborative Research

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

8.A Collaborative Research with Other UI Personnel

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

8.B Collaborative Research with non-UI Entities

In the conduct of cooperative research projects, each institution (entity) is responsible for safeguarding the rights and welfare of human subjects and for complying with any applicable regulations. Federal regulations from DHHS and FDA [45 CFR 46.114 and 21 CFR 56.114] allow for cooperative research projects which involve more than one institution (or entity). To avoid duplication of review efforts by IRBs, institutions can choose to conduct joint reviews, rely upon the review of another qualified IRB, or make other arrangements to establish oversight responsibilities.

Discussion of how to assure the rights and welfare of human subjects in research at each entity involved in the research usually begins with an evaluation of whether or not each entity is “engaged” in human subjects research. An entity becomes “engaged” in human subjects research when its employees or agents (agents include all individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility):

- 1) intervene or interact with living individuals for research purposes OR
- 2) obtain individually identifiable private information for research purposes

An entity is automatically considered to be “engaged” in human subjects research whenever it receives a direct DHHS award to support such research. In these cases, the awardee institution bears ultimate responsibility for protecting human subjects under the award.

OHRP has provided guidance and examples for when institutions are considered to be “engaged” in research and examples of when institutions are NOT “engaged” in research. The UI IRB makes a determination about whether or not a cooperating outside institution is engaged in human subjects research. This determination is made by the appropriate UI IRB Chair based on the outside institution’s role and whether or not that role meets any of the criteria for “engaged in research” as defined in the guidance above.

Any questions an IRB chair might have regarding making that determination are posed to OHRP by phone call or e- mail. Please call the HSO for more information if there is any question about the involvement of outside institutions in human subjects research.

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

When the outside institution is receiving federal funds through a subcontract with the UI, the UI Division of Sponsored Programs requires documentation that the outside institution holds a Federalwide Assurance (FWA) through the subcontract process. If the outside institution does not hold its own FWA, the UI requires that they obtain one prior to finalization of the subcontract. If this is the case, and the other institution obtains its own FWA, there are a few methods of IRB oversight that the UI IRB would consider acceptable based on the circumstances of the project and the role of the other institution.

The UI IRB could either:

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

Under limited circumstances, when the UI is able to assure understanding of the local context in relation to the proposed research and has sufficient resources to provide appropriate oversight during the conduct of the research, the UI may choose to extend its FWA to cover the outside institution's role in the individual project. This agreement is formalized using an Individual Investigator's Agreement.

There are two instances whereby this mechanism will NOT be allowed:

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

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

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

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

For each of these mechanisms of collaborative research oversight, the investigator must have the approval of the designated IRB(s) of record prior to conducting any research that involves human subjects. Documentation of complete contact information at each applicable collaborative site will also be required prior to the start of any research activity. The

investigator must have the signed agreements and requirements finalized prior to receiving UI IRB approval and before conducting multi-institutional research projects that involve human subjects. The final determination to enter into any agreements described in this section is made by the UI Institutional Official.

8.C International Research

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

Special attention should be given to local customs and to local cultural and religious norms in drafting written consent documents or proposing alternative consent procedures. Protections afforded subjects must be equivalent to those provided to subjects in the United States.

For some research proposals, it may be appropriate to request a waiver of consent or the elements of consent. Such proposals should include explanations of cultural norms or conditions requiring such a waiver. For example, societies where no written language is used or societies where signatures might represent something quite different than what they represent in the United States.

The first step in the review process is to make a determination about whether or not the project meets the definition of human subjects research. If unsure about whether the project constitutes human subjects research, the investigator should submit a Human Subjects Research Determination (HSRD) form in HawkIRB to receive a documented determination from the IRB Chair.

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

using the International Research Local Context Review Form before it gives final approval of the project. This form is available on the attachments page in the HawkIRB application.

8.D Multi Center Studies

Section VII.A of the HawkIRB application asks if investigators at other institutions or sites are conducting the research study, including some or all of the study procedures or receiving identified study data (identified with a study ID number for which there is a link to the subject identifiers).

Examples include:

- Sending data or samples with identifying information (name, date of birth, study ID code, etc.) to a non-UI researcher or location
- A researcher at another institution that is conducting study procedures in conjunction with this study
- Studies that involve collaboration with a contract research organization, coordinating center, central laboratory or statistical/data management center or some other organization or entity
- Community-Based Research in which a UI investigator collaborates with research affiliates outside of the UI

The UI research team conducting study procedures at an outside organization or institution does not constitute “collaboration.” The conduct of the research study at an outside organization or institution should be indicated in Section VII.A.1 and described in Section VII.D and VII.E.

8.D.i Lead Site Responsibilities

If the UI is the lead institution or coordinating center, additional information must be provided in the HawkIRB application. Investigators should provide detailed information regarding the procedures requested in Section VII.A of the HawkIRB application including the methods used, communication channels, and the process for responding to serious problems occurring at the participating sites.

One responsibility of the lead institution is to ensure IRB approval for the project and any protocol modifications. The lead institution must also ensure that participating sites maintain continuing approval from their local IRB on an annual basis. The investigator should describe plans for tracking documentation of IRB approval for each participating site in Section VII.A of the HawkIRB application.

8.E Collaborative Group studies

Refer to the section on Collaborative Research.

8.F Community Based Research

Refer to the HSO Community Based Research page here.

Part 9: HawkIRB Section VII.B. Study Design

9.A Clinical Trial

In a clinical trial (also called an interventional study), participants receive specific interventions according to the research plan or protocol created by the investigators. These interventions may be medical products, such as drugs or devices; procedures; or changes to participants' behavior, for example, diet. Clinical trials may compare a new medical approach to a standard one that is already available or to a placebo that contains no active ingredients or to no intervention. Some clinical trials compare interventions that are already available to each other. When a new product or approach is being studied, it is not usually known whether it will be helpful, harmful, or no different than available alternatives (including no intervention). The investigators try to determine the safety and efficacy of the intervention by measuring certain outcomes in the participants. For example, investigators may give a drug or treatment to participants who have high blood pressure to see whether their blood pressure decreases.

Clinical trials used in drug development are sometimes described by phase. These phases are defined by the FDA.

9.A.i Phases of Clinical Trials

Refer to The FDA's Drug Review Process here.

9.A.ii ClinicalTrial.gov reporting

Review information about clinical trials requirements for registration with ClinicalTrials.gov here.

9.A.iii FDA Clinical Trials and Human Subject Protection

9.B Repositories

Refer to the Specimen or Data Repository Procedures at the UI here.

9.B.i Data/Specimen Use Agreements

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

Purpose for Establishing a Formal Repository:

- 1) To give the “collector investigator” authority and responsibility for distributing specimens or data from the repository if certain pre-determined guidelines are met
- 2) To minimize the paperwork burden on “recipient investigators” (those individuals with whom the PI intends to share the specimens or data)
- 3) Features of a Formalized Repository:
- 4) Repository PI (“collector”) obtains IRB approval for establishing and maintaining the repository
- 5) Repository PI determines the conditions under which s/he will share specimens or data from the repository with Recipient Investigators
- 6) Repository PI develops a “Usage Agreement” that describes those conditions
- 7) Repository PI is responsible for maintaining a copy of the signed Usage Agreements

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

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

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

application a copy of the funding agency grant, and a copy of the signed Usage Agreement so that the IRB knows that the terms of the Usage Agreement will be followed. IRB approval of the Recipient's use of the specimens or data will be classified as exempt from the federal regulations. The funding agency will be notified by the Division of Sponsored Programs (via the DHHS 310 form) that the PI has obtained IRB approval for an exempt project, and the PI will not have to submit continuing review applications for the duration of that grant.

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

9.C Registries

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

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

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

Not all compilations of individuals' names and associated data constitute a research registry.

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

9.D Investigational Drugs or Biologics

9.D.i IND – Investigational New Drug

Federal law requires that a drug be the subject of an approved marketing application (i.e. an application for Food and Drug Administration (FDA) approval to market or sell the drug) before it is transported or distributed across state lines. Because a sponsor will probably want to ship the investigational drug to clinical investigators in many states, it must seek an exemption from that legal requirement. The Investigational New Drug (IND) application is the means through which the sponsor technically obtains this exemption from the FDA.

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

The FDA's role in the development of a new drug begins when the drug's sponsor (usually the manufacturer or potential marketer) has screened the pharmacological activity and acute toxicity potential of the drug in animals and wants to test its diagnostic or therapeutic potential in humans.

There are three IND types:

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

9.D.i.a 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:

- 1) 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;
- 2) 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;
- 3) 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;
- 4) The investigation is conducted in compliance with the requirements for institutional review and with the requirements for informed consent; and
- 5) 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:

- 1) it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure and
- 2) it is shipped in compliance with 21 CFR 312.160.
- 3) A drug intended solely for tests in vitro is exempt from the requirements of an IND if it is shipped in accordance with 21 CFR 312.160.
- 4) 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
- 5) Once the IND is submitted to FDA, the sponsor must wait 30 calendar days before initiating any clinical trials. During this time, FDA has an opportunity to review the IND for safety to assure that research subjects will not be subjected to unreasonable risk. For more information on IND's, refer to the following link: FDA (CDER) website. UI\VAHCS investigators conducting studies with an IND are required to submit documentation from the sponsor (either a letter or email from the FDA or sponsor, or indication on the commercial sponsor's protocol) of the IND number assigned by the FDA. If the IND is an investigator held IND, the entire IND application and the FDA Form 1571 (IND application cover page) are required. This documentation must be attached to the New Project application in HawkIRB.

Promotion and Charging for Investigational New Drugs (21 CFR 312.7)

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

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

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

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

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

- 1) There is adequate enrollment in the ongoing clinical investigations under the authorized IND;
- 2) Charging does not constitute commercial marketing of a new drug for which a marketing application has not been approved;

- 3) The drug is not being commercially promoted or advertised; AND
- 4) The sponsor of the drug is actively pursuing marketing approval with due diligence.

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

9.D.ii Expanded Access

Refer to the FDA's Access to Investigational Drugs Outside of a Clinical Trial (Expanded Access) [here](#).

9.D.iii Investigational Use of FDA-approved Drugs or Biologics

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

- 1) It is not intended to be reported to FDA in support of a new indication for use or to support any other significant change in the labeling for the drug;
- 2) It is not intended to support a significant change in the advertising for the product;
- 3) It does not involve a route of administration or dosage level, use in a subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
- 4) It is conducted in compliance with the requirements for IRB review and informed consent;
- 5) It is conducted in compliance with the requirements concerning the promotion and sale of drugs; and
- 6) It does not intend to invoke the exception for informed consent requirements (21 CFR 50.24).

9.D.iv Investigator-Initiated Research with Drugs or Biologics

The following information is intended to provide sponsor-investigators with information to guide them through the FDA requirements for sponsor-investigators who hold an IND. The federal regulations for INDs are found under 21 CFR 312. Responsibilities of sponsors and

investigators are also contained in the International Conference on Harmonisation (ICH) Guidance for Industry, E6 Good Clinical Practice. For more information, review the FDA's Center for Drug Evaluation and Research (CDER) web site www.fda.gov/cder.

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

Sponsor-investigators are also required to follow all federal regulations and University of Iowa policies and guidance for Human Subjects research, and VAHCS requirements as applicable.

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

9.D.iv.a Sponsor-Investigator Reporting Requirements

9.D.iv.a.i New Protocol 21 CFR 312.30(a)

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

9.D.iv.a.ii Changes in the protocol 21 CFR 312.30(b)

The following protocol changes must be submitted to the FDA:

- 1) For Phase 1 studies, any change that significantly affects the safety of subjects.
- 2) For Phase 2 and 3 studies, any change that significantly affects the safety of subjects, the scope of the investigation, or the scientific quality of the study.

9.D.iv.a.iii New investigator 21 CFR 312.30(c)

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

9.D.iv.a.iv Information amendments 21 CFR 312.31

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

9.D.iv.a.v IND safety/adverse events reports 21 CFR 312.32

An investigator shall promptly report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug. If the adverse effect is alarming, the investigator shall report the adverse effect immediately (21 CFR 312.64). Guides to adverse event reporting are indicated below:

- 1) Unexpected fatal or life-threatening suspected adverse reactions that are associated with the investigational drug must be reported to the FDA by fax or telephone as soon as possible, but no later than 7 calendar days after the sponsor-investigator initially receives the information.
- 2) Serious and unexpected suspected adverse reactions associated with the use of the drug that are not fatal or life-threatening only if there is evidence to suggest a causal relationship between the drug and the adverse event. These must be submitted to the FDA as soon as possible, but no later than 15 days after the sponsor-investigator initially receives the information.
- 3) Findings from other studies that suggests a significant risk in humans exposed to the drug whether or not conducted under an IND or not conducted by the sponsor-investigator. This includes any findings from epidemiological studies, pooled analysis of multiple studies, or clinical studies.
- 4) Findings from animal or in vitro testing that suggests a significant risk in humans exposed to the drug whether or not conducted by the sponsor-investigator. This includes reports of mutagenicity, teratogenicity, or carcinogenicity, or reports of significant organ toxicity at or near the expected human exposure.
- 5) Increased rate of occurrence of serious suspected adverse reactions that are a clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor should consider a variety of factors (study population, nature and seriousness of the reaction and the magnitude of the observed increase in rate).
- 6) Additional information that must be included in each IND safety report including all IND safety reports previously submitted to the FDA concerning a similar suspected adverse

reaction and the significance of the suspected adverse reaction in light of previous, similar reports or any other relevant information.

9.D.iv.a.vi Annual reports 21 CFR 312.33

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

9.D.iv.a.vii Withdrawal of an IND 21 CFR 312.38

Sponsor-investigators must inform the FDA of desire to withdraw an IND.

9.D.iv.a.viii Discontinuation of an investigation 21 CFR 312.31(a)2

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

9.D.iv.a.ix Financial disclosure reports 21 CFR 312.57d

Any changes to financial disclosure information must be promptly reported to the FDA during the investigation and for 1 year following completion of the study.

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

9.D.iv.a.x Drug accountability 21 CFR 312.57a

The sponsor-investigator must maintain records showing receipt, shipment, or other disposition of the investigational drug.

9.D.iv.a.xi Financial interest 21 CFR 312.57b

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

9.D.iv.a.xii Case Histories 21 CFR 312.62b

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

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

9.D.iv.b General responsibilities of sponsors 21 CFR 312.50

The sponsor-investigator is responsible for:

- 1) Selecting qualified investigators and providing them with the information they need to conduct an investigation properly.
- 2) Ensuring proper monitoring of the investigation.
- 3) Ensuring that the investigation is conducted in accordance with the general investigational plan and protocols contained in the IND.
- 4) Maintaining an effective IND with respect to the investigations.
- 5) Complying with FDA regulations with regard to the promotion and charging for investigational new drugs.
- 6) Ensuring that FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug.

9.D.iv.b.i Selection and monitoring of investigators 21 CFR 312.53 – 312.56

The sponsor-investigator is responsible for:

- 1) Selecting qualified investigators and monitors.
- 2) Ensuring that the study drug is shipped only to participating investigators.
- 3) Informing co-investigators of new observations with regard to the investigational drug and progress of the study.
- 4) Reviewing on-going investigations, including assuring compliance of all investigators with the protocol, reviewing and evaluating safety and efficacy data of the investigational drug, and discontinuing studies that are deemed to pose an unreasonable and significant risk to subjects.

9.D.iv.b.ii Recordkeeping and record retention 21 CFR 312.57

The sponsor-investigator is responsible for maintaining study records, as described above. Inspection of sponsor's records and reports 21 CFR 312.58

The sponsor-investigator must allow FDA employees access to all records and reports at their request. Drug Enforcement Administration and Department of Justice employees must be given access to records and reports involving controlled substances at their request.

9.D.iv.b.iii Disposition of unused supply of investigational drug 21 CFR 312.59

If the investigation is terminated, suspended, discontinued, or completed, the sponsor-investigator is responsible for assuring that all co-investigators return any unused supplies of the investigational drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug under 21 CFR 312.59 [21 CFR 312.62]. The sponsor-investigator must maintain records of the disposition of the drug as described above.

As an investigator, the sponsor-investigator has all the responsibilities of investigators in any clinical trial.

9.D.iv.c General responsibilities of investigators 21 CFR 312.60

The sponsor-investigator is responsible for:

Ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations.
Protecting the rights, safety, and welfare of subjects under the investigator's care
Ensuring the control of drugs under investigation.

9.D.iv.c.i Control of the investigational drug 21 CFR 312.61

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

9.D.iv.c.ii Investigator recordkeeping and record retention 21 CFR 312.62

The sponsor-investigator is responsible for maintaining adequate records of the disposition of the drug, including dates, quantity, and use by subjects. This is described above.

9.D.iv.c.iii Investigator reports 21 CFR 312.64

The sponsor-investigator must provide reports to the FDA as described above.

9.D.iv.c.iv Assurance of IRB review 21 CFR 312.66

The sponsor-investigator is responsible for:

- 1) Assuring that a qualified IRB will be responsible for initial and continuing review and approval of the investigation.
- 2) Providing a letter or email from the FDA (as an attachment to the HawkIRB new project application) giving the IND number assigned by the FDA.
- 3) Assuring that he/she will report to the IRB all changes and unanticipated problems involving risk to human subjects or others.
- 4) Assuring that he/she will not make any changes in the investigation without prior IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

9.D.iv.c.v Inspection of investigator's records and reports 21 CFR 312.68

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

9.D.iv.c.vi Handling of controlled substances 21 CFR 312.69

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

9.D.v Emergency Settings: Research in the Emergency Setting (Planned Emergency Research)

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

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

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

9.D.vi Emergency Use of an Investigational Drug or Device

9.D.vi.a Exemption from Prospective IRB Approval

Emergency use is defined as the use of an investigational drug or biological product with a human subject in a life-threatening or severely debilitating situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval [21 CFR 56.102(d)]. The emergency use provision in the FDA regulations [21 CFR 56.104(c)] is an exemption from prior review and approval by the IRB.

The exemption, which may not be used unless the subject is in a life-threatening or severely debilitating situation in which no standard acceptable treatment is available, allows for one emergency use of a test article without prospective IRB review. Life threatening means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life threatening do not require the condition to be immediately life threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible. Severely debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

Not all emergency use requires an exemption from prospective IRB review. When there is time for prospective IRB approval, the University of Iowa IRB expects the investigator to complete a New Project application describing the emergency use. The application will be scheduled for review at the next IRB meeting. The FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval. [21 CFR 56.104(c)] Therefore, if the first use does not have prospective review, the IRB notifies the investigator that if it is possible subsequent use of the agent will occur, a New Project application should be submitted for IRB review immediately following the first emergency use. The FDA defines emergency use as the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval (21 CFR 56.102(d)). However, it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

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

Some manufacturers will agree to allow the use of the test article, but their policy requires "an IRB approval letter" before the test article will be shipped. If it is not possible to convene a quorum of the IRB within the time available, the IRB Chair will send the sponsor a written statement that the IRB is aware of the proposed use and considers the use to meet the requirements of 21 CFR 56.104(c).

9.D.vi.b Obtaining an Emergency IND

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

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

9.D.vi.c Exception From Informed Consent Requirement (21 CFR 50.24(a)(1))

Even for an emergency use, the investigator is required to obtain informed consent of the subject or the subject's legally authorized representative unless both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:

- 1) The subject is confronted by a life-threatening situation necessitating the use of the test article.
- 2) Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject.
- 3) Time is not sufficient to obtain consent from the subject's legal representative.
- 4) No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.
- 5) If, in the investigator's opinion, immediate use of the test article is required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the clinical investigator should make the determination and, within five working days after the use of the article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. The investigator must notify the IRB within 5 working days after the use of the test article.

9.D.v Placebo-Controlled Trials

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

investigator is bound to follow the risk management procedures as with any other provision of the approved protocol.

Use of placebos may be appropriate where the investigator demonstrates that:

- 1) standard therapy is unavailable or is of unproved efficacy, or
- 2) standard therapy possesses unacceptable side effects, or
- 3) minimal harm may result from the use of placebo (e.g., ongoing disease has little adverse effect on the patient during the course of the trial and is reversible), or
- 4) placebo itself may be an effective therapy, or the disease process is characterized by exacerbation and remission.
- 5) The risk management procedures should be in the written protocol, with the same level of detail as in the protocol itself. The following issues should be specified:
- 6) the frequency of monitoring,
- 7) whether monitoring is in person or by telephone,
- 8) the criteria for managing a subject in the event of worsening, and
- 9) how 24 hour-per-day, 7 day-per-week, medical care is made available in the event of questions, emergencies, worsening, or withdrawal from the protocol.

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

9.D.vi Washout Issues in Drug Treatment Studies

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

Once an approval is granted, the investigator is bound to follow the risk management procedures as with any other provision of the approved protocol. The risk management procedures should be in the written protocol, with the same level of detail as in the protocol itself. The following issues should be specified:

- 1) careful definition as to when a subject would be withdrawn from the study,
- 2) the frequency of monitoring,

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

9.E Physiology intervention studies

Physical procedures by which data are gathered (e.g. drawing blood).

9.F Behavioral intervention studies

Manipulations of the subject or the subject's environment that are performed for research purposes.

9.G Diagnostic trial

A protocol designed to evaluate one or more interventions aimed at identifying a disease or health condition (ClinicalTrials.gov)

9.H Investigational Medical Devices

When research is conducted to determine the safety or effectiveness of a device: The device fulfills one of the IDE exemption categories:

- 1) A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time.
- 2) A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence.
- 3) A diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) and if the testing is noninvasive, does not require an invasive sampling procedure that presents significant risk, does not by design or intention introduce energy into a participant, is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure, a device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put participants at risk.

A custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

9.H.i Investigational Device Exemption (21 CFR 812)

An investigational device is a medical device which is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. Clinical investigations undertaken to develop safety and effectiveness data for medical devices must be conducted according to the requirements of the Investigational Device Exemption (IDE) regulations. An IDE study may not necessarily commence 30 days after an IDE submission to FDA. Certain clinical investigations of devices (e.g., certain studies of lawfully marketed devices) may be exempt from the IDE regulations.

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

Significant and Nonsignificant Risk Medical Device Studies

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

- 1) is intended as an implant; or
- 2) is used in supporting or sustaining human life; or
- 3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or
- 4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject

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

Unless exempt from the IDE regulations, an investigational device must be categorized as either "significant risk" (SR) or "nonsignificant risk" (NSR). The determination that a device presents a

nonsignificant or significant risk is initially made by the sponsor. The proposed study is then submitted either to FDA (for SR studies) or to an IRB (for NSR studies).

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

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

Once the final SR/NSR decision has been rendered by the IRB (or FDA), the IRB must consider whether the study should be approved. In considering whether a study should be approved, the IRB should use the same criteria it would use in considering approval of any research involving an FDA regulated product (21 CFR 56.111). FDA considers all SR studies to present more than minimal risk, and thus, full IRB review is necessary. In making its determination on approval, the IRB should consider the risks and benefits of the medical device compared to the risks and benefits of alternative devices or procedures.

Distinguishing between SR and NSR Device Studies (21 CFR part 812)

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

If an IRB believes that a device study is SR, the investigation may not begin until both the IRB and FDA approve the investigation. To help in the determination of the risk status of the device, IRBs should review information such as reports of prior investigations conducted with

the device, the proposed investigational plan, a description of subject selection criteria, and monitoring procedures. The sponsor should provide the IRB with a risk assessment and the rationale used in making its risk determination.

9.H.ii The IRB and the NSR/SR Decision

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

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

For nonsignificant risk devices, the investigator must maintain the following:

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

9.H.iii Investigator-Initiated Research with Medical Devices

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

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

Sponsor-investigators are also required to follow all federal regulations and University of Iowa policies and guidance for Human Subjects research, and VAHCS requirements as applicable.

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

9.H.iii.a Sponsor-investigators Reporting Requirements

9.H.iii.a.i Changes in the protocol 21 CFR 812.35

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

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

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

9.H.iii.a.ii IDE safety/adverse device effects 21 CFR 812.150(b)

The sponsor-investigator must report all unanticipated adverse device effects to the FDA and the IRB within 10 working days of receiving the first notice of the event.

9.H.iii.a.iii Withdrawal of IRB approval 21 CFR 812.150(b)

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

9.H.iii.a.iv Withdrawal of FDA approval 21 CFR 812.150(b)

The sponsor-investigator must notify all reviewing IRBs and participating investigators of any withdrawal of FDA approval. This notification must occur within 5 working days after receipt of the withdrawal of approval.

9.H.iii.a.v Current investigator list 21 CFR 812.150(b)

The sponsor-investigator must provide the FDA with a current list of investigators participating in the investigation. This list must be provided to the FDA every 6 months.

9.H.iii.a.vi Annual reports 21 CFR 812.150(b)

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

9.H.iii.a.vii Recall and device disposition 21 CFR 812.150(b)

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

9.H.iii.a.viii Discontinuation of an investigation 21 CFR 812.150(b)

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

9.H.iii.a.ix Informed consent 21 CFR 812.150(b)

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

9.H.iii.a.x Financial disclosure reports 21 CFR 812.43

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

The sponsor-investigator is responsible for maintaining the following records during and for 2 years after completion or termination of the investigation or 2 years after the records are no longer needed to support a premarket approval application or a notice of completion of a product development protocol. 21 CFR 812.140d. The sponsor-investigator must make these available to FDA inspectors at their request.

9.H.iii.a.xi Correspondence 21 CFR 812.140

The sponsor-investigator must maintain copies of all correspondence with other investigators, reviewing IRBs, monitors, and the FDA including required reports.

9.H.iii.a.xii Financial interest 21 CFR 812.140

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

9.H.iii.a.xiii Device records 21 CFR 812.140

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

An investigator or sponsor may withdraw from the responsibility to maintain records for the period required in 21 CFR 812.140(d) and transfer custody of the records to any other person who will accept responsibility for them under 21 CFR 812.140, including the requirements of 21 CFR 812.145 (21 CFR 812.140(e)). Notice of this transfer shall be given to the FDA not later than 10 working days after transfer occurs.

9.H.iii.a.xiv Case Histories 21 CFR 812.140

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

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

9.H.iii.b General responsibilities of sponsors 21 CFR 812.40

The sponsor-investigator is responsible for:

- 1) Selecting qualified investigators and providing them with the information they need to conduct an investigation properly.
- 2) Ensuring proper monitoring of the investigation.
- 3) Ensuring that IRB review and approval are obtained.
- 4) Submitting an IDE application to the FDA.
- 5) Ensuring that any reviewing IRB, FDA, and participating investigators are promptly informed of significant new information about an investigation.

9.H.iii.b.i Selecting and monitoring investigators 21 CFR 812.43 – 812.46

The sponsor-investigator is responsible for:

- 1) Selecting qualified investigators and monitors.
- 2) Ensuring that the investigational device is shipped only to participating investigators.
- 3) Obtaining investigator agreements.
- 4) Obtaining statements from participating investigators attesting to their commitment to the proper conduct of the investigation.
- 5) Obtaining accurate financial disclosure statements from participating investigators.
- 6) Providing participating investigators with the investigational plan.
- 7) Informing co-investigators of new observations with regard to the investigational device and progress of the study.

- 8) Reviewing on-going investigations, including assuring compliance of all investigators with the protocol, reviewing and evaluating safety and efficacy data of the investigational device, and discontinuing studies that are deemed to pose an unreasonable and significant risk to subjects.

9.H.iii.b.ii Adverse device effects and study termination 21 CFR 812.46

The sponsor-investigator must immediately evaluate any unanticipated adverse device effect. If the sponsor-investigator determines that the device presents an unreasonable risk to the safety of subjects, the sponsor-investigator must terminate the study within 5 working days after making this determination, but not later than 15 working days after first receiving notice of the adverse effect.

If the device is significant risk, the sponsor-investigator may not resume a terminated investigation without IRB and FDA approval. If the device is nonsignificant risk, the sponsor-investigator may not resume a terminated investigation without IRB approval.

9.H.iii.b.iii Recordkeeping and record retention 21 CFR 812.140

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

9.H.iii.b.iv Inspection of sponsor's records and reports 21 CFR 812.145

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

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

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

As an investigator, the sponsor-investigator has all the responsibilities of investigators in any clinical trial.

9.H.iii.c General responsibilities of investigators 21 CFR 812.100

An investigator may determine whether potential participants would be interested in participating in an investigation, but shall not request the written informed consent of any participant to participate, and shall not allow any participant to participate before obtaining IRB and FDA approval. [21 CFR 812.110].

The investigator is responsible for providing a letter or an e-mail from the FDA giving the IDE number, if applicable, as assigned by the FDA. The sponsor-investigator is responsible for:

Ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable FDA regulations.
Protecting the rights, safety, and welfare of subjects under the investigator's care
Ensuring the control of devices under investigation.

9.H.iii.c.i Compliance with protocol 21 CFR 812.110b

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

9.H.iii.c.ii Device use and disposition 21 CFR 812.110c

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

9.H.iii.c.iii Investigator recordkeeping and record retention 21 CFR 812.140a

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

9.H.iii.c.iv Investigator reports 21 CFR 812.150

The sponsor-investigator must provide reports to the FDA as described above.

9.H.iii.c.v Inspection of investigator's records and reports 21 CFR 812.145

The sponsor-investigator must allow FDA employees access to all records and reports at their request.

Part 10: HawkIRB Section VII.C. Genetic Research

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

The IRB considers the following issues in its review of the application and the Informed Consent Document:

- 1) Information that can be obtained from DNA samples in general, and the specific questions to be addressed in this study.
- 2) The extent of subject and sample confidentiality if the sample and subsequent information will be part of a registry or database (required for all studies, regardless of being a registry or database).
- 3) The rights and limitations of subjects to require destruction of their sample and/or associated data at a future date. The rights and limitations of subjects to require that their sample and or associated data be stripped of any identifying information.
- 4) Identifying information available to other researchers if their sample and/or associated data are part of a registry or database (required for all studies, regardless of being a registry or database)
- 5) Mechanisms for maintaining confidentiality in long-term studies, registries, or databases.
- 6) Potential for commercial profit by the institution, investigator or sponsor from information gathered in this study.
- 7) The availability or access to genetic counseling in cases where a study may reveal genetically important information (i.e., possessing genetic defects which could be passed on).
- 8) Subjects must have the right to decline receiving genetic information (required for all studies).
- 9) In the absence of a specific authorization to maintain a DNA sample beyond the initial project, DNA samples collected, stored, and/or analyzed in connection with a research project must be destroyed upon completion of the project or withdrawal of the individual from the project. This information must be clearly stated in the Informed Consent Document.

Before involving children in DNA research, the parent(s) or legal guardian(s) must review and sign the Informed Consent Document. The Informed Consent Document must give parents/guardians the option of whether or not they want the results (if available) of the

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

10.A GWAS

Refer to the NIH Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS) [here](#).

The UI IRB must review and approve data submission plans for institutional certifications under NIH's GWAS Policy

10.B dbGap

Refer to information about the National Center for Biotechnology Information's (NCBI) database of Genotypes and Phenotypes (dbGaP) [here](#).

Refer to the NIH Points to Consider for IRBs and Institutions in their Review of Data Submission Plans for Institutional Certifications under NIH's Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (GWAS) [here](#).

10.C Storage of genetic samples for future use

Investigators must describe how requests for genetic samples will be received, reviewed and approved. Plans for data/specimen sharing should also be described in the Consent Document. If the samples have been stripped of identifiers, subjects will not be able to request at a later time that they be destroyed.

Samples must be destroyed when the study is closed in HawkIRB unless the study is approved by the IRB to store samples for future research.

10.C.i Incidental findings

The IRB considers availability or access to genetic counseling in cases where a study may reveal genetically important information (i.e., possessing genetic defects which could be passed on). Subjects must have the right to decline receiving genetic information.

Before involving children in DNA research, the parent(s) or legal guardian(s) must review and sign the Informed Consent Document. The Informed Consent Document must give parents/guardians the option of whether or not they want the results (if available) of the genetic analysis disclosed to them. Whenever appropriate, the child's assent should be solicited. Upon reaching the age of majority, if the subject may request his or her information be disclosed that should be included in the Consent Document.

10.D HIPAA Compound Authorization

An institution providing health care must notify patients regarding how it will use and disclose the patients' health information for treatment, payment, and health care operations. Patient permission is not required for the institution to carry out these activities. The privacy rule stipulates that research is not included in the definition of treatment, payment, and health care operations and patients must give their permission for the research use or disclosure of their health information, even if the researcher is the same individual who provides treatment to the patient outside of a research context.

When an authorization for the use or disclosure of protected health information is combined with another authorization, such as an Informed Consent Document for research, it is called a compound authorization. The IRB allows investigators to obtain informed consent and a HIPAA authorization using a compound authorization. ~~However, for a few specific types of research scenarios, the HIPAA Privacy Rule requires an additional signature to be collected. If a subject is enrolled in a clinical trial in which research-related treatment is conditioned on the individual's signing the research HIPAA authorization for the clinical trial, that research authorization may not be combined with any other research authorization (such as optional tissue banking or ancillary studies that do not directly affect the research related treatment) . If a clinical trial or other study offering research related treatment wishes to combine optional studies that do not directly affect the research related treatment on the same document, the subject must be offered the choice to "opt in" to participate in the optional component and to authorize release of PHI for the optional component. This may be accomplished by use of a space to initial or check that the subject agrees to participate in that portion of the study.~~

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- The VAHCS does not allow the use of a compound authorization, all HIPAA authorizations are collected on a separate document from the informed consent.

10.E GINA

The Genetic Information Nondiscrimination Act (GINA) makes it illegal for health insurance companies, group health plans, and employers of 15 or more persons to discriminate against individuals based on genetic information. GINA prohibits health insurance companies and

group health plans from requesting genetic information collected for research purposes. Health insurance companies and group health plans may not use genetic information when making decisions regarding eligibility for insurance coverage or the amount of insurance premiums. GINA does not protect individuals from genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. The law also does not prohibit discrimination if the individuals already have a manifest genetic disease or disorder.

The Informed Consent Document template available in HawkIRB includes template language describing GINA. All studies that involve research on genes or genetic testing/research are required to include this template language in the Consent Document.

Part 11: HawkIRB Section VII.D. Recruitment & Consent Process

11.A IRB Expectations for a successful Research Recruitment portfolio

The IRB must review and approve all recruitment methods and materials used to describe a research study to potential subjects. All recruitment materials must have IRB approval prior to their use. Investigators should select all items that may be used for recruiting subjects in Section VII.D and attach all related materials to be used for recruitment to the HawkIRB application.

11.A.i Partial Waiver of HIPAA Authorization for recruitment purposes

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

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

The request for a partial waiver of HIPAA authorization opens up in the application based on the PI's response to Section VII, Question D.1, "Check all materials/methods that will be used in recruiting subjects (you will need to attach copies of all materials at the end of the application)". In order for the waiver justification questions to open up, the PI must select the

option, "Use of any information available to the researchers or their colleagues because this person is a patient OR use of any information considered to be Protected Health Information (PHI) OR review of patient/clinic records, Describe source of records". Selecting this option opens up questions VII.D.2-VII.D.7 which address the waiver criteria listed above. However, it may be necessary to 'read between the lines'. Researchers often describe access to PHI in the "describe" comment boxes for the options "Existing Registry/database", "Referral from colleague", and "Other". The waiver justification questions will not open up if the use of PHI is described under any of these options.

11.A.ii Recruitment materials & methods

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

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

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

Any material aimed at recruiting potential subjects into a study (including the final copy of the printed advertisement, audio or video tapes or websites) must be reviewed and approved by the IRB prior to being used. Recruitment messages in any form should not be coercive or perceived as "marketing" of the study.

Advertisements or recruitment letters should:

- 1) Include the purpose of the project and/or briefly state what is expected of the subject
- 2) Include the time commitment required of the subject.

- 3) Include the investigator's University department affiliation and where the research will take place
- 4) List a contact name and phone number.
- 5) Include in summary form, the criteria that will be used to determine eligibility for the study.
- 6) Include a brief list of benefits, if any

Advertisements or recruitment letters should not:

- 1) Emphasize (for example, in large or bold type) the payment amount.
- 2) Include the name of commercial sponsors or products.
- 3) Use phrases such as "help needed" or "subjects wanted." Instead use "you are invited" or "participants invited."
- 4) State or imply a certainty of a favorable outcome or other benefits beyond what is outlined in the consent document and protocol.
- 5) Emphasize how "important" the study is or include exculpatory language (language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence).
- 6) Make exaggerated marketing claims or sales pitches
- 7) Make claims that the drug, biologic or device is safe or effective for the purposes under investigation.
- 8) Make claims, that are inconsistent with FDA labeling, that either explicitly or implicitly that the drug, biologic or device is known to be equal or superior to any other drug, biologic, or device
- 9) Use terms such as "new treatment," "new medication," or "new drug" without explaining that it is investigational.
- 10) Promise "free medical treatment," when the intent is only to say subjects will not be charged for taking part in the investigation.
- 11) Allow compensation for participation in a trial offered by a sponsor to include a coupon good for a discount on the purchase price of the product once it has been approved for marketing.

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

- 1) Invite subjects to participate
- 2) The title or invitation to participate should be brief and informative for potential subjects. The title should state that this is a research study. Avoid phrases such as "help needed" or "research subjects wanted." The recommended wording is "you are invited" or "participants invited."
- 3) Identify who is conducting study
- 4) State that the research study is a University of Iowa study and give the name of the department or college in which the study is conducted.

- 5) State the purpose of the study:
 - a. Use lay terms to address briefly why the study is being done.
- 6) Describe what subjects will be asked to do:
 - a. Provide a brief description of the study procedures subjects will be asked to do for participation in the study.
- 7) Describe the primary inclusion / exclusion criteria:
 - a. Potential subjects need to know whether or not they would be eligible to participate. Only include the criteria that subjects would know about themselves. Limit the exclusion criteria to the most common reasons a person would be ineligible to participate. If there are a lot of inclusion/exclusion criteria, it is not necessary to list all of them.
- 8) Include the time commitment:
 - a. Provide a general statement about the overall time commitment for the subject.
- 9) Describe the primary study procedures:
- 10) Provide a brief overview of the main study procedures. If the study protocol includes many study activities for the subject, it is not necessary to list them all in the recruitment poster or brochure.
- 11) State whether subjects will be paid for participation:
 - a. Do not emphasize (large font or bold type) that payment is offered.
- 12) Provide contact information:
 - a. Provide the name and/or contact information for a member of the research team that the potential subject can call to find out more information about the study or to volunteer to participate. The contact information does not have to be the name and contact information for the Principal Investigator.

11.A.ii.a Use of Research subject compensation in recruitment materials

It is acceptable to include the compensation amount in recruitment materials. However, study materials should not over emphasize the amount of compensation for participation. This policy applies to recruitment materials such as posters or flyers, mass mail or e-mail messages, or newspaper, radio or television advertisements, etc. that provide information about a research study. Read the Inclusion of Compensation Amount in Recruitment Materials policy here.

11.A.ii.b Use of University of Iowa ITS mass email

The IRB allows targeted or mass e-mail for the purpose of recruiting subject participants for research studies.

Requests for a mass e-mail announcement are received via fax, e-mail, campus delivery or hand delivery to the HSO. The written request is reviewed to verify that the IT form has been printed and delivered with the request. This form has the information that was given electronically to IT'S, and is the information that needs to be verified by reviewing the HawkIRB application. If

this form is not submitted, the research team member needs to be contacted and this form submitted to HSO.

Once the form is received, it is reviewed for the following:

- 1) E-mail is listed as a recruitment methods in Section VII.D of the HawkIRB application
- 2) Mass e-mail is described as a recruitment method in VII.D.29 (and VII.D.30, if applicable)
- 3) The email script in the IT form is identical to the mass e-mail attached to the application

Access the required IT form to request the use of mass-email [here](#).

11.A.iii Cold Calling

UI policy generally restricts the use of “cold calls” to recruit subjects to research studies. An introductory letter or other informational material must first be sent or given directly to subjects prior to telephone contact. Read the HSO cold calling policy [here](#).

The VAHCS prohibits the use of cold calls to recruit subjects to research studies.

Finder’s Fees and Recruitment Incentives

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

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

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

11.A.iv ResearchMatch

ResearchMatch is the product of the Clinical and Translational Science Awards (CTSA) Consortium, which is led by the National Center for Research Resources, a part of the National Institutes of Health (NIH). The UI participates in the CTSA Consortium through its Institute for Clinical and Translational Science. ResearchMatch.Org is a national volunteer recruitment

registry to connect online with potential research study volunteers. To recruit volunteers using ResearchMatch the investigator must be the primary Principal Investigator on an active University of Iowa IRB-approved study. The IRB approved project must be approved to use Research Match as a recruitment method in Section VII.D.

The PI is required to register the study on ResearchMatch.org. The investigator will be asked to submit contact and study information and sign a Researcher Acknowledgment Form (RAF), agreeing to treat volunteers' personally identifiable data obtained from ResearchMatch as confidential information. The information may only be used to recruit patients to participate in the study. This RAF must be attachment to the HawkIRB application.

Any communications with volunteers via ResearchMatch will utilize content and/or recruitment language, with the removal of direct study contact information. The investigator is also required to attach a copy of the e-mail notification ResearchMatch sends to potential subjects. This email should provide enough information about the study that potential subjects can make an informed decision about participation.

11.B The Full Informed Consent Process

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 at the time of consent:

- 1) The name of the study
- 2) The person obtaining the subject's consent.
- 3) A statement that the subject or the subject's legally authorized representative is capable of understanding the consent process.
- 4) A statement that the study was explained to the subject.
- 5) A statement that the subject was given the opportunity to ask questions.
- 6) The investigator must enter a progress note in the subject's medical record when:
- 7) The subject is entered into the study.
- 8) The subject's participation is terminated
- 9) 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.

When participants withdraw from a clinical trial, the IRB determines that:

- 1) The data collected on the participant to the point of withdrawal remains part of the study database and may not be removed. The consent document cannot give the participant the option of having data removed.
- 2) A researcher may ask a participant who is withdrawing whether the participant wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study.
 - a. Under this circumstance, the discussion with the participant distinguishes between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the participant's information.

- b. The researcher must obtain the participant's consent for this limited participation in the study (assuming such a situation was not described in the original consent document). The IRB must approve the consent document.
- 3) If a participant withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the researcher must not access for purposes related to the study the participant's medical record or other confidential records requiring the participant's consent. However, a researcher may review study data related to the participant collected prior to the participant's withdrawal from the study, and may consult public records, such as those establishing survival status.

11.B.i Consent and Assent

11.B.i.a Standard Informed Consent Document

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

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

11.B.i.a.i Basic Elements of Informed Consent

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

- 1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.
- 2) A description of any reasonably foreseeable risks or discomforts to the subject.
- 3) A description of any benefits to the subject or to others which may reasonably be expected from the research.
- 4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
- 5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained. For studies regulated by the FDA, note the possibility that the Food and Drug Administration may inspect the records. [21 CFR 50.25(a)(5)]
- 6) For research involving more than minimal risk, an explanation as to whether payments or medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
- 7) An explanation of who to contact for answers to pertinent questions about the research and research subjects' rights, and who to contact in the event of a research-related injury to the subject.
- 8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

11.B.i.a.ii Additional Elements of Informed Consent

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

- 1) A statement that the particular treatment or procedure may involve risks to the subject or to the embryo or fetus, if the subject is or may become pregnant which are currently unforeseeable.
- 2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
- 3) Any additional costs to the subject that may result from participation in the research.
- 4) Adverse consequences (physical, social, economic, legal or psychological), if any, of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
- 5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.
- 6) The approximate number of subjects involved in the study.

11.B.i.a.iii Consent Template and HawkIRB

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

For all New Project applications, investigators must begin with the consent template that is available at the end of the HawkIRB application. In HawkIRB, the consent document is populated with template language based on responses to various questions within the application. Thus, when downloaded, many of the pertinent sections of the consent template are already included.

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

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, 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) Contact information for questions about the research project, and research subjects' rights, and whom to contact in the event of research-related injury.
- 13) 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.
- 14) The signature and signature date for subject and/or legally authorized representative.
- 15) Signature and date lines for person providing verbal explanation of study and obtaining consent (where study appropriate).

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:

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

- 1) 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.
- 2) Anticipated circumstances under which participation may be terminated by the investigator.
- 3) Any additional costs to the subject that may result from participation in the research.
- 4) Consequences of the subject's decision to withdraw from the research.
- 5) Procedures for orderly termination of participation by the subject.
- 6) 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.
- 7) The approximate number of subjects involved

11.B.i.a.iv Teenage Subjects and How to Handle Wording on the Consent Document

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

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

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

If you are a teenager reading this document because you are being invited to be in this study, the word “you” in this document refers to you. You will be asked to read and sign this document to indicate your willingness to participate.

11.B.i.a.v Signature Lines

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

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

11.B.i.a.vi Exceptions

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

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

When there is no verbal communication with potential subjects (e.g., mail-out surveys), the signature of the person who obtained consent may also be deleted. ~~(Does not apply to studies conducted at or using resources of the Veterans Affairs Health Care System (VAHCS)).~~

An auditor/witness signature line is needed only if specifically required by the IRB or the funding agency/company. However, if this line is included on the consent, the consent must always be witnessed and this line signed.

Except in certain minimal risk studies, the Informed Consent Document:

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

11.B.i.a.vii Plain language

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

Perhaps the most common problem with Informed Consent Documents is that they are written at a reading level several grades higher than the average subject would understand.

Informed Consent Documents should be written at a reading level that potential subjects would understand. For most projects, an eighth grade reading level is suggested. Most word processing programs can determine a document's reading level.

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

- 1) Write the Consent as though you were speaking to the person who will read it, using "you" and "your," "we" and "our," rather than third person.
- 2) Use language that could be understood by a junior high student.
- 3) Put technical jargon into lay terms (e.g., describe the amount of a blood draw in teaspoons rather than milliliters; use "cancer" rather than "carcinoma").
- 4) Clearly define complicated terms (e.g., randomization means the study treatment you'll receive will be decided by chance, like flipping a coin).
- 5) Don't give a lot of technical information that participants don't need to know (e.g., complicated methods of determining drug doses, exhaustive lists of specific lab tests).
- 6) Use bulleted lists rather than long sentences.
- 7) Use headings and subheadings as appropriate with logical and consistent formatting.
- 8) Use tables and charts to explain when/where each procedure will take place.
- 9) Use pictures and diagrams to help describe devices.
- 10) Number each page of the document.
- 11) Use hard page breaks to eliminate "widow" and "orphan" lines of text.

- 12) Use consistent and reasonable font size (e.g., 12 point).
- 13) Do not “right justify” the text.

11.B.i.a.viii VA requirements

The Veterans Affairs Health Care System requires that the standard Informed Consent Document be copied onto its own form. This form is a template choice on the Consent/Assent attachments page of HawkIRB.

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 statement that in the event of a research-related injury the VA has to provide necessary medical treatment to a subject injured by participation.

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.

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.

11.B.i.a.ix IRB Stamp

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

Only the current, approved Consent Document may be used for documenting informed consent. Documenting consent on a Consent Document on or after the expiration date

stamped on that document is not permitted and may not constitute valid consent. With each Continuing Review, the investigator receives newly stamped versions with the approval notification. Even if the content is identical, the research team is expected to use the current, stamped version of all stamped materials.

11.B.i.a.x Sponsor template Consent

When a template consent document is available from the study sponsor, the investigator should attach it in the Miscellaneous attachments category of the HawkIRB application. The template should be attached even if the investigator is not proposing to use the template consent to enroll subjects.

A complete submission for IRB review includes sample Informed Consent Document(s). When federally funded and available from the industry or federal (DHHS, NIH, FDA, etc.) sponsor, the IRB must be provided with the template consent document to review any deviations.

11.B.i.a.xi What additional data/info can be added to the consent?

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

11.B.i.a.xii Where are consent documents stored? (Section X Privacy & Confidentiality)

The Investigator must adhere to the confidentiality protections for paper records, including signed consent documents, paper data collection forms, etc. described in the HawkIRB application and approved by the IRB.

11.B.i.b Assent

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. 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.

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

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

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

For studies involving children, the IRB may recommend that this form be used with children, but it may also be used when teenagers are being recruited to enhance their comprehension if the study involves complicated procedures. Investigators are asked to select and describe plans for the assent process for children/minors in the HawkIRB application.

Options for assent procedures include the following:

- 1) Children/minors will sign an assent or consent document
- 2) Children/minors will be given an assent or consent document to read, but will provide only verbal assent
- 3) Children/minors will be given only a verbal description of the study and asked to assent verbally
- 4) No assent procedure because some or all of the children/minors do not have the capability to assent or their capability is so limited that they cannot reasonably be consulted to provide assent
- 5) No assent procedure because the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children/minors and is available only in the context of the research
- 6) No assent procedure because although children are capable of assenting, we are requesting a waiver of assent (NOTE: must be minimal risk study for children and request must be justified in writing by answering questions to follow)

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

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

11.B.i.b.i Waiver of Assent

The IRB may waive assent of children with life-threatening illnesses who are eligible for research treatment protocols.

11.B.ii Legally Authorized Representative

A legal guardian in the state of Iowa is defined [in the termination of parental rights chapter of Iowa law](#) as a person who is not the parent of a [minor](#) child, but who has been appointed by a court or juvenile court having jurisdiction over the [minor](#) 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 [district](#) court ~~(a district court)~~ or a juvenile court, rather than an individual. ~~(Iowa Code 600A.2)~~

Unless otherwise expanded or restricted by a [district](#) court or juvenile court having jurisdiction over the [minor](#) child or by operation of law, the rights and duties of a guardian with respect to a [minor](#) child shall be as follows:

- 1) **To consent to marriage, enlistment in the armed forces of the United States, or medical, psychiatric, or surgical treatment.**
- ~~2) To serve as a guardian ad litem (a person appointed by a court or juvenile court having jurisdiction over the minor child to represent that child in a legal action. A guardian ad litem appointed under Iowa code must be a practicing attorney) unless the interests of the guardian conflict with the interests of the child or unless another person has been appointed guardian ad litem.~~
- ~~3)2) To serve as custodian, unless another person has been appointed custodian~~
- ~~4)3) To make periodic reasonable visitations if the guardian does not have physical possession or custody of the [minor](#) child.~~
- ~~5)4) To consent to adoption and to make any other decision that the parents could have made when the parent-child relationship existed.~~
- ~~6) To make other decisions involving protection, education, and care and control of the child.~~

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

- 1) the parent, OR
- 2) the court-appointed guardian

In studies conducted in the state of Iowa involving cognitively impaired adults (adults who may be incompetent or have limited decision-making capacity), the legally authorized representative is:

- 1) The designated proxy ~~(such as an individual named by the study participant in a Durable Power of Attorney for Health Care. (see Iowa Code Chapter 144B))~~
- 2) ~~A~~ court-appointed guardian for the study participant [see Iowa Code § 633.551 et seq.]
- 3) The study participant's Spouse.
~~3) Spouse (This does NOT include "common law" spouses)~~
- 4) ~~An adult child of the study participant, or if the study participant has more than one adult child, a majority of the adult children. Adult child~~
A Parent parent of the study participant, or both parents
- 5) ~~An Adult sibling of the study participant~~

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In studies involving cognitively impaired adults, permission-consent must be sought from the first existing person reasonably available in the above list, even if another relative-person is more conveniently available. Not reasonably available means the person is deceased, unknown, incompetent, or unable to provide permission-consent due to inability to communicate with the research team (e.g. the individual is stationed outside the United States in the armed services and does not have access to phone, email, or fax).

11.B.iii Non-English Speaking Subjects & Consent

11.B.iii.a Short Form Consent process

See the Short Form Consent policy outlined on the HSO Website found here.

11.B.iii.b Translators

A list of individuals who have given the HSO permission to share their contact information with investigators in need of translation services is available here.

11.B.iv VA Consent Process

Refer to VA requirements or to the VHA Handbook 1200.05

11.B.v Record of Consent

When a research project involves any physical interaction or specimen collection at the University of Iowa Health Care (UIHC), it is UIHC policy (IM-MR-06.21) that a signed copy of the Record of Informed Consent (RIC) be placed in the subject's medical record chart. All content added within the Record of Consent must be approved by the IRB prior to use. The Informed Consent Document signed by the subject (or a copy) is NOT placed in the medical record. The RIC provides a link between the UIHC patient and the study in which they participate, however, it protects the privacy and confidentiality by providing limited information about the research study. The RIC is signed by the research team member who obtained consent from the subject and documents that consent has been obtained.

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

11.B.vi Screening procedures

All screening procedures conducted before and after the subject gives consent to participate in the study must be described in the HawkIRB application and approved by the IRB. This includes questions asked directly of the subject (or his/her Parent/Legal Guardian/Legally Authorized Representative) prior to consent and any additional questions asked or procedures conducted to determine whether or not the subject qualifies to continue in the study after consent is obtained.

Sensitive and/or medical-related questions and procedures should be asked and/or conducted after consent has been obtained.

11.C Waiver of Documentation of Consent

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

- 1) The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality;

- 2) Example: Some types of studies that fall into this category are survey or interview studies that contain highly sensitive (e.g., criminal behavior, sexual behavior) questions.
- 3) 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.
- 4) Example: Studies that may meet these criteria include mail out surveys about topics that could not reasonably damage a participant's reputation or employability or be otherwise stigmatizing.

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

- 1) the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context;
OR
- 2) the requirements in 21 CFR 50.24 for an exception from informed consent for emergency research are met.

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

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

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

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

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

11.C.i Consent by mail

For minimal risk mail-out or web-based surveys or questionnaires, it may be appropriate to request a waiver of documentation of consent. When the subject's signature requirement is waived, generally the investigator provides all of the required elements of consent in a cover letter, with a statement that returning the survey or questionnaire will be considered voluntary agreement to participate.

11.C.ii Consent via online

In some cases, a waiver of documentation of consent may be granted by the UI IRB for research conducted online (i.e. a web-based survey). Investigators may use a consent letter or information sheet containing the elements of consent (template provided in the attachments section of HawkIRB) to provide consent information to participants. For studies with a waiver of documentation of consent collecting data online, a web portal or screen may be used to present the consent information to the participant, allowing for the individual to indicate consent by selecting a button to proceed with their participation.

If the research is greater than minimal risk, written consent will be required. Currently, the UI IRB does not allow for the collection of electronic signatures to document informed consent over the Internet. Investigators will need to have subjects submit a signed consent document in order to access the web site to participate in the study.

Survey instruments, such as those provided by the University of Iowa Qualtrics account, should be designed in such a way that allows participants to skip questions or provide a response such as "I choose not to answer."

11.D Coercion & Undue Influence

In order to be voluntary, consent must be given under conditions that are free of coercion and undue influence. Consent is valid only if the agreement to participate in the research is given voluntarily.

11.E. Use of Deception in Research

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

In a minimal risk study involving playing a computer game to test subjects' responses to differential pay-offs or reinforcements, the investigator might indicate in the Informed Consent Document that the purpose of the study is to test reaction time. This deception may be necessary because the study would be compromised if subjects were told the true purpose.

In this scenario, one of the basic elements of consent -- the purpose of the study -- could be waived by the IRB chair, and not included in the Informed Consent Document.

11.E.i Waiver of Informed Consent

11.E.ii Rationale

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

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

11.E.iii Debriefing

When requesting a waiver of the elements of consent for the use of deception, the IRB will require that participants be debriefed as soon as possible after the conclusion of the experiment. The HawkIRB application should include a description of the debriefing process and who will conduct it. The debriefing statement or information sheet provided to subjects should be attached to the HawkIRB application. The individual conducting the debriefing should not be in a position of authority over the participant.

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.

Part 12: HawkIRB Section VII.E. Study Procedures – What will happen during the course of the study?

12.A Randomization

Randomization refers to different conditions or study procedures. It does not refer to the random selection of subjects to be involved in the study. The randomization of subjects to different conditions or study procedures should be described in the HawkIRB application and the Informed Consent Document.

12.B Surveys, Questionnaires, and Interview Studies

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

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

12.B.i Distribution/storage by use of Redcap

REDCap is a data management tool that provides a secure multi user web based interface for storing study information. REDCap is supported by the Institute for Clinical and Translational Science (ICTS) and is the UI IRB preferred web-based data collection tool. Investigators who use REDCap for the distribution and storage of study data must describe its use in Section X of the HawkIRB application. More information about REDCap is available [here](#).

12.B.ii Distribution/storage by use of Internet

Reserved for forthcoming Internet Research and Use of Social Media Policy

12.C Audio/Video Taping

Study procedures may require the videotaping, audio recording, or photographing of subjects. These media provide potential means for subject identification. Investigators must secure subject consent after explicitly describing these practices in the Informed Consent Document.

12.D Pregnancy screening

Pregnancy screening must be described in the Informed Consent Document and HawkIRB application, and must be done after the subject signs the Consent Document.

12.D.i Pregnancy Screening In Minors

When a minor is required to have a pregnancy test as part of a screening visit (or study procedure), the Informed Consent Document or Assent Document must describe this information. Minors in research must be given the same rights to privacy pertaining to their pregnancy that they would be given in a clinical setting. Therefore, minors 12 years of age or older can choose whether to share the pregnancy results with their parents/legal guardians. For children less than 12 years of age who have a positive pregnancy test, the research team must inform the parents or guardians of the pregnancy. The research team is required to inform proper authorities if a child of any age has a positive pregnancy test and if abuse is expected. The Appendix section of the Informed Consent Document in HawkIRB provides the template language that is to be included in the Informed Consent Document.

12.D.ii Drug Studies Requiring Consent of Subject's Spouse or Significant Other

In certain instances, it may be advisable to have a consent for a Subject's Spouse or Significant Other. A sponsor may request this, or the IRB may decide it is necessary. For additional information contact the Human Subjects Office.

12.D.iii Vulnerable Populations

12.E Use of Social Media/Internet

Reserved for forthcoming Internet Research and Use of Social Media Policy

12.F Lost to Follow up

Lost to follow up refers to the research team's inability to locate enrolled subjects during the study using the contact information the subject provided (i.e. if the subject changed address or phone number). This does not refer to planned follow-up phone calls outlined in the study procedures. This also does not refer to attempts to contact subjects after the completion of this study (i.e. about participation in future research studies). The investigator should describe all efforts that will be made to locate subjects that they are unable to reach during the study (for example, use of on-line databases, web-based searches, commercial services, etc.).

12.G Subject Compensation

Payment for participation in research should be a form of recognition for the investment of the subject's time, loss of wages, or other inconvenience incurred. Payments should be based on the research subject's time and/or reimbursement for reasonable expenses incurred during his/her participation in the research study. This could include payment for parking, lodging or transportation. Payment should not be excessive to the nature of the project or be offered to the subject as a means of coercive persuasion or undue influence.

Subjects may be compensated for blood donation as part of their participation in a research study. The compensation amount should not be reflective of the amount of blood donated but rather one set amount that will be compensated to subjects regardless of the amount of blood donated.

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

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

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

12.G.i Cash Handling Policy

UI Policy University Cash Handling Policies and Procedures apply when the type of research subject compensation using cash, check, or cash equivalent (Cash or cash equivalent is defined as coin, currency, checks, money orders, credit cards, accounts receivable charges, electronic

funds transfers, tokens, gift cards, parking tickets and/or stamps) From more information about the University of Iowa policy on cash handling, go to: <http://afr.fo.uiowa.edu/cash-handling>.

To review a template for use when creating a cash handling procedure, go to the Accounting and Financial Reporting web site.

12.G.ii W-9 substitute documentation

For each individual payment to a research subject exceeding \$75, the Research Participant/Substitute W-9 form must be completed prior to research activities occurring. This form and the Accounts Payable Policy can be found on the Accounts Payable website.

The participant must provide their:

- 1) Name
- 2) U.S. address
- 3) Social Security or Taxpayer Identification Number
- 4) Mailing Address
- 5) Amount paid or value of items given as compensation
- 6) Citizenship Status
- 7) If not a U.S. Citizen, the following information will be needed:
- 8) Immigration(visa) status
- 9) Tax residency country (may differ from citizenship country)
- 10) Permanent foreign address
- 11) All participants must certify the information is accurate by signing the substitute W-9. The completed substitute W-9 form should be faxed or hand delivered to Accounts Payable by a research team member for processing. Do not email this form. Once the substitute W-9 form has been submitted to Accounts Payable and a Vendor ID# has been assigned, it must be confidentially discarded.
- 12) For compensation of \$75 or less, the Accounts Payable Office will require all of the above information except for the Social Security Number/Taxpayer Identification Number.
- 13) Subjects must be given the option to waive compensation if they do not want to disclose their Social Security Number or Taxpayer Identification Number for the purposes of compensation for research participation.

12.G.iii Compensation vs. Travel reimbursement

Payments to subjects in research studies are a form of compensation. Payments may be any type of remuneration including, but not limited to checks, cash, gift cards, or any other items of value. Reimbursement for travel or other costs is not considered compensation.

Reimbursements for travel or per diem are not subject to the requirement to collect SSN/TIN regardless of the amount of reimbursement.

Reimbursements of this nature are expected to be supported with receipt or mileage documentation.

This type of reimbursement without supporting documentation could be construed as tax avoidance.

Flat rate reimbursements are considered to be compensation if it is not reimbursement at cost or at the designated mileage reimbursement rate.

Any questions related to this requirement should be referred to Grant Accounting.

Because federal regulations do not require collection of a SSN for travel or per diem reimbursement, investigators are encouraged to use ProTrav to process payments. ProTrav does not require a SSN or TIN for purposes of providing travel or per diem reimbursements so long as they are within the currently UI approved mileage rate or at cost. Travel or per diem reimbursement requires either an explanation within the ProTrav submission accounting for the reimbursement or supporting receipts as documentation. For more information, refer to the Grant Accounting Office site [here](#).

Part 13: Section VIII Risks to Subjects

13.A What are the risks?

Section VIII of the HawkIRB application must describe all known and potential risks and indicate whether the study has any of the following types of risks:

- 1) Emotional or psychological
- 2) Financial
- 3) Legal or social
- 4) Physical

If there are no known risks, the investigator may state that there are “no foreseeable risks” to participating. Depending on the type of study, risks may be described as discomforts or something that might make the subject “uncomfortable,” such as fatigue or embarrassment. The Consent Document must also describe these risks.

Examples of non-physical risks include loss of confidentiality, discomfort from being asked sensitive information, disclosure of illegal activities, disclosure of mental health condition, etc.

13.A.i Suicidality and IRB expectations

Refer to the Section on Legal Requirements for IRB Review.

In its review of studies, the IRB complies and expects investigators to comply with Iowa common law (not statute) which generally requires that one report a demonstration of a current intent to hurt oneself or others.

Based on the nature of study and subject population, the investigator may be asked to describe a response plan in the HawkIRB application and Consent Document if subjects may be identified as suicidal or at risk of harming themselves or others.

13.B How to minimize risks

The IRB reviews the risks and considers whether the risks to subjects are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, or whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

13.C Data Safety Monitoring

13.C.i Frequency

Studies that plan to have an individual or committee review combined data from all subjects on a periodic basis (such as summary or aggregate safety and/or efficacy data) must describe what data will be summarized and reviewed and how frequently the data will be reviewed in Section VIII of the HawkIRB application.

Refer to Federal & State Regulations & Guidance Materials

13.C.ii Reporting

Studies that plan to have an individual or committee review combined data from all subjects on a periodic basis must provide reports from the data safety monitoring committee at the time of Continuing Review.

Refer to Federal & State Regulations & Guidance Materials

13.C.iii Medical Monitor

Reserved

13.C.iii.a DoD requirements

Research conducted or supported by the Department of Defense (DoD), including its separate components (i.e., the Army, Navy, Air Force and Marine Corps) requires compliance with additional federal regulations, directives and instructions. The DoD has adopted 32 CFR 219, a version of the Common Rule that mirrors 45 CFR 46. The Department of Defense Instruction 3216.02 (DoDI 3216.02) establishes policy and assigns responsibilities for implementation of 32 CFR 219 in protecting human subjects in DoD-supported research. The University of Iowa, its IRBs and investigators involved in DoD research must be knowledgeable about these obligations in order to adhere to them. The Education and Compliance Program has implemented a program to monitor the adherence with the additional requirements for DoD-supported research.

Part 14: Section IX Benefits

14.A Direct benefits to Subject

Direct benefits include benefits that subjects will definitely receive from participating in the research. Often there are no direct benefits to subjects and should be described as such in the HawkIRB application and Consent Document.

Benefits may not promise a cure or a great discovery. Benefits may not include compensation or payment for participation.

14.B Benefits to Society

Potential benefits may include the hypothesized results of the study, benefits to society or the knowledge that the investigator hopes to gain from conducting the study. Potential benefits to society may be described in Section IX of the HawkIRB application.

The IRB determines whether risks to subjects are reasonable in relation to anticipated benefits (if any) to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB will consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB does not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

Part 15: Section X Privacy & Confidentiality

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

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

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

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

15.A Certificate of Confidentiality

Certificates of Confidentiality are issued by the National Institutes of Health (NIH) to protect the privacy of research subjects by protecting investigators and institutions from being compelled to release information that could be used to identify subjects with a research project. Certificates of Confidentiality are issued to institutions or universities where the research is conducted. They allow the investigator and others who have access to research records to refuse to disclose identifying information in any civil, criminal, administrative, legislative, or other proceedings, whether at the federal, state, or local level.

Identifying information in this context is broadly defined as any item or combination of items in the research data that could lead directly or indirectly to the identification of a research subject. By protecting researchers and institutions from being compelled to disclose information that would identify research participants, Certificates of Confidentiality help achieve the research objectives and promote participation in studies by assuring privacy to subjects.

Investigators who intend to apply for a Certificate of Confidentiality should contact the Human Subjects Office regarding procedural steps for IRB approval and communicating with NIH. Complete information regarding the NIH Certificate of Confidentiality is available on the NIH Office of Extramural Research web site.

15.A.i University of Iowa [or VA PI requesting the CoC](#)

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

When VA conducts a study that is protected by a Certificate of Confidentiality, the following health record documentation provisions apply:

(1) For studies that do not involve a medical intervention (e.g., observational studies, including interview and questionnaire studies), no annotation may be made in the health record.

(2) For studies that involve a medical intervention, a progress note entry should indicate that an individual has been enrolled in a research study, any details that would affect the subject's clinical care, and the name and contact information for the investigator conducting the study. Subjects' informed consent forms and HIPAA authorization documents are not to be included in the health record.

Investigators should work with the research office in their facility to assure that when Veterans are enrolled in a study protected by a Certificate of Confidentiality, they are not simultaneously enrolled in other interventional studies unless it is absolutely clear that this enrollment does not raise safety issues.

15.A.i.a Process

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

UI IRB procedures are as follows:

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

15.A.i.b Consent language

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

15.A.i.c Requirements

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

15.A.i.d Expiration

A Certificate of Confidentiality protects personally identifiable information about subjects in the research project while the Certificate is in effect. Generally, Certificates are effective on the date of issuance or upon commencement of the research project if that occurs after the date of issuance. The expiration date should correspond to the completion of the study. The Certificate will state the date upon which it becomes effective and the date upon which it expires. A Certificate of Confidentiality protects all information identifiable to any individual

who participates as a research subject (i.e., about whom the investigator maintains identifying information) during any time the Certificate is in effect. An extension of coverage must be requested if the research extends beyond the expiration date of the original Certificate. However, the protection afforded by the Certificate is permanent. All personally identifiable information maintained about participants in the project while the Certificate is in effect is protected in perpetuity.

15.A.ii Reserved

15.B Data and/or Specimen protections

Confidentiality protections for data and/or specimens must be described in Section X of the HawkIRB application. The description should include the storage location, who has access to the data and/or specimens, and the individual responsible for maintaining IT security (typically the investigator's departmental IT person), as well as the person responsible for the storage of specimens. Investigators must describe how specimens are labeled (i.e. ID codes, subject's initials, date of collection, etc.). Confidentiality protections must also be described in the Informed Consent Document.

15.B.i VAHCS requirements for data and specimen storage outside of the VAHCS

If the project involves the VAHCS and tissue/sample storage for future use, the investigator should check with the VAHCS Research Office (338-0581; from within the University, dial 158, extension 7666) to determine if this is allowable prior to adding the other site to the tissue storage section of the consent document. VAHCS investigators should include a written statement from the VAHCS research office acknowledging permission to store tissue/samples for future use as an attachment to the HawkIRB application.

15.C Use of SSN

15.C.i UI Policy requirements

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

Services (ITS) department and may result in additional reporting requirements as mandated by UI ITS.

The collection of a subject's Social Security Number (SSN) may be legally required. For example, IRS regulations require collection of the SSN if the subject is to be paid or if there is a business necessity for its collection. When neither of these situations exist, a subject may voluntarily provide his or her SSN. Whether collection is required or voluntary, the researcher is obligated to inform the subject of ALL intended SSN use(s). If collection of the SSN is not legally required or if there is no business necessity for collection of the SSN, the subject must approve all uses of the SSN by initialing his/her choice in the Informed Consent Document.

15.C.ii UI ITS requirements

Investigators should review the UI Information Security and Policy Office's Information Security Guidance for Researchers.

15.C.iii IRB approved uses of SSN

Unless the collection of the SSN is legally required or there exists a business necessity for collection, collection of the SSN is strictly optional on the subject's part and is not required for participation in the study. The only exception to this policy is for research projects that occur at the VAHCS. The VAHCS requires the collection of the SSN for any payment. This action can be completed by adding the new social security template section immediately following the "What Will Happen" section of the consent to inform the subject of the following information:

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

15.C.iv Confidential discarding of SSN

If Social Security Numbers (SSN) are collected from subjects for compensation purposes, the research team should not retain them electronically or in paper/hard copy form. The eVoucher and ProTrav systems assign a separate University ID number (Univ ID) that can be used for future payment requests. Paper and electronic documents containing SSNs should be removed as soon as possible.

15.D Access and/or storage protections for data/specimens

Refer to the section on Privacy & Confidentiality

15.D.i Storing research records separate from clinical records

The Health Insurance Portability and Accountability Act (HIPAA) or Privacy Rule protects the privacy of individually identifiable health information or Protected Health Information (PHI), while at the same time ensuring that researchers continue to have access to medical information necessary to conduct vital research. Whether in healthcare or research, the Privacy Rule requires that PHI be communicated on a “minimum necessary” basis. In other words, research team members should only have access to the individually identifiable information necessary for the research. Therefore, even if members of the research team are the subject’s clinicians, only the IRB-approved clinical records, described in the HawkIRB application and the Informed Consent Document, should be stored in research records. Clinical records that are not approved by the IRB for use in the study must be stored separately from the research records.

Part 16: Section XI Data Analysis

16.A Analysis methods

The investigator must provide a detailed plan for data analysis in the HawkIRB application. This includes details about the variables that will be analyzed, the comparisons that will be made, the analysis that will be done on the variables and the relationship of these analyses to the indicated study aims, etc. Justification for the number of subjects the investigator proposes to enroll in the study should also be provided. A formal power analysis is not necessary. If the project described in the HawkIRB application is a pilot study, this should be indicated that in the response. The investigator should also describe how s/he has assessed whether the number of subjects proposed will provide meaningful information to answer the study questions.

Part 17: Section XII Future Research

Investigators do not need IRB permission to store data collected in this study for future research. However, IRB approval is necessary to conduct research in the future using identified data collected in a previous research study (including data with an ID code for which there is a link between the code number and subject identifiers). In this case, the investigator must submit a new HawkIRB application describing the use of the identifiable data, reference the previous IRB ID# and await IRB approval before beginning the study.

17.A Contacting subjects for future research

Investigators may request to keep subject contact information so members of the research team may contact them about their own future research studies. A statement must be in the Informed Consent Document so subjects are aware they may be contact about other studies.

17.A.i Consent process

Refer to the section on Recruitment & Consent Process

17.A.ii Minors aging up process (Minors Reaching the Legal Age of Consent While Enrolled in a Study Policy)

Informed consent should be viewed as an ongoing process throughout the duration of a research study. Long-term studies may involve subjects who are minors at the time of enrollment but who reach the legal age of consent while study or follow-up procedures are still ongoing. The UI IRB considers on a study-by-study basis whether obtaining new consent from each subject is required or whether a waiver of consent may be granted.

If there is continued interaction with subjects who were first enrolled as minors, obtaining a new consent when a subject reaches the legal age of consent will usually be required. Investigators enrolling minors who may reach the legal age of consent during the course of the study, and will have interactions with the subject after they turn 18, should describe in Section VII.D.29 of the HawkIRB application how they plan to obtain a new consent from these subjects. Options may include in-person consents, mail out consents, use of email with a pdf. version of the consent form attached, or faxed consent forms.

All materials utilized to obtain the new consent, such as a letter, phone script, or email explaining the requirement, should be attached to the HawkIRB application.

If the investigator will not have any interaction with the subject after they turn 18, but would like to continue to analyze the data or specimens collected under the legally effective consent obtained from the parent or guardian, s/he should either describe the plan to obtain a new consent or request a waiver of consent.

For continued collection of new data from record reviews after the subject reaches the legal age of consent, the IRB may approve a waiver of consent under 45 CFR 46.116(d) if the required conditions are met.

17.B Sharing contact information with researchers outside the research team

Investigators who want to share their enrolled subjects' contact information with other researchers who are not on the research team should request IRB approval to do so in Section XII of the HawkIRB application. Template language describing the registry should also be included in the Consent Document.

Part 18: Research Related Study Materials

Investigators may keep contact information so other researchers can contact subjects for future research. This must be described in Section XII of the HawkIRB application and the Informed Consent Document. However, this does not authorize the PI to share data collected in the current study with researchers outside the research team.

18.A What does the IRB expect to see as part of the IRB application

The New Project Application must be accompanied by some basic materials, when appropriate. HawkIRB will prompt the investigator to attach materials based on responses to questions in the application. The investigator is required to attach any required materials electronically. If only a hard copy of the supporting documentation is available, the investigator will need to convert the document to a single electronic file (for example, scanning the document), so that it can be attached to the HawkIRB application. There are detailed instructions within HawkIRB on how to attach materials. There are also instructions regarding attachments on the HawkIRB FAQ page. Materials that may need to be attached to the HawkIRB application include the following:

18.A.i Consent materials

To create any of these documents, the investigator or his/her delegate will need to start with the template provided in HawkIRB, download them to a computer, make edits, and re-attach the documents to the HawkIRB application.

- 1) Consent document
- 2) Assent document
- 3) Record of Consent
- 4) Exempt information sheet
- 5) Consent letter
- 6) WIRB consent template

18.A.ii Recruitment materials

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

Phone script(s) need to be included for situations that involve screening or providing consenting information to participants via telephone.

18.A.iii Grant application

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

18.A.iv Surveys

This includes questionnaires, surveys, stimuli, etc., that will be used in the study.

18.A.iv.a How to attach if online

Investigators using online survey instruments (such as Qualtrics) to collect data from subjects must attach screen shots of the survey as it would be presented to subjects. Investigators may also provide a survey link in Section VII.E to the HSO/IRB for review.

18.A.iv.b Where to document URL (section VII.E)

The URL for survey instruments should be provided in Section VII.E.4 of the HawkIRB application for IRB review and approval.

18.A.v Protocol

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

18.A.vi Investigator Brochures

For studies that require review by the Pharmacy & Therapeutics Committee or involve investigational drug interventions, attach a copy of the Investigator's Brochure for the investigational drug under study.

18.A.vii G-12

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

18.A.viii Drug package inserts

For studies administering drugs within the FDA approved population, indication, dose or route of administration, the drug package insert(s) must be attached to the HawkIRB application for IRB review.

18.A.ix Questionnaires

All questionnaires administered to subjects (in paper or electronic form) must be attached to the HawkIRB application for IRB review and approval.

18.A.x CRFs

Unless a form is completed by the subject in order to collect data directly from the individual, Case Report Forms (CRFs) should not be attached to the HawkIRB application.

CRFs are paper or electronic forms typically used in clinical trial research. The CRF is a tool used by the sponsor to collect data from each participating site. All data on each subject participating in a clinical trial are documented in the CRF. The IRB does not require investigators to attach CRFs as the information collected on these forms should be described in the attached protocol. Additionally, a Modification to the HawkIRB application would have to be submitted each time the attached CRF was revised.

18.A.xi Screening logs

Screening logs that may include subject identifiers (name, date of birth, medical record number, etc.) must be attached to the HawkIRB application for IRB review and approval.

18.A.xii Letters of Agreement

For collaborations with non-UI entities, attach the Individual Investigator's Agreement. See the section on Collaborative Research.

18.A.xiii IND documentation

If the study involves an investigational drug, attach the following documentation:

- 1) IND application
- 2) Including documentation of the IND number from the sponsor (if this is not indicated on the Investigator's Brochure or protocol).
- 3) In the case of investigator-held INDs, attach a copy of the FDA letter that informed the PI of the IND number.

18.A.xiv FDA response

Investigator/sponsor correspondence with the FDA documenting that an IND is or is not required must be attached to the HawkIRB application.

18.A.xv Tracking information

Detailed procedures for tracking use and disposition of medical devices and the person responsible for maintaining the use and disposition tracking records must be provided in Section VII.B of the HawkIRB application.

Part 19: PI Responsibilities after initial IRB approval

19.A Modifications

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

Modifications include, but are not limited to:

- 1) Changes to study procedures,
- 2) Adding or removing investigators or research team members,
- 3) If a PI is leaving the institution, a new PI must be submitted and approved prior to the current PI's departure. A signed assurance document is required of a newly named PI of a research study. If a PI is on extended leave from the institution, contact the HSO to discuss continued oversight of any open studies.
- 4) Changes to the title of the project,
- 5) Requests for additional subjects beyond the original approved number,

- 6) Change in funding sources,
- 7) Changes in how subjects are being recruited or followed-up,
- 8) New or revised advertisements,
- 9) Changes to Informed Consent Documents, surveys, questionnaires, correspondence with potential or current subjects, or additional new items, protocol changes.
- 10) Modifications to an approved project should be submitted on a Modification/Update Form. A modification may be submitted at the same time as a continuing review. Instructions for the completion of these applications are contained within HawkIRB.

Modifications to an approved project that pose no additional risk to subjects (e.g. changes in title, co-investigator(s), funding sources) are eligible for expedited review. To be eligible for expedited review, the modification must maintain similar or increased safeguards to protect the subject. Expedited modifications are reviewed and approved by the IRB chair or designee. More extensive modifications, or modifications that pose additional risk to subjects, may require full board review. In either case, revisions or clarifications may be required. All modifications must be approved by the IRB prior to implementation (see exception noted above).

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

For projects that have received Concept approval, to obtain approval for enrolling human subjects the investigator should submit a Modification/Update Form in HawkIRB. In the Modification/Update Form, the investigator should change Question IV.1 to indicate that the project should receive Regular review. This change will open up additional questions for the investigator to answer in order to complete the application. An Informed Consent Document and any other materials, such as interview scripts or questionnaires, should be attached to the Modification/Update Form.

19.A.i Section XIV Modification checklist

Refer to the IRB Primary Reviewer Checklist

19.B Reportable Events

Investigators are required to report to the appropriate UI IRB if any of the above items occur in a study where IRB-01, IRB-02, IRB-03 is the IRB of record. (For WIRB studies, events are reportable directly to WIRB.). When IRB-03 is the IRB of record, all VHA reporting actions are in accordance with the requirements of the *VHA Handbook 1058.01 "Research Compliance Reporting Requirements found [here](#).*

Field Code Changed

19.B.i -Unanticipated Problems Involving Risks to Subjects or Others

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

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

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.

Examples of unanticipated problems involving risks to subjects or others include, but are not limited to:

- 1) A breach of confidentiality
- 2) A subject complaint when the complaint indicates unexpected risks or cannot be resolved by the investigators,
- 3) A research team member experiences harm in the conduct of the study
- 4) A new risk of the study drug, device, or study procedure is identified by an outside source (sponsor, federal regulatory agency, outside site, etc.)

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

within 10 working days of the PI becoming aware of the event. For IRB-03 studies, reporting must occur within five working days.

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

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

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

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

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

- 1) Death
- 2) Life-threatening adverse drug experience
- 3) Inpatient hospitalization or prolongation of existing hospitalization
- 4) A persistent or significant disability/incapacity
- 5) A congenital anomaly/birth defect
- 6) Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug event when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed above (21 CFR 312.32).
- 7) An unexpected adverse drug event is any adverse drug experience (associated with the use of the drug), the frequency, specificity, or severity of which is not consistent with the current investigator brochure; or, if an investigator brochure is not required or

available, the specificity or severity of which is not consistent with the risk information provided to the subjects and the IRB (21 CFR 312.32) .

Investigators must report any serious adverse drug event using the Reportable Event Form (REF). This form includes a description of the event, the date of occurrence, the type of risk, whether the event was unexpected, the outcome, and an assessment of degree of relatedness to the research. The form also includes the proposed actions to be taken by the investigator with regard to modifying approved study materials (including change in consent documents or other notification procedures) and notifying current subjects. Reports from the investigator to the IRB must be submitted via HawkIRB within ten working days of the event or within 10 working days of the PI becoming aware of the event. For IRB-03 studies, reporting must occur within five working days.

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

All reports of serious and unexpected adverse drug events occurring in a UI/VAHCS subject are reviewed by the IRB Chair and/or the IRB in the following manner:

The IRB chair compares the content of the REF with the previously approved project materials such as applications, informed consent document(s), protocols, investigator brochures, or other supporting documents to determine whether this event meets the definition of an unanticipated problem involving risk to subjects or others.

If the chair agrees the event meets the definition of an unanticipated problem involving risks to subjects or others, the chair determines whether the event represents minimal risk of harm or more than minimal risk of harm to subjects enrolled under the UI study.

If the event represents minimal risk of harm, the chair reviews and signs the report through the HawkIRB system.

If the event represents more than minimal risk of harm to subjects enrolled under the UI\VAHCS study, the report is referred to the convened IRB for review. The full board determines whether subjects must be notified of the new information, and if so, the method of notification and whether any study materials (e.g. consents, protocol) must be updated to reflect the new information.

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

on a monthly basis. [For IRB-03, they are reviewed by the full board at regular monthly IRB meetings.](#)

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

19.B.iii Serious adverse device effects (either anticipated or unanticipated) occurring in a UI subject

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

An unanticipated adverse device effect is 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 (21 CFR 812.3).

Investigators must report any serious adverse device effect occurring in a UI\VAHCS subject to IRB-01 or IRB-03 using the Reportable Event Form (REF). This form includes a description of the effect, the date of occurrence, the type of risk, whether the effect was unanticipated, the outcome, and an assessment of degree of relatedness to the research. The form also includes the proposed actions to be taken by the investigator with regard to modifying approved study materials (including change in consent documents or other notification procedures) and notifying current subjects. Reports from the investigator to the IRB must be submitted via HawkIRB within ten working days of the event or within 10 working days of the PI becoming aware of the event.

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

Reports of serious and unanticipated adverse device effects occurring in a UI\VAHCS subject are reviewed by the UI\VAHCS IRB Chair and/or UI IRB in the following manner:

- 1) The IRB chair compares the content of the REF with the previously approved project materials such as applications, informed consent document(s), protocols, investigator

brochures, or other supporting documents to determine whether this event meets the definition of an unanticipated problem involving risk to subjects or others.

- 2) If the chair agrees the event meets the definition of an unanticipated problem involving risks to subjects or others, the chair determines whether the event represents minimal risk of harm or more than minimal risk of harm to subjects enrolled in the research study.
- 3) If the event represents minimal risk of harm, the chair reviews and signs the report through the HawkIRB system.
- 4) If the event represents more than minimal risk of harm to subjects enrolled under the UI\VAHCS study, the report is referred to the convened IRB for review. The full board determines whether subjects must be notified of the new information, and if so, the method of notification and whether any study materials (e.g. consents, protocol) must be updated to reflect the new information.

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

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 to all reviewing IRBs and participating investigators. Any such reports are initially received by the investigator who is in turn responsible for reporting this information to the IRB-01 or IRB-03. By definition, these effects must be associated with the use of the device.

Investigators must report any evaluation of unanticipated serious adverse device effects conducted by the sponsor occurring in a non-UI\VAHCS subject to IRB-01 or IRB-03 using the Reportable Event Form (REF). This form includes a description of the effect, the date of occurrence, the type of risk, the outcome, and an assessment of degree of relatedness to the research. The form also includes the proposed actions to be taken by the investigator with regard to modifying approved study materials (including change in consent documents or other notification procedures) and notifying current subjects. Reports from the investigator to the IRB must be submitted via HawkIRB within ten working days of the event or within 10 working days of the PI becoming aware of the event. [For IRB-03 studies, reporting must occur within five working days.](#)

All reports of unanticipated serious device effects occurring in a non-UI\VAHCS subject are reviewed in the following manner:

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

All reports of unanticipated serious adverse device effects occurring in a non-UI\VAHCS subject are electronically filed with the appropriate research study. These reports are also reviewed by the IRB at the time of continuing review. In addition, reports of all unanticipated serious adverse device effects for all projects reviewed by the full board are provided by e-mail to all IRB-01 ~~or IRB-03~~ members on a monthly basis. [For IRB-03, they are reviewed by the full board at regular monthly IRB meetings.](#)

19.B.iv Unanticipated Problem Involving Risk to Subjects or Others

Refer to the section on Unanticipated Problems Involving Risks to Subjects or Others

19.B.v Receipt of new information

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

Investigators must report any new information that may impact the willingness of subjects to participate to IRB-01, IRB-02, or IRB-03 using the Reportable Event Form (REF). This form includes a description of the new information and its potential impact on subjects. Reports from the investigator to the IRB must be submitted via HawkIRB within ten working days of the event or within 10 working days of the PI becoming aware of the event. In addition, a

modification form must be submitted describing the investigator's proposed method for providing this information to subjects.

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

19.B.vi Noncompliance

Noncompliance is a failure to follow the federal regulations (45 CFR 46; 21 CFR 50) 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.

Investigators who are self-reporting noncompliance with federal regulations or the requirements or determinations of the IRB to IRB-01, IRB-02, and IRB-03 use the Reportable Event Form (REF). This form includes a description of the noncompliance and description of impact on the rights, safety, or welfare of subjects or others. Reports from the investigator to the IRB must be submitted via HawkIRB within ten working days of the event or within 10 working days of the PI becoming aware of the event.

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

Part 20: Continuing Review

The IRB is required to review and approve all non-exempt research projects at intervals appropriate to the degree of risk, but not less than once a year [45 CFR 46.109(e) (DHHS) and 21 CFR 56.109(f) (FDA)]. This is called "continuing review." Continuing review for non-exempt research is required to occur as long as the research remains active for long-term follow-up of the research subject, even when the research is permanently closed to the enrollment of new subjects and all subjects have completed all research-related interventions and to occur when the remaining research activities are limited to collection of private identifiable information.

As described above, the Informed Consent Document(s) indicate the project's expiration date. If a project initially received expedited review and risks to subjects remain minimal, the continuing review may be expedited (reviewed by the chair alone). If a project initially received full board review, the project generally requires full board continuing review. The calculation of

the approval period for research is based on the date and length of time at which the IRB approved the protocol by either a convened Full Board meeting or through the expedite review process.

20.A Due date for submitting an application for continuing review

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

A reminder memo is sent via email 60, 30, 14, 7 and 1 day before the LPSD of the project.

On the day prior to the date of expiration, the Principal Investigator, his or her delegates, and contact persons will receive notice that the project will lapse and that no human subjects activity may take place after 12:01 a.m. on the expiration date. The Principal Investigator will have 10 working days from the date of this notice to obtain review and approval of the continuing review for the project or it will be administratively closed by the IRB through the Human Subjects Office.

On the day of the LPSD (if a continuing review application has not yet been received by the HSO) the investigator and his/her HawkIRB contacts will receive notice by email that there will not be sufficient time prior to the expiration of the project for review and approval. This notice will state that IRB approval will lapse as of 12:01 a.m. on the expiration date and no further research activity may occur on or after that date. The Principal Investigator will be asked to submit a continuing review application or a project closure form in HawkIRB to close the project.

No human subjects activity (which includes the enrollment and follow-up of subjects and the collection and/or use of research data) may take place on or after the expiration date unless there is an over-riding safety concern (as determined by an IRB Chair) and until the continuing review application is approved by the IRB and released by the HSO. In the event a Continuing Review lapses for studies greater than minimal risk, the Principal Investigator must immediately submit to the IRB chair a list of research participants who could be harmed by stopping study procedures. The IRB chair, with appropriate consultation with the chief of staff for any studies enrolling VA subjects, determines whether participants on the list may continue participating in the research interventions or interactions. In these situations, IRB approval of a continuing

review must be obtained immediately.

If the HSO closes the study due to no response, the HSO sends the Principal Investigator a notification via email of study closure. The investigator's departmental executive officer (DEO) may also receive notification of closure. In cases of on-going externally funded projects, the Division of Sponsored Programs also receives a copy of the closure notice and make an independent determination regarding the need to notify the sponsor. Once the HSO closes a project, the only way for the project to resume is for the investigator to submit a New Project Application (via the HawkIRB system) for IRB review and approval.

20.B How to submit a continuing review application

The continuing review information is required to be submitted via HawkIRB. The investigator or his/her delegate should log onto the HawkIRB system and choose the open project from the inbox. From there, the investigator/delegate can choose to open either of the following forms: Continuing review form [Use this form if the investigator is not submitting a modification/update in conjunction with the continuing review] Modification/Update + Continuing Review Form.

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

20.B.ii Review and Approval Process for Continuing Reviews

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

Although the IRB does not require submission of Continuing Review forms for studies determined to be Exempt, if the study involves the VA, The VA Research and Development committee will require submission of continuing review information to that committee. This review is not conducted in HawkIRB.

Part 21: Reporting Complaints or Concerns

Refer to Human Subjects Research Related Complaint or Concern

Part 22: Project Closure

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

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

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

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

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

If the project was started in the HawkIRB system or has been transferred to the HawkIRB system, the investigator or his/her delegate should use HawkIRB to close the project. Log-on to HawkIRB and select the project that should be closed. Choose the "Project Close Form" and follow the directions to submit the project closure. Take care not to close the project too soon. Once a Project Closure Form is submitted, no more data may be collected about any of the subjects in the study and no more contact with subjects for research purposes is allowed. There is no mechanism to re-open a closed study.

In adherence with federal regulation once a research project is formally closed with the IRB via the HawkIRB electronic system, all research related activity must halt. Research activity includes contact with subjects, review of identifiable subject data, analysis of identifiable subject data, etc. If new information that may affect the safety or medical care of enrolled subjects is discovered or provided to the research team after a project has been closed, notification to the IRB must occur within ten working days of the event or notification to the investigator of the event. In order to inform subjects of the new information, IRB approval is

required prior to subject notification of such information. In order to provide the appropriate IRB approval to notify subjects of the new information, a HawkIRB new project application submission will be required for a previously closed project.

The project application will require an explanation including the new information that was discovered or provided to the research team and a plan for how the information will be disseminated to the enrolled subjects. If the new information requires action to be taken, or information to be provided to subjects, prior to IRB review in order to avoid immediate harm to the subjects, an IRB chair should be consulted to determine if the action or notification can be undertaken prior to IRB review. In such cases IRB review should be still be carried out eventually as described. All relevant materials in connection with the method of dissemination will need to be included in the HawkIRB application for IRB approval. In most cases, a waiver of informed consent can be obtained in order to provide the new information to the enrolled subjects.

Part 23: Record Keeping

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

23.A How long to keep records

Copies of all research records for studies that do not involve protected health information must be kept for at least three years after the close of the study.

Copies of all research records for studies that involve protected health information must be kept for at least six years after the close of the study. HIPAA regulations provide individuals the right to receive an accounting of certain disclosures of protected health information made by a covered entity. This accounting must include disclosures of protected health information that occurred during the six years prior to the individual's request for an accounting and must include specified information regarding each disclosure.

Copies of all research records for VAHCS studies must be kept indefinitely after the close of the study. Studies that involve drugs or devices seeking FDA approval must be kept for two years after the FDA has taken final action on the marketing application. Sponsors may require a longer retention rate.

Ultimately, it is the Principal Investigator's responsibility to maintain accurate files of IRB correspondence, approvals, and research records during the life of the study and after

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

Part 24: Principal Investigator leaves the University of Iowa

The UI owns the primary research results generated from all research conducted under its jurisdiction. Therefore, when a PI plans to leave the UI and wants to take the original data to the new institution, the transfer of the data/samples must proceed according to established guidelines.

If the PI will not have continued access to identifiable research data /samples and is not taking data to the new institution:

- 1) If the study is not complete - submit a Modification form in HawkIRB to change the PI named on the application
- 2) If the study is complete - submit a Project Closure form in HawkIRB

If the PI will take identifiable research data /samples to the new institution, or plans to have continued access, s/he should:

- 1) Submit a Modification form in HawkIRB requesting IRB approval to take the data/samples or to have continued access
- 2) Contact Division of Sponsored Programs (DSP) to determine whether s/he needs a Materials Data Transfer Agreement
- 3) Obtain a letter from the PI's UI department head that documents awareness/approval of the transfer of the data/samples and outlines the department expectations for the transfer and use of the data/samples