



UnityPoint Health
Des Moines



UnityPoint Health – Des Moines

Human Research Protection Program Procedures

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UnityPoint Health – Des Moines

Eric Crowell
President and Chief Executive Officer

Mark Purtle, MD
Vice President of Medical Affairs
Institutional Official for Research Subjects Protections

Kathryn Karpowicz, BSN, RN, MA Director of Ethics and Human Research
Protection Program (HRPP)

Jody Weese, BA
Coordinator, Human Research Protection Program (HRPP)

Kenneth McCann, DO
Chair, Institutional Review Board

Timothy Drevyanko, MD, MS
Vice-Chair, Institutional Review Board

Kathryn Karpowicz, RN, MA
Research Subject Advocate

All local documents and forms are available on the IRB web page

www.unitypoint.org/irb



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I. Introduction

This document describes the Policy and Procedures governing the Program of Human Subjects Protection and the operations of the Institutional Review Board of UnityPoint Health - Des Moines (UPHDM).

The UPHDM Institutional Review Board is responsible for overseeing research conducted within UnityPoint Health – Des Moines, which includes Iowa Methodist Medical Center, Iowa Lutheran Hospital, Methodist West Hospital, Blank Children’s Hospital, Blank Physicians Group, UnityPoint Health Foundation and John Stoddard Cancer Center.

II. Charge

UnityPoint Health – Des Moines is committed to the highest standards of clinical research and to protecting the rights and welfare of participants in clinical research endeavors.

The **Institutional Review Board** is charged with the responsibility for reviewing and overseeing all research involving human participants conducted within UnityPoint Health – Des Moines.

Eric Crowell
President and Chief Executive Officer
UnityPoint Health – Des Moines



III. Policy

Research involving human participants conducted within UnityPoint Health – Des Moines will:

- Scrupulously safeguard the rights and welfare of research participants and be guided by the ethical principles of respect for persons, beneficence, and justice as set forth in the Belmont Report.
- Be consistent with the Values and Mission of the System.
- Obey laws and regulations as set forth in:
 - Federal Policy for Protection of Human Subjects (Common Rule, 45CFR46, Part A),
 - Additional Protections for Vulnerable Populations (45CFR46, Parts B (revised December 2001), and D),
 - Food and Drug Administration Regulations for Protection of Human Subjects (21CFR50 and 21CFR56),
 - Standards for Privacy of Individually Identifiable Health Information (Privacy Rule, 45CFR160 and 164),
 - The Standards of DNV; and
 - Relevant portions of the Code of Iowa and the Iowa Administrative Code.

IV. Basic Procedures for Human Research Protections

A. Scope and Authorities

[45CFR46.101]

(1) Research Involving Human Participants

An activity is defined as research involving human participants if either:

(1) it meets the following definitions of research and human subject as defined in DHHS regulation 45CFR46.102(d) and 45CFR46 102(f), respectively, or

(2) it meets the definitions of clinical investigation and human subject as defined in FDA regulation 21 CFR 50.2(c) and 21 CFR 50.2(g), respectively.

The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. (21 CFR 50.3(c), 21 CFR 56.102(c)).

When medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimens as human subjects.

Human research must be reviewed and carried out according to the procedures set forth in this document.

(2) Activities and entities covered by these procedures

These procedures apply to all human research or clinical investigations - regardless of the source of support - conducted, supported or otherwise the sole responsibility of UnityPoint Health – Des Moines (UPHDM) or any of its components, including Iowa Methodist Medical Center, Iowa Lutheran Hospital, Methodist West Hospital, Blank Children's Hospital, Blank Physicians Group, UnityPoint Health Foundation and John Stoddard Cancer Center.

Such research cannot begin until it has been approved by the UPHDM Institutional Review Board. Authority to approve, suspend, or terminate such research rests solely with the UPHDM Institutional Review Board. Decisions made by the UPHDM IRB cannot be over-ridden by any



institutional authority.

As explained in the next section, certain kinds of research are exempt from review by the IRB. Only the IRB chair, Vice-chair, or designee can make this determination.

(3) Exempt research activities

Certain research activities are exempt from review and institutional oversight 45CFR46.101(b). Research in the following categories may generally qualify for exemption:

Category 1.

- a. The research conducted in established or commonly accepted educational settings.
- b. The research involves normal educational practices such as:
 - Research on regular and special educational instructional strategies.
 - Research on the effectiveness of the comparison among instructional techniques, curricula, or classroom management methods.
- c. The research does not involve prisoners as participants
- d. The research is not FDA-regulated.

Category 2.

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.

Category 3.

Research involving the use of educational tests that is not exempt under paragraph (b)(ii) of this section, if: (i) the human subjects are elected or appointed public officials or candidates for public office; or (ii) Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.


Category 4.

Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. Such research must be in compliance with HIPAA regulations (Section X).

Category 5.

Research and demonstration projects designed to study, evaluate, or otherwise examine:


- public benefit or service programs;
- procedures for obtaining benefits or services under those programs;
- possible changes in or alternatives to those programs or procedures; or
- possible changes in methods or levels of payment for benefits or services under those programs.
- The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act).
- The research or demonstration project must be conducted pursuant to specific federal statutory authority.
- There must be no statutory requirement that the project be reviewed by an IRB.
- The project must not involve significant physical invasions or intrusions upon the privacy of participants.
- The exemption should have authorization or concurrence by the funding agency.

Category 6.

Taste and food quality evaluation and consumer acceptance studies.

Note: This list is edited: consult 45CFR46.101(b) for full details regarding the exemptions.

Restrictions. Research that meets the federal criteria for exemption may not be approvable at UPHDM. Examples of such research include, but are not limited to, studies that are inconsistent with the primary mission of the institution; research that is inconsistent with local regulations or laws




or professional codes of conduct; research requiring unplanned expenditure of institutional resources; research involving prisoners; and research involving children when the investigator participates in the observation of public behavior, or when the researcher includes interviews or surveys of children.

Application for exemption. An investigator who believes a project may qualify for exemption should submit a request in writing to the IRB Chair. Supporting documents demonstrating why the investigator believes the work qualifies for exemption under one of the above-listed categories should be submitted with the request. The investigator must give assurance that the research will be conducted in accordance with any applicable regulations, laws or codes. If necessary, the chair will seek expert opinion regarding the proposed research and conformity to applicable codes.

Determinations. Authority to classify research as exempt rests with the Chair of the Institutional Review Board and not with an investigator. In making a determination whether to grant an exemption, the chair will use the “Exemption Checklist” to evaluate whether the research conforms to one of the categories enumerated above and conduct an ethical analysis using the principles of respect for persons, beneficence and justice. The ethical analysis will include an examination of the following elements:

- The research holds out no more than minimal risk to subjects;
- Selection of subjects is equitable;
- If there is recording of identifiable information, there are adequate provisions to maintain the confidentiality of the data;
- If there are interactions with subjects, there will be a consent process that will disclose such information as:
 - The activity involves research
 - A description of the procedures
 - Participation is voluntary
 - Name and contact information of the investigator
 - Provisions to maintain the privacy interests of subjects.

The “Exemption Checklist” will be used to document the chair’s determination and retained as a record of the application in the IRB office. The Director of HRPP must acknowledge research exempt from IRB oversight. It must be emphasized that exemption from IRB oversight does not mean that the research is totally exempt from institutional oversight. In particular, the protocol should document mechanisms, when appropriate, for obtaining informed consent and responding to concerns or complaints.



Notification. All requests for exemption are answered promptly by determination letters, signed by the IRB chair, which describe the regulatory basis for granting exempt status as well as any additional requirements that may be imposed in order to assure protection of the rights and welfare of research subjects, or the reasons for denying exempt status. Letters granting exempt status must be reviewed by the Director of HRPP, who must either countersign them or explain in separate communications the basis for disapproving the requests. Exemption decisions are noted in agendas and minutes of convened meetings and filed in the IRB Office.


(4) Quality assessment and quality improvement (QA/QI) studies

Studies to assess or improve quality of healthcare operations are generally not considered research unless they meet the regulatory definition under 45 CFR 46.102(d) : “Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.” Planning to publish an account of a quality improvement project does not necessarily mean that the project fits the definition of research; people seek to publish descriptions of non-research activities for a variety of reasons, if they believe others may be interested in learning about those activities. Conversely, a quality improvement project may involve research even if there is no intent to publish the results. If the quality study involves research, as defined above, then the study requires IRB review. Depending on the level of risk involved, the study may require full board review, or be eligible for an expedited review process.

(5) Case reports

Case reports, that is, descriptions of unusual or unique presentations of a disease or condition are not considered reports of research and do not require review by the IRB or verification of exempt status if the following conditions are satisfied:

- a. record review is done by persons already involved in patient's care (so that no new confidentiality risks created by the activity);
- b. information about the patient is presented in an anonymous fashion or with the explicit consent of the patient to the report; and
- c. no changes were made in the patient's care or diagnostic testing for the sake of reportability.



On the other hand, case reports are reports of research and require verification of exemption or IRB review if:


- a. they are presented in a manner that states or implies generalizability;
- b. changes were made in the patient's care for the sake of reportability; or
- c. the patient's records were examined for reasons not directly related to patient care or quality assurance.

If any of these above circumstances apply, investigators are advised to contact the IRB Office for consultation on a case-by-case basis. Regardless of whether a particular case report does or does not qualify as a report of research, investigators must at all times be sensitive to protecting the privacy and confidentiality of the subjects of the reports.

(6) Determination about whether an activity qualifies as human research

In most cases, investigators readily understand the definition of human subjects research and abide by the provisions of this Policy & Procedures when it is appropriate. Investigators who request advice in determining whether a given project meets the regulatory definitions are invited to discuss the matter with the IRB Chair or the Director of HRPP, who will explain the definitions and use the OHRP decision chart and guidance document. Determinations about whether an activity qualifies as human subjects research will be documented in determination letters to the prospective investigator from the chair of the IRB. These letters will include the determination as well as the rationale leading to the determination.

In rare instances, it may happen that a person claims that a particular activity is not human subjects research and thus not subject to these Policy & Procedures or to oversight by the IRB. The IRB Chair, the Director of HRPP and the Vice President for Medical Affairs are authorized to make determinations about whether a given project meets the regulatory definitions of DHHS and FDA for human subjects research, and which would be subject to these Policy & Procedures. The Vice President for Medical Affairs is authorized to make the determination when the activity has elements of a quality assurance/quality improvement project. The person making the determination evaluates the protocol according to the above definition of human research. He or she may consult the decision chart published by OHRP for assistance to decide whether the activity is research or involves human subjects as defined by



DHHS regulations. If an investigator does not accept the determination, the matter will be treated as an instance of non-compliance with the human research protection program requirements and handled according to the procedures described in Sec IV.Y.

(7) Other laws and regulations

Compliance with this policy requires compliance with pertinent State and Federal laws or regulations, which may provide additional protections for human subjects.

This policy does not affect any State or local laws or regulations which may otherwise be applicable and which provide additional protections for human subjects.

(8) Research subject to FDA regulations

On the application of a sponsor or sponsor-investigator, the FDA may waive any of the requirements contained in its regulations, including the requirements for IRB review, for specific research activities or for classes of research activities, otherwise covered by FDA regulations at 21CFR56.105.

(9) Research in foreign countries

When research covered by this policy takes place in foreign countries, procedures normally followed in the foreign countries to protect human subjects may differ from those set forth in this policy. In these circumstances, if the CEO of UPHDM, or his designee, in consultation with the Institutional Review Board (IRB) and, if necessary, the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA), determines that the procedures prescribed by the institution afford protections that are at least equivalent to those provided in this policy, the CEO of UPHDM, or his designee, may approve the substitution of the foreign procedures in lieu of the procedural requirements provided in this policy.

(10) Research involving Vulnerable Populations

Research involving prisoners does not qualify for exemption. Research involving children does not qualify for exemption under Category 2 unless the research involves the use of educational tests or the observation of public behavior where the investigator(s) do not participate in the activities being observed. Research that is FDA

regulated does not qualify for exemption under Categories 1-5.

(11) Reserved authorities

The CEO of UPHDM, or his designee, may require that specific activities conducted, supported, or otherwise subject to regulation by UPHDM but not otherwise covered by this policy, comply with some or all of the requirements of this policy.

B. Definitions

[45CFR46.102 and 21CFR56.102]

(1) Certification means the official notification by the institution to a supporting Department or Agency of the federal, local or state government or a sponsor, in accordance with the requirements of this policy, that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.

(2) Generalizable knowledge means research findings that contribute to a theoretical framework of an established body of knowledge, enhances scientific or academic understanding, and is relevant to a larger population beyond the local site of the data collection.

(3) Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care when general medical care includes participation in research. For purposes of subpart D of this part, a guardian also means an individual who is authorized to consent on behalf of a child to participate in research. When research is conducted outside of Iowa, the UPHDM law department will be consulted to determine applicable state laws. [21CFR50.3]

(4) Human research is an activity is human research if it is either research involving human subjects, as defined below, or a clinical investigation, as defined below.


(5) Human Participants means a living individual about whom a Researcher conducting research obtains data through intervention or interaction with the individual, or identifiable private information.




(6) Human subject

- a. HHS definition: a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject. 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 (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects. The preceding definition of "human subject" will only apply to the Department of Health and Human Services definition of "research." (45 CFR 46.102 (f))
- b. FDA definition: Subject means a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used. A Human Subject is 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 human or may have a medical condition or disease. When medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissues specimens as human subjects. The preceding definition of "human subject" will only apply to the Food and Drug Administration definition of "research." (21 CFR 50.3 (g))

- (7) Institution** includes UPHDM and its components, namely Iowa Methodist Medical Center, Iowa Lutheran Hospital, Methodist West Hospital, Blank Children's Hospital, Blank Physicians Group, UnityPoint Health Foundation and John Stoddard Cancer Center.

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- (8) **Interaction** includes communication or interpersonal contact between investigator and subject.
- (9) **IRB** means an Institutional Review Board established in accord with and for the purposes expressed in this document.
- (10) **IRB approval** means the determination of the IRB that the research has been reviewed and may be conducted at the institution within the constraints set forth by the IRB.
- (11) **Intervention** includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- (12) **Legally authorized representative** means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research (45CFR46 and 21CFR50.) Iowa Code defines legally authorized representatives as follows: Substitute medical decision-making board [Iowa Code 135.29]. Guardian for minor or person with impaired decision-making capacity [Iowa Code 633.562, 633.552]. Attorney-in-fact, guardian, spouse, adult child, parent, adult sibling [641 Iowa Admin. Code 857]. Durable power of attorney for health care [Iowa Code 1999: Section 144B.2, 144B.3, 144.B.5]. When research is conducted outside of Iowa, the UPHDM law department will be consulted regarding applicable state law.
- (13) **Minimal risk** means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
- (14) **Principal Investigator** is a person qualified by education, training or experience to assume responsibility for the conduct of a research protocol.

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- (15) **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.
- (16) **Research** means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes.
- (17) **Research subject to regulation**, and similar terms, are intended to encompass those research activities for which a Federal Department or Agency has specific responsibility for regulating as a research activity.
- (18) **Systematic Investigation** means a methodical activity that involves a prospective research plan which incorporates data collection, either quantitative or qualitative, and data analysis to answer a defined research question.

The following definitions relate to research regulated by FDA (21CFR50 and 56):

- (19) **Clinical investigation** means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions regarding non-clinical laboratory studies.
- (20) **Sponsor** means a person or other entity that initiates a clinical investigation, but that does not actually conduct the investigation, i.e., the test article is administered or dispensed to, or used involving a subject under the immediate direction of another individual. A person other than an individual (e.g., a corporation or agency) that uses one or more of its own employees to conduct an investigation

that it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators.

- (21) Sponsor-investigator** means an individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include any person other than an individual, e.g., it does not include a corporation or agency. The obligations of a sponsor-investigator under this part include both those of a sponsor and those of an investigator.
- (22) Test article** means any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 or 354-360F of the Public Health Service Act [42USC262, 42USC263].
- (23) Family member** means any one of the following legally competent persons: Spouse; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.

C. Assuring Compliance with this Policy


[45CFR46.103]

(1) Federal-Wide Assurance

UPHDM will provide written assurance to the Department of Health and Human Services (DHHS), in the form of the federal-wide assurance (FWA), that it will comply with the requirements set forth in 45CFR46. Such assurance will be reviewed yearly and updated as necessary.

The FWA shall at a minimum include the following information:

- a. A statement that UPHDM will be guided by the ethical principles set forth in the Belmont Report - namely, respect for persons, justice, and beneficence - in the discharge of its responsibilities for protecting the rights and welfare of human subjects of research conducted at or sponsored by UPHDM, regardless of whether the research is subject to Federal regulation.

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- b. A statement that the IRB is established in accordance with the requirements of 45CFR46, and that the IRB is administered and supported by the Director of HRPP.
 - c. A list of IRB members identified by name, earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution. Changes in IRB membership shall be reported to OHRP.
 - d. A statement that the IRB will follow written procedures: (i) for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution; (ii) for determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review; and (iii) for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.
 - e. A statement that written procedures will be followed for ensuring prompt reporting to the IRB, appropriate institutional officials, and, as appropriate, the sponsor, funding agency or regulatory agency of: (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval [Sections IV. N(3) and (5)].

(2) Individuals authorized to execute the Federal-Wide Assurance

The assurance shall be executed by an individual authorized to act for the institution and to assume on behalf of the institution the obligations imposed by this policy and shall be filed in such form and manner as the DHHS prescribes.

Implementation. The CEO of UPHDM has authorized the Vice President for Medical Affairs, the Director of HRPP and the HRPP Coordinator to submit, or make changes in, the FWA on behalf of UPHDM.



D. IRB Membership

[45CFR46.107] (21CFR56.107)

(1) General considerations

The IRB shall have at least twelve (12) members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas.


Membership includes at least two physicians and representatives from Pharmacy, Nursing, Social Services, Pastoral Care, Executive Leadership, and a person otherwise unaffiliated with UPHDM. This IRB regularly reviews research that involves a vulnerable category of subjects, viz children; therefore, the IRB shall include one or more individuals who are knowledgeable about and experienced in working with children.

(2) Appointment to the IRB

The Vice President for Medical Affairs is authorized by the CEO of UPHDM to appoint members of the IRB. Appointments are for a calendar year and may be renewed. All appointments are documented by letters, which are kept on file in the office of the IRB.

(3) IRB leadership

- a. Eligibility criteria. The Chair and Vice Chair will possess significant, documented involvement in the practice or oversight of research; at least 1 year experience as a voting member of an IRB; formal training in human subjects protection at the minimal level required of all investigators and research



staff; ability to articulate the mission of the IRB and the human research protections program to persons and audiences of different backgrounds; ability to work well with persons from different backgrounds and professional qualifications; appreciation for diversity of opinion.

- b. Service criteria. Commitment to and active involvement in continuing education in human subjects protection; commitment to continuous improvement in IRB processes; maintenance of good working relationships with IRB members, investigators and institutional administrators; efficient management of IRB meetings.

Evaluation. The HRPP Coordinator meets with each Chair and Vice Chair once a year to specifically evaluate their performance. according to the above criteria.

The chair and vice chair of the IRB are named by the Vice President for Medical Affairs and serve for a calendar year. Appointments may be renewed each year. The chair signs all correspondence dealing with decisions and other actions taken by the IRB and conducts IRB meetings. The vice chair may exercise all functions of the chair when the chair is absent or otherwise unavailable. In the event that neither the chair nor the vice chair is available to respond to an urgent matter, the HRPP Coordinator will contact as many members as possible who will confer on the matter and appoint one person to make a decision as chair pro tempore in the name of the IRB. In the event that neither the chair or the vice chair is available to conduct the regular meeting, the HRPP Coordinator will contact an IRB member with at least one year of experience as a voting member of the IRB and formal training in human subjects protection to request that they run the scheduled meeting. Neither the chair, vice chair, nor any member may make a decision individually on behalf of the IRB that is appropriately a matter for determination by the Board as a whole.

(4) Categories of membership

- a. Regular. A regular member of the IRB participates in all activities of the IRB and has the privilege of voting for all motions presented to the IRB.
- b. Alternate. An alternate member of the IRB may attend all meetings of the IRB and participate in all discussions, but may not vote unless the regular member, for whom the alternate member is designated, is absent or recused

because of a conflict of interest. An alternate member may be designated to serve in place of more than one regular member. Wherever possible, the professional status of the alternate member will be equivalent, or at least closely related to, the status of the corresponding regular member.

(5) Gender equality

Every nondiscriminatory effort will be made to ensure that the IRB does not consist entirely of men or entirely of women, including the institution's consideration of qualified persons of both genders, so long as no appointment is made to the IRB on the basis of gender.

(6) Primary concerns of members


The IRB may not consist entirely of members of one profession. The IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. The Director of HRPP confers periodically with the Chair to determine whether the expertise and representative capacity among the IRB members is adequate to meet the regulatory requirements for the protocols being reviewed. If a determination is made that additional members should be appointed, then the Director identifies appropriate candidates, who are then appointed as described in IV. D. (2) . Individuals who are responsible for business development of the organization are not eligible to serve as IRB members, alternate members, or ex-officio members.

(7) Unaffiliated member

The IRB shall include 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.

(8) Conflict of interest

An IRB member may not participate in the initial or continuing review or the review of unanticipated problems, noncompliance, or requests for exemption of any project if the member expects to participate, or has participated, in any aspect of the research including recruitment of subjects; informed consent process; treatment of subjects or evaluation of the outcome of treatment; analysis or presentation of the data. Neither may a member participate in the initial or continuing review if the member has a significant financial interest, as defined in UPHDM Policy on Individual Conflict of Interest in



Research. Members who have these conflicts must recuse themselves from discussing (except to provide information requested by the IRB) and voting on the protocol and leave the room. These members are not counted toward quorum. At the time of IRB appointment, and annually thereafter, a person will be required to complete a “Conflict of Interest Disclosure” form. The process to identify IRB members and consultants with a conflict of interest is outlined in Section AA. Conflict of Interest Disclosure of this procedure manual.

These policies cover each type of review, such as review by the expedited procedure and review by convened IRB.

IRB members or consultants are defined when they have a conflicting interest as follows:


- Definition:
- “Immediate Family” means spouse and dependent children.

(9) Use of consultants

The IRB may, at its discretion, invite consultants with competence in special areas to assist in the review of issues which require expertise beyond, or in addition to, expertise of the IRB members. The participation of a consultant in any matter before the IRB shall be documented in the minutes of the meeting at which the matter was discussed. Consultants may not vote or be present when the IRB votes on a protocol.

Consultants can become involved in the review of a protocol in various ways:

- a. If the HRPP Coordinator thinks that a protocol falls outside the normal range of protocols reviewed by the IRBs, she will bring it to the attention of the chair who may request outside review.
- b. IRB members are reminded each month that they may request additional expert advice to review any protocol for scientific content or for any other matter. The IRB staff will make the necessary arrangements for obtaining the services of an appropriate consultant. Depending on the nature of the request, resources at other medical centers in the Des Moines metro area or at neighboring research universities will be identified.

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- c. The IRB, after consideration of a protocol at a convened meeting, may decide that advice from a consultant is needed, and request the IRB staff to secure such services. The consultant may submit a written report to the chair, which will then be shared with the IRB at or before a convened meeting and included in the protocol file, or present a report at a convened meeting. The contribution of the consultant will be documented in the minutes of the meeting.
 - d. If an investigator or the institution assumes the role of sponsor in research on a drug or a device that is subject to FDA regulations, then the IRB will engage the services of a consultant with expertise in the area of sponsor's responsibilities (drugs, 21CFR312.50-53; devices, 21CFR812.40-43) to evaluate whether these responsibilities are being met.


(1) Conflict of interest.

Prior to being engaged formally as a consultant, a person would be required to complete a "Conflict of Interest Disclosure" form as well as required to disclose whether he or she expected to participate, or has participated, in any aspect of the research under consideration, including recruitment of subjects; informed consent process; treatment of subjects or evaluation of the outcome of treatment; analysis or presentation of the data would not be eligible to serve as a consultant. If any of these criteria applied, the person would not be engaged as a consultant.

(10) Training of IRB members

UPHDM will support various educational activities designed to develop and maintain the competencies of IRB members in the discharge of their responsibilities.

- a. Minimal training that must be completed prior to a new IRB member reviewing research: completion of the NIH training found at, <http://phrp.nihtraining.com>. Documentation of this training must be submitted to the IRB office prior to the new member participating in review of research. If more than two months pass without completion of initial minimal training, the new IRB member will be asked to resign their appointment due to lack of commitment.
- b. Continuing education of IRB members: UPHDM subscribes to "IRB Ethics and Human Research", and distributes these



materials to IRB members bi-monthly via the IRB SharePoint website.

- c. Members are expected to participate in educational activities afforded them, such as attendance at local, regional and national conferences, and webinars during the year. This will be reviewed and discussed with IRB members each year at the time of annual review of IRB members by the IRB chair.
- d. Periodically, IRB members will be surveyed in order to illicit their input regarding the focus of continuing education.

(11) Evaluation of IRB members

UPHDM will assure the continued competency of IRB members. To this end, the HRPP Coordinator, along with the IRB chair as available, will evaluate the performance, effectiveness and commitment of each individual IRB member. IRB members will be evaluated annually. The IRB member will have completed the NIH “Protecting Human Research Participants” training at: <http://phrp.nihtraining.com> prior to the evaluation. The HRPP Coordinator may choose to be the sole evaluator of individual members, or may incorporate a process of peer review into the evaluation at his/her discretion. The evaluation documents will be kept on file in the IRB office. The evaluation assessment will be shared with each IRB member in their annual appointment letter.

(12) Liability

IRB members, including unaffiliated members, participating in IRB activities are covered by the general liability insurance policy of UPHDM.

(13) Removal


IRB members may be removed by the Vice President for Medical Affairs for failure to discharge assigned tasks (such as protocol review), poor attendance at regularly scheduled meetings, or other actions that are, in the opinion of the Vice President for Medical Affairs in consultation with the IRB chair, inconsistent with service on the IRB.


E. IRB Functions and Operations

[45CFR46.108; 21CFR56.108(b)]

(1) General operations and definition of quorum

In order to fulfill the requirements of 45CFR46 and 21CFR56 the IRB shall:

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- a. Follow written procedures for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution; for determining which projects require review more often than annually and which projects need verification from sources other than the investigator that no material changes have occurred since previous IRB review; for ensuring prompt reporting to the IRB of changes in research activity; and for ensuring that changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the human subjects.
 - b. Follow written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the Food and Drug Administration of: any unanticipated problems involving risks to human subjects or others; any instance of serious or continuing noncompliance with these regulations or the requirements or determinations of the IRB; or any suspension or termination of IRB approval.
 - c. Except when an expedited review procedure is used, review of proposed research at convened meetings, at which a majority of the members of the IRB are present, including at least one member who is a physician and at least one member whose primary concerns are in nonscientific areas. Additionally, at least one unaffiliated member and one member who represents the general perspective of subjects must be present to constitute a quorum. The unaffiliated member, the non-scientific member, and the member representing the general perspective of subjects may be the same person, two different persons, or three different persons. The HRPP Coordinator is responsible for determining that the constituted group meets regulatory requirements for quorum and membership. When a protocol involves children, pregnant women, or other populations considered to be vulnerable (such as mentally disabled persons, or economically or educationally disadvantaged persons) then a member of the IRB with appropriate expertise must be present during the discussion and voting.
 - d. In order for the research to be approved by the IRB, it shall receive the affirmative voice vote of a majority of those members present at the meeting. The members remaining after a member recuses for conflict of interest or leaves the



meeting for any other reason must meet regulatory requirements for quorum and membership.

- e. Occasionally, it may be necessary to hold a convened meeting of the IRB using a teleconference process. In these cases, the meeting format, including quorum requirements, and documentation of minute requirements, will be the same as for a convened meeting of the IRB in person. The minutes will also reflect that the IRB members received all pertinent material prior to the meeting, and all members can actively and equally participate in the meeting.

(2) Administrative support

Administrative support for IRB functions is provided by the IRB Office of UPHDM. The HRPP Coordinator is responsible for receiving and docketing new protocol applications and revisions and yearly reports submitted for continuing review; assigning reviewers for new and continuing applications; preparing correspondence on behalf of the IRB; arranging meetings; taking minutes of IRB meetings and distributing them to members; and overseeing safe storage of IRB files.

(3) Delivery and disposal of documents

All documents to be considered at a convened meeting of the IRB are delivered to IRB members or uploaded to the IRB SharePoint website, at least one week before the meeting. Members may not retain personal copies of sensitive documents, such as protocols and consent forms. Paper documents considered at a convened meeting are collected and destroyed after each meeting. Documents are removed from the SharePoint website immediately after the convened board meeting.

(4) Confidentiality

Members are expected to hold in confidence all matters coming before the IRB and comply with all State and Federal regulations regarding confidentiality, including HIPAA.

(5) Attendance of visitors at IRB meetings

Persons who are not IRB members may, at the discretion of the chair, attend meetings. Such persons will sign a statement agreeing to keep the meeting proceedings confidential, and their attendance will be noted in the minutes of the meeting.



F. Initial Review of Research by IRB

[45CFR46.109] [21CFR56.111]

(1) Functions and authority of the IRB

The IRB shall review and have sole authority to approve, require modifications in (to secure approval), or disapprove all research activities involving human subjects conducted at UPHDM.

The CEO of UPHDM, or his designee, may require that specific activities conducted, supported, or otherwise subject to regulation by UPHDM but not otherwise covered by this policy, comply with some or all of the requirements of this policy.

Research involving prisoners is not contemplated at this time.

(2) Format for submitting applications to the IRB

Investigators are expected to use the approved application form “Application to Conduct Research Involving Human Subjects” when submitting new protocols for consideration by the IRB.

(3) Format for presentations to the IRB


Except in the case of protocols submitted for expedited review, the principal investigator is usually required to make an oral presentation of the protocol to the IRB and be available to answer questions. Investigators are not present during deliberations about a protocol or voting.

The suggested format for making an oral presentation to the IRB is posted on the IRB Web Page

(4) Procedure for evaluating protocols

a) The HRPP Coordinator will assign a board member as primary reviewer with the appropriate scientific expertise to conduct an in-depth review of the protocol. Four reviewers, usually two physicians and two non-physicians, serve each month.

(b) The HRPP Coordinator, in consultation with the IRB chair, will determine for each protocol application whether or not it involves subjects likely to be vulnerable or subject to coercion. If this is the



case, then the HRPP Coordinator will ensure that at least one IRB member knowledgeable about or experienced in working with such subjects will be present at the meeting.

(c) Each primary reviewer receives copies of all new protocols or protocol amendments, protocol applications, and consent documents.

(d) A copy of the final contract with the sponsor will be submitted for each new protocol to be reviewed. The HRPP Coordinator may make exceptions to this requirement and permit an “all but signed”, verbally approved, version of the contract to be submitted if the signed copy is not available at the time of submission deadline. The final contract will be reviewed by the board member serving as community legal representative on the IRB for:

- Consistency regarding provisions for medical care or other care or services for research-related injury;
- to ensure that it indicated who would provide care and who was responsible to pay for it;
- to ensure that the final contract obligated the sponsor to report to the organization, within 30 days of availability for routine safety monitoring and within 7 days for urgent monitoring, any finding of the study monitors that could affect the safety of participants, affect the willingness of participants to continue participation, influence the conduct of the study, or alter the IRB’s approval to continue the study; to ensure that it described the communication of results from a closed research study to participants when those results directly affected their safety or medical care, findings should be communicated within two years after study closure, or as appropriate for the specific study.

(e) Board members who are not primary reviewers receive copies of the protocol applications and consent documents. For amendments, members receive a summary of the requested changes and the revised consent document. If there are no changes in the consent document, then the members receive a complete copy of the amendment.

(f) When it is determined that consultants or experts are required to advise the IRB in its review of a protocol, the protocol shall be distributed to consultants prior to the meeting.

(5) **Information to be provided in the informed consent document**

Information provided to subjects as part of informed consent must be in accordance with 45CFR46.111; 45CFR46.116; 45CFR46.117; 21CFR50.20; 21CFR50.23; 21CFR50.25; 21CFR50.27; 21CFR56.111. Refer to procedures in IV.S. of this documents.

(6) **Research involving children**

For research involving children, the IRB shall make an explicit determination of the degree of risk to the subject, and such determination shall be documented in the minutes. The risk checklist is completed by the IRB Chair and filed in the study file in the IRB Office.

(7) **Research involving participants with diminished capacity**

For research involving participants with diminished capacity, the IRB shall make a determination of risk level associated with the protocol and document this in the minutes. Refer to procedure IV.U. of this document.

(8) **Research Involving drugs or biologics**


- a. **Investigational drugs.** An application to conduct research involving an investigational new drug in humans must have a Notice of Claimed Investigational Exemption for a New Drug with FDA (synonymous with an Investigational New Drug application) and the drug must be labeled "For investigational use only." [Iowa Code 126.12]

In the rare circumstance that the IRB reviews research in which the organization or the investigator holds the IND, the IRB will require written documentation that the investigator or the organization is knowledgeable about and will follow FDA regulatory requirements. This documentation should be submitted with the application for research.

- b. **Approved drugs.** The clinical investigation of a drug product that is lawfully marketed in the United States is exempt from the requirements of this part if all the following apply:

Exemption #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;

- 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;
- 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;
- The investigation is conducted in compliance with the requirements for institutional review set forth in 21CFR56 (Sec F) and with the requirements for informed consent set forth in 21CFR50 Sec Q); and
- The investigation is conducted in compliance with the requirements of 21CFR 312.7 (Promotion and charging for investigational drugs).

Exemption #2:

- The clinical investigation is for an in vitro diagnostic biological product that involves one or more of the following:
 - Blood grouping serum
 - Reagent red blood cells
 - Anti-human globulin

Exemption #3:

- The diagnostic test is intended to be used in a diagnostic procedure that confirms the diagnosis already made by another, medically established, diagnostic product or procedure.
- The diagnostic test is shipped in compliance with 21CFR312.160.

Exemption #4:


- A clinical investigation involving use of a placebo if the investigation does not otherwise require submission of an IND.

(9) Research involving medical devices

For research involving medical devices, the IRB must determine that one of the following three items is true:

- The device has an IDE and the IDE number that is supported by one of the following sources of documentation submitted to the IRB office and confirmed by the HRPP Coordinator: (the Investigator Brochure may not be used for this purpose)
 - Sponsor protocol imprinted with the IDE number.
 - Written communication from the sponsor documenting the IDE number.
 - Written communication from the FDA documenting the IDE number. (Required if the investigator holds the IDE.)

- The device meets the requirements for an abbreviated IDE:
 - The device is not banned
 - The device is not a significant risk device;
 - The sponsor (or investigator) will label the device in accordance with 21 CFR 812.5;
 - The sponsor (or investigator) will comply with the requirements of 21 CFR 812.46 with respect to monitoring investigations;
 - The sponsor (or investigator) will maintain the records required under 21 CFR 812.140(b) (4) and (5) and make the reports required under 21 CFR 812.150 (b) (1) through (3) and (5) through (10);
 - The sponsor (or investigator) will ensure that participating investigators maintain the records required by 21 CFR 812.140. (a) (3) (i) and make the reports required under 21 CFR 812.150 (a) (1), (2), (5), and (7)
 - The sponsor (or investigator) will comply with the prohibitions in 21 CFR 812.7 against promotion and other practices.
 - The sponsor obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval.
 - The sponsor ensures that each investigator participating in an investigation of the device obtains



from each subject under the investigator's care, consent under 21 CFR 50 and documents it, unless documentation is waived.

- The device falls into one of the categories of exemption from an IDE:
 - **Exemption #1**
 - Is not a transitional device.
 - Has been in commercial distribution immediately before May 28, 1976
 - Is being used or investigated in accordance with the indications in labeling in effect at the time.
 - **Exemption #2**
 - Is not a transitional device
 - Was introduced into commercial distribution on or after May 28, 1976
 - The FDA has determined it to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976
 - Is being used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence.
 - **Exemption #3**
 - Is a diagnostic device
 - The sponsor will comply with applicable requirements in 21 CFR 809.10.
 - The testing:
 - Is noninvasive
 - Does not require an invasive sampling procedure that represents significant risk.
 - Does not by design or intention introduce energy into a subject.
 - Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

- **Exemption #4**

- 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 subjects 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.

(10) Documentation of informed consent

The IRB shall require documentation of informed consent or may waive documentation in accordance with Section R [§46.117].

(11) Deferred (tabled) applications

The IRB may defer (or table) a protocol because it lacks important information, or because significant changes are required in either the consent form or protocol. The reasons for deferring an application will be communicated in writing to the investigator. In such cases, the investigator is expected to respond in writing within 90 days and the responses are considered at a convened meeting of the IRB. In the event that the IRB stipulates revisions requiring simple concurrence by the investigator, then the IRB Chair, or an IRB member delegated by the chair may review the changes and grant final approval. All changes required by the IRB must be incorporated into a final document, which will constitute the approved protocol. If the investigator does not respond within 90 days, then the application is deactivated and will not be considered further.

(12) Contingent approval

The IRB may require, as a condition for approval, minor changes in the protocol that require only simple concurrence by the investigator. The changes can be reviewed by the IRB Chair (or Vice Chair), who will verify that the stipulation for approval has been met. In this case, the notification to the investigator of the IRB determination will not be sent until the required contingency has been satisfied. The IRB will be notified of the status of each required stipulation in the meeting agenda for the following month.

Additionally, the IRB may approve a protocol involving a significant risk device contingent upon receipt of documentation that FDA has



granted the IDE. The IRB staff can make this determination.

(13) Approval period

Protocols may be approved for periods up to, but no greater than, one year. If a protocol is approved at a convened meeting without any conditions, or with requirements for minor changes that can be reviewed and accepted administratively, then the approval period begins on the date of the meeting.


(14) Investigators are notified of IRB actions

The IRB shall notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity or of modifications required to secure IRB approval of the research activity. The notification to the investigator will be in the form of a letter and will specify determinations that the IRB was required to make such as degree of risk for research involving children or whether a device poses a significant or non-significant risk; notification will also specify any modifications or clarifications required by the IRB as conditions of approval. Notification to the investigator in writing will occur after any modifications or stipulations have been met by the investigator. The notification to the institution will be in the form of the minutes of the meeting, which are sent to institutional officials.

If a protocol was reviewed by expedited procedures, then the determination letter will document that all the applicability criteria are satisfied and indicate the specific permissible category(ies) justifying the expedited review; documentation of the review and action taken by the reviewer; and any findings required under the HHS regulations along with protocol-specific findings that justify those determinations.

If the IRB disapproves or defers (tables) a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing. If the IRB disagrees with a sponsor's recommendation that a device poses a non-significant risk, then the determination letter will explain the reasons that led to the IRB's decision. If necessary, a copy of the letter will be sent to the sponsor.

Changes in wording or organization of the consent document that are required or suggested by the IRB are communicated directly to



the investigator during the meeting or by e-mail or fax to the investigator or research coordinator immediately after the meeting. Minor changes (e.g., spelling errors or semantic changes to wording) can be reviewed and approved by the HRPP Coordinator as directed by the IRB chair, however major changes must be reviewed and approved by the Chair or the Chair's designee. All written communications between the IRB and investigators are maintained in the protocol files. Telephone conversations that relate to matters that pertain to the conduct of the protocol are documented in notes and filed in the study file.

(15) Requests for reconsideration of protocols that are disapproved or deferred

An investigator may request that the IRB reconsider a protocol that was disapproved or deferred. Such requests should be made in writing to the IRB chair and explain why reconsideration is requested. The IRB chair may invite the investigator to re-present the protocol at a convened meeting. In responding to such requests, the board may reverse itself and approve the protocol; table consideration in order to obtain more information; or affirm its original decision to disapprove or table the protocol. In general, investigators are to be discouraged from requesting reconsideration more than once.

(16) Institutional officials are notified of IRB actions


The minutes of each meeting are sent to the Vice President for Medical Affairs and the Director of HRPP.

G. Unanticipated Problems Involving Risks to Research Participants or Others

[45CFR46.103(b)(5); 45CFR46.111(a)(6); 21CFR812.150(a)(1)]


(1) Definitions

- a. Unanticipated problems involving risks to participants or others are defined as problems that are unforeseen, related to the research and indicate that participants or others are at increased risk of harm. Events occurring prior to the study opening at the local site do not need to be submitted to the IRB for review. However, it will be beneficial to inform the IRB of these events at the time of presenting the new study for approval.

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- b. Internal event. The event occurred at a study site under the jurisdiction of the UPHDM IRB.
 - c. External event. The event occurred at a site not under the jurisdiction of UPHDM IRB. External events do not need to be reported to the IRB as the local IRB does not oversee this research.

(2) Reportable events: Principal Investigators must report to the IRB as soon as possible, but in all cases within 7 working days any:

- a. Adverse event (any harm experienced by a participant regardless of whether the event meets the FDA definition of “serious adverse event”), which in the opinion of the principal investigator are both **unexpected, related to the research and poses a risk to subjects or others.**
Adverse events that are expected and unrelated to the research do not need to be reported to the IRB. The IRB would like, however, to be notified of all deaths of human subjects that occur within a study.
 - An adverse event is “unexpected” when its specificity and severity are not accurately reflected in the informed consent document.
 - An adverse event is “related to the research procedures” if in the opinion of the principal investigator, it was more likely than not to be caused by the research procedures or if it is more likely that not that the event affects the rights and welfare of current participants.
- b. Information that indicates a change to the risks or potential benefits of the research. For example:
 - An interim analysis or safety monitoring report indicates that frequency or magnitude of harms or benefits may be different than initially presented to the IRB.
 - A paper is published from another study that shows that the risks or potential benefits of your research may be different than initially presented to the IRB.
- c. A breach of confidentiality.

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- d. Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
 - e. Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to research participants.
 - f. Incarceration of a participant in a protocol not approved to enroll prisoners.
 - g. Event that requires prompt reporting to the sponsor.
 - h. Sponsor imposed suspension for risk.
 - i. Complaint of a participant when the complaint indicates unexpected risks or cannot be resolved by the research team.
 - j. Protocol violation (meaning an accidental or unintentional change to the IRB approved protocol) that harmed participants or others or that indicates participants or others may be at increased risk of harm.
 - k. Protocol deviations within a particular study that occur with such frequency that this may have an adverse effect on the risk/benefit analysis of the study.
 - l. Unanticipated adverse device effect (Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.)
 - m. IRB members or staff who become aware of an event that would require reporting by an investigator from a source other than the investigator or the sponsor; for example, newspaper accounts of deaths associated with the drug in a different trial, must report this information to the IRB.
 - n. Investigators may be required by the sponsor to report some events within 24 hours of discovery. In those cases,


the investigator may utilize the “24 hour SAE notification” form available on the IRB website.

o. The Non-Compliance with the Protocol, Board Requirements or Regulations Report Form is to be used to report all internal Unanticipated Problems and Protocol Deviations and Violations.

The 24-Hour Serious Adverse Event Notification is to be used to notify the IRB of any Serious Adverse Event that occurs that is unexpected, related to research and poses risk to subjects or others. This form is also used to report the death of a subject. Both forms are available on the IRB website.

(3) Evaluation of reported events

- a. All internal reported events will be received in the IRB Office and reviewed by the [HRPP Coordinator or a](#) designated non-compliance subcommittee. The [coordinator/subcommittee](#) will review each event, gather additional information from the PI/study coordinator. [Events that are reviewed by the HRPP Coordinator are put on the agenda for the next convened IRB meeting for review/discussion where the board will make a determination on the event. If the subcommittee reviews an event, they will make a recommended determination to the full convened IRB.](#)
- b. At the meeting, the IRB will review the event *and/or* the subcommittee’s recommendation then determine and document in the minutes the following:
 - if the event meets the definition of serious non-compliance
 - if the event meets the definition of continuing non-compliance.
 - if the event increases the risk of harm to subjects or others
 - Whether the event represents an unanticipated problem involving risks to subjects or others (as defined above)
 - Whether any further actions should take place.
- c. If the convened IRB determines that a problem is NOT an unanticipated problem involving risks to participants or others, no further action is required.
- d. If the convened IRB determines that the problem is an unanticipated problem involving risk to participants or others, the IRB will consider the following actions at a minimum:
 - No action
 - Requiring a modification of the research protocol

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- Requiring a modification of the information disclosed during the consent process
 - Requiring additional information be provided to past participants
 - Requiring notification of current participants (required when such information may relate to participants' willingness to continue to take part in the research)
 - Requiring that current participants re-consent to participation
 - Modifying the continuing review schedule
 - Monitoring of the research; monitoring the consent process
 - Suspending or terminating the research; (which would activate procedures described in Section IV.N)
 - Seeking additional information pending a final decision; referring the matter to other organizational entities (e.g., Law Department)
 - If the evaluation indicates that non-compliance occurred, then the procedures described in Section IV.W are activated.

If the convened IRB determines that there is insufficient information to make a determination of whether an event is an unanticipated problem involving risks to participants or others, the event will be tabled and the HRPP Coordinator will make a request in writing to the PI, or study coordinator, following the convened meeting. The communication to the PI will include a request for additional information, as well as a completion date for that request.

(4) Reporting of findings

- a. In all cases when the IRB determines that there is an unanticipated problem involving risks to participants or others, the IRB will report its findings and actions to the investigator.
- b. If the IRB determines that the event was not an unanticipated problem involving risks to participants or others, no further reporting is required. Otherwise the following reporting steps will be followed and completed within 30 days following the IRB's final determination.
- c. The IRB Coordinator will prepare a report of the event describing:

- The nature of the event.
 - The findings of the organization.
 - Actions taken by the organization or IRB.
 - Reasons for the organization's or IRB's actions.
 - Plans for continued investigation or action.
- d. The report will be reviewed and approved by the HRPP Director and the IRB chair.
- e. IRB staff will provide a copy of the report to:
- The IRB in the next agenda packet.
 - The Director of HRPP
 - OHRP
 - FDA, if the research is subject to FDA regulations
 - Other federal agencies that have regulatory oversight
 - Vice President of Medical Affairs
 - The sponsor
 - The Principal Investigator
 - The study file

H. Continuing Review of Research by the IRB


45CFR46.109 OHRP Guidance on Continuing Review

(1) Frequency of review

The IRB shall conduct continuing review of research covered by this policy at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research. The IRB can review any protocol at any time. Continuing review of research shall occur as long as the research is active, including for long term follow-up of participants, even when the research was permanently closed to enrollment of new participants and all participants had completed all research related interventions. Continuing review of research shall also occur when the research activity only includes collection or analysis of private identifiable information.

(2) Timing of continuing review

If a protocol is initially approved for one year and the investigator wishes to continue the research, then the IRB will review the research at a convened meeting the month before the anniversary month of initial approval. If the IRB approves continuation of the research, then the protocol is assigned a new approval date corresponding to the first day of the original anniversary month.



(This reassignment of approval date is necessary to assure that the most recent review always occurs no more than 30 days before expiration of approval.) If the IRB office does not receive the necessary information from the investigator or research coordinator/contact and the IRB does not approve a protocol by the expiration date, the research must be suspended.

(3) Changes to previously approved research:

Changes in an approved protocol or consent form may not be implemented without prior IRB review and approval except when necessary to eliminate immediate hazard to subjects. Requests for changes in approved protocols or consent forms must be submitted in writing to the IRB. A copy of the protocol with proposed changes is submitted to the IRB office. Usually, only the amendment is distributed to the members of the board. Substantive changes in the informed consent document must be indicated by different typography, and the revised document is distributed to the board.

A change in an approved protocol that is implemented in order to eliminate immediate hazard to subjects, is an Unanticipated Problem and the investigator is required to follow the procedures described in Section G. If it is necessary to terminate or suspend a protocol, the investigator must follow procedures described in Section N. Those sections describe the procedures for evaluating the matter and for reporting the matter.

(4) Mechanisms of continuing review

Reminder notices are sent to principal investigators or their contact 2 months before an application to Continue Research on Human Subjects is due. The HRPP Coordinator checks whether the consent document currently used by the investigator corresponds to the document most recently approved by the IRB. Continuing review of a protocol is conducted at a convened meeting of the IRB unless the protocol qualified originally for expedited review. All members of the board receive copies of the continuation application, original application, most recently signed consent document, currently approved consent document, and all reports from sponsor. At least one member also receives a copy of the complete protocol, including any modifications previously approved by the IRB. Furthermore, upon request, any IRB member may have access to the complete IRB protocol file and relevant IRB minutes prior to or during the convened IRB meeting.



(5) Criteria for determining frequency of review

Criteria which may be used in determining whether a specific protocol should be reviewed more frequently than once a year include, but are not limited to, greater than minimal risk to subjects; high frequency of serious adverse events; emergence of unexpected side effects; and an investigator's history of noncompliance with IRB policies and procedures. The IRB will give serious consideration to requiring review at 6-month intervals to protocols involving one or more of the following elements: radiopharmaceuticals; modification in procedure for informed consent; subjects lacking decision-making capacity; and research conducted under the emergency research consent exemption.

(6) Criteria for approval of research undergoing Continuing Review


The regulatory criteria for initial approval of research are used for the continuing review of research as well. The IRB may refer to the "Criteria for Approval of Research" checklist during continuing review of research to ensure that all regulatory criteria are satisfied.

(7) Response to concerns about a protocol

If the IRB becomes aware of concerns about a protocol, then the IRB may require verification from sources other than the investigator that no material changes have occurred since the previous IRB review. Such verification process may involve, but not be limited to, detailed examination of records by IRB members; interviews with staff; and interviews with subjects enrolled in the protocol.

The IRB will require verification from sources other than the investigator that no material changes have occurred since the previous IRB review when the IRB doubts the veracity of the information provided by the investigator for continuing review, the information is inconsistent with other information provided to the IRB, or when there has been serious or continuing non-compliance involving continuing review.

If, through continuing review of a protocol or by other means, the IRB becomes aware of problems involving unforeseen or undocumented risks to subjects or others, or of serious continuing noncompliance, then the matter will be considered at a convened meeting of the IRB. In such instances consideration may be given to suspending or terminating an approved protocol. (See Section N for provisions regarding suspension or termination of a protocol.)



Such matters will be reported promptly and in writing by the IRB chair to the Vice President for Medical Affairs and the Director of HRPP, and as appropriate, by the Director of HRPP to the sponsor, OHRP and FDA.

(8) Format of reports submitted for continuing review

The form used by investigators to submit reports for continuing review by the IRB can be downloaded from the IRB website. This form is distributed to all members of the IRB.

(9) Research not approved by the expiration date

If an investigator does not provide continuing review information to the IRB or the IRB has not approved a protocol by the expiration date, the IRB will ensure that:


- All activities stop, including recruitment, advertising, screening, enrollment, consent, interventions, interactions, and collection of private identifiable information.
- Interventions and interactions on current participants continue only when the IRB finds an overriding safety concern or ethical issue involved such that it is in the best interest of the individual participants.

I. Expedited Review Procedures for Certain Kinds of Research Involving No More than Minimal Risk, and for Minor Changes in Approved Research

[45CFR46.110]

(1) Applicability Criteria


- a. Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

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

(2) Categories of research eligible for expedited review

Research in the following categories may be reviewed by the IRB through an expedited procedure.

- a. Clinical studies of drugs and medical devices only when one of the following conditions is met. (i) Research on drugs for which an investigational new drug application (21CFR312) is not required. (ii) Research on medical devices for which an investigational device exemption application (21CFR812) is not required; or the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
- b. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows: (i) from healthy, non-pregnant 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 (ii) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.
- c. Prospective collection of biological specimens for research purposes by noninvasive means.
- d. 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.)

- e. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis).
- f. Collection of data from voice, video, digital, or image recordings made for research purposes.
- g. 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.
- h. Continuing review of research previously approved by the convened IRB as follows: (i) where the research is permanently closed to the enrollment of new subjects; all subjects have completed all research-related interventions; and the research remains active only for long-term follow-up of subjects; or (ii) where no subjects have been enrolled and no additional risks have been identified; or (iii) where the remaining research activities are limited to data analysis.
- i. Continuing Review of research, not conducted under an investigational new drug application or investigational device exemption where categories (a) through (h) do not apply but the IRB has determined and documented in the minutes at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified. There is no distinction between documentation requirements for expedited continuing



review and for full board continuing review.

(3) Expedited review of amendments to approved protocols


The IRB may use the expedited review procedure to review either or both of the following:

- a. Some or all of the research appearing on the list and found by the IRB chair, or designee, to involve no more than minimal risk,
- b. Minor changes in previously approved research during the period (of one year or less) for which approval is authorized. Examples of minor changes include, but are not limited to, clarification of eligibility criteria; changes in consent form to clarify original meaning or update information; and changes in analytic procedures or statistical methods that do not change the original intent of the protocol. A change in protocol that involves procedures that are greater than minimal risk; procedures that did not fall into categories (a) – (g) above, or changes in protocol that alters the risk profile, or might affect a subject's willingness to participate in a protocol would not qualify as minor.

(4) Procedures for conducting expedited review

A subcommittee of the IRB consists of 2-4 IRB members who have at least 2 years of IRB experience. The subcommittee will be supported by the HRPP Coordinator who reviews new submissions, amendments and applicable continuing reviews for complete paperwork.

- a. The HRPP Coordinator ensures that NIH Training Certificates and Conflict of Interest Disclosure Forms are on file with the IRB office prior to processing the submission for review.
- b. Once the submissions are verified as complete, the HRPP Coordinator prepares approval letters and expedited checklists and delegates each submission to the appropriate subcommittee member.
- c. The subcommittee member reviewing the submission



documents the protocol specific determinations of the Expedited review on the Expedited Review Checklist. The checklist will be signed by the IRB subcommittee member who reviewed the submission and supporting documents.

- d. For expedited review of pediatric studies, the Subpart D checklist will be completed on new submissions, continuing reviews, and amendments to approved research. The Subpart D checklist is completed by the subcommittee member and filed in the study file in the IRB office.
- e. When the subcommittee member has reviewed and approved the submission, the approval letter and expedited checklist are signed and returned to the HRPP Coordinator.
- f. The HRPP Coordinator copies the approval letter and checklist, enters the submission into the IRB database and enters the approval on the Expedited Review on the board meeting agenda. The paperwork is then filed in the study file in the IRB office.
- g. For expedited continuing review of research, the subcommittee may exercise all of the authorities of the IRB except that the reviewer may not disapprove the research. The subcommittee may require changes in the proposed research protocol or associated documents as a condition for approval. If an investigator declines to make required changes, then the protocol is referred for full board review. A research activity may be disapproved only after review in accordance with the non-expedited procedure set forth in 45CFR46.108(b). Additionally, the subcommittee may recommend that a protocol be referred for review by the IRB at a convened meeting of the IRB. If at any time the subcommittee member(s) feel that a study is too high risk for expedited review, they can defer the review of the study to the IRB Chair.

(5) Documentation of determinations:

A written determination that all the applicability criteria were met and which category applied will be placed in the protocol file. The Expedited Review Checklist signed and dated by the reviewer, will be used for this purpose. The determination must also describe and justify any modifications to the informed consent process.



(6) Informing IRB members of expedited reviews

The agenda of each regularly scheduled IRB meeting shall contain a complete list of all protocols and amendments that were reviewed and approved by the expedited procedure since the submission deadline for the last regularly scheduled meeting.

(7) Implementation

Investigators may request that a protocol receive expedited review, however, the IRB Chair makes the final decision regarding type of review.


J. Criteria for IRB Approval of Research

[45CFR46.111; 21CFR56.111]

(1) Requirements to be Satisfied

In order to approve research covered by this policy, the IRB shall determine that all of the following requirements are satisfied:

- a. Physical, psychological, social, legal and economic risks to participants are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose participants to risk.
- b. Physical, psychological, social, legal and economic risks to participants are minimized whenever appropriate, by using procedures already being performed on the participants for diagnostic purposes.
- c. Physical, psychological, social, legal and economic risks to participants are reasonable in relation to anticipated benefits, if any, to participants, and the importance of the knowledge that may reasonably be expected to result.
- d. Selection of Participants is equitable.
- e. Informed consent will be sought from each prospective participant or the participant's legally authorized representative. The Informed Consent process may be waived or altered under specific circumstances. See Section IV.S.(5) – (6).
- f. Informed consent will be documented in writing in



accordance with the regulations. The requirement for written documentation may be waived or altered under specific circumstances. See Section IV. T. (2)-(3).

- g. Research involving no greater than minimal risk does not require a Data Safety Monitoring Board.
- h. The research plan makes adequate provision for monitoring the data collected to ensure the safety of participants. The IRBs may consider the following criteria to determine whether data and safety monitoring is required:
 - Studies that involve a greater than minimal risk to subjects
 - Research with a particularly large study population.
 - Research conducted at multiple sites.
 - Research involving dangerous procedures.
 - Research with a high chance of study termination.
- i. There are adequate provisions to protect the privacy of participants.
- j. There are adequate provisions to protect the confidentiality of the data.
- k. Additional safeguards have been included in the study to protect the rights and welfare of participants likely to be vulnerable to coercion or undue influence.

(2) Test articles are controlled

The site where research involving test articles, i.e. drugs and medical devices used in a protocol subject to FDA regulations should have policies and procedures for control of the test articles. At a minimum, such a plan will conform to FDA regulations at 21CFR312 for drugs and 21CFR812 for devices.

The plan for control of investigational drugs, biologics, or devices will be submitted to the IRB for review. This plan should reflect that the test articles are used only in approved research protocols and under the direction of approved investigators.

(3) Adequate provisions are made in research involving radiopharmaceuticals

Iowa has specific rules governing human subject research involving radiopharmaceuticals, such as providing information to a patient regarding precautions when he/she leaves the facility, misadministration, safety instructions and precautions. [641 Iowa Admin Code 40, 41]

K. Information to be Submitted for Review by the IRB


(1) Initial Review

- a. Application form. Investigators will submit protocols using the form Application to Conduct Research on Human Subjects. Completion of this form is the responsibility of the investigator. If the investigator delegates completion of the form to a member of the research staff, then the investigator should thoroughly review the content of the form prior to signing and submission. All elements of the form must be specifically addressed. This form can be downloaded from the IRB web page. If the Principal Investigator is unable to sign the form, the Co-Investigator may sign it.
- b. Informed Consent document. Investigators are strongly advised to use the template available on the IRB web site.
- c. Additional materials. The following documents should be submitted with the protocol application form:
 - Complete protocol
 - Investigator's Brochure (if one exists)
 - Grant Application (if one exists)
 - For Industry sponsored Clinical Trials:
 - Copy of the Final Contract and budget, if available.
 - Copy of a "good faith" preliminary Contract, if final contract not available at the time of submission.
 - Validation of IND or IDE as indicated in the Application form.
 - Documentation of Completion of the NIH human subjects protection training found at, <http://phrp.nihtraining.com> , if not already on file in the IRB office. Other forms of ethics training completed within the last 5 years may be submitted for IRB review (i.e. CITI training).
 - Updated "Conflict of Interest Disclosure" form if indicated in the requirements of the Application.
 - For DHHS-supported multicenter clinical trials:

- DHHS-approved sample informed consent document (if one exists)
 - Complete DHHS-approved protocol (if one exists)
- d. Protocol. Much of the information needed to address the criteria listed in Section J will usually be presented in a formal protocol written by the principal investigator or by a sponsor. A suggested format for a protocol is available on the IRB web page.
- e. Advertisements and other materials. All materials that will be presented to research subjects or potential subjects must be submitted to the IRB for review. This requirement covers all printed matter such as the consent document; explanatory material; recruiting materials; and letters attempting to reestablish contact with subjects who do not keep scheduled appointments or who appear lost to follow-up. This requirement also covers all advertising material such as pamphlets, posters and audio and visual promotions. Any such materials developed after initial approval of a protocol are considered changes to the protocol and must be submitted for review as explained in Section H (3).
- f. All board members receive (a), (b) and (e). Primary reviewers receive all materials.
- g. The HRPP Coordinator is responsible for reviewing and verifying the accuracy of all documents submitted prior to scheduling the protocol review date.

(2) Continuing Review

- a. Documentation. The amount and kind of documentation required will vary with the status of the research:
- 1) Continuing Review Application
 - 2) Most recently approved informed consent document
 - 3) Most recently signed informed consent document
 - 4) Summary of amendments and changes approved since last review
 - 5) Current protocol incorporating all approved amendments and changes
 - 6) Statements or reports from safety monitor or data safety monitoring board (if available)




7) Current list of study investigators and study personnel and contact information for each person

- b. Studies open to enrollment. All board members receive (1), (2), (3), (4), (5), (6), (7). Primary reviewers receive all documents.
- c. Studies closed to enrollment but with continuing treatment or active follow up. All board members receive (1), (4),(6), (7), primary reviewers receive all documents.
- d. Studies closed to enrollment and treatment; follow up continues on an annual basis. All members receive (1), (6) and (7). These studies may be reviewed using the expedited procedure.

L. Principal Investigator

(1) Qualifications and responsibilities

- a. A principal investigator must be qualified by education, training or experience to assume responsibility for the conduct of a research protocol.
- b. A principal investigator must have a formal appointment to the staff of one of the constituent units of UPHDM or be employed by UPHDM.
- c. For projects that are developed locally, as opposed to projects developed by commercial, government, or nonprofit sponsors, the principal investigator must also assume responsibility for the experimental design and for analysis and presentation of the data.
- d. A principal investigator must have completed training in Human Subjects Protection prior to the initiation of research approved by the IRB. This training must be repeated or enhanced with additional training at least every 5 years. A record of the training must be submitted to the IRB office before the study is processed for review.
- e. The principal investigator is responsible for ensuring that all members of the Research Staff have completed training in Human Subjects Protection prior to the initiation of research




approved by the IRB. This training must be repeated or enhanced with additional training at least every 5 years. A record of the training must be submitted to the IRB office before the study is processed for review.

- f. A principal investigator must have on file in the IRB office a current “Conflict of Interest Disclosure Form” prior to the initiation of research approved by the IRB.
- g. The principal investigator is responsible for ensuring that all members of the Research Staff have on file in the IRB office a current “Conflict of Interest Disclosure Form” prior to the initiation of research approved by the IRB.
- h. The principal investigator will attest to a commitment to uphold the Principles stated in the Belmont Report and to follow the HRPP procedures with every application to conduct research. This attestation is on the form, “Application to Conduct Research on Human Subjects,” and the “Application for Continuing Review” form.

(2) Trainees, students and visiting investigators

Research proposed by a resident or by an investigator affiliated with another institution, e.g., a visiting scientist or a student conducting thesis research, must be sponsored by a member of the UPHDM staff who qualifies to be a principal investigator. Before a student submits proposed research to the UPHDM IRBs, they must first have the approval of the IRB at the educational institution where they are enrolled. The written determination must be submitted to the UPHDM IRB with the student’s proposed research. If the educational institution does not have an IRB, then the student must state that clearly at the time the proposal is submitted to the UPHDM IRB. The trainee, student or visiting investigator must have completed training in Human Subjects Protection prior to the initiation of research approved by the IRB.



(3) Monitoring of education and conflicts of interest reporting requirements

Monitoring of the fulfillment of human subjects protection education and conflict of interest reporting requirements will be the responsibility of the HRPP Coordinator. Monitoring will be performed before the initiation of a new protocol and yearly thereafter.

M. Review by Institution

[45CFR46.112]


(1) Further review

Research that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of UPHDM. However, those officials may not approve the research if it has not been approved by an IRB.

(2) Reporting and responding to efforts to unduly influence IRB staff and members

Undue influence refers to efforts to induce an IRB member or staff to act in way contrary to performing their duties as described in this document or federal regulations governing protection of human research subjects. The influence may take the form of threats about employment status, offers of money or other items of value, or intimidating behavior.

- a. Relevant UPH Policy. All IRB members and staff, regardless of employment status, are subject to afforded the protections of and subject to provisions of the UPH Code of Conduct (1.CE.2).
- b. Reporting undue influence. IRB staff may report attempts to exert undue influence to the Director of HRPP, the Corporate Compliance HelpLine (1-800-548-8778) or the UPHDM Compliance Executive Director. IRB members appointed by UPHDH may report attempts to exert undue influence to the Director of HRPP, the Corporate Compliance HelpLine or the UPHDM Compliance Executive Director.
- c. Institutional response to attempts to exert undue influence. The institutional response to attempts to exert undue influence on IRB members or staff will depend on the nature of the original event and how the report was made. It is



anticipated that matters brought directly to the attention of the Director of HRPP involving members of the UPHDM medical staff can be appropriately addressed by the Vice President for Medical Affairs or the Director of HRPP, who would confer with the physician and attempt to resolve the matter; matters involving ancillary research personnel or sponsors would be addressed by the Director of HRPP. Complaints made to the Compliance Executive Director would be processed initially as described in the institutional policy and eventually referred to the Director of HRPP for resolution or advice. In all cases, the institutional representative handling the matter will stress to the person who attempted to exert influence the importance of maintaining the independence of the IRB in protecting human research subjects.

N. Suspension or Termination of IRB Approval of Research

[45CFR46.113]

(1) Authority of the IRB

The IRB shall have 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. Termination means that the IRB approval of research is withdrawn permanently and the same research protocol cannot resume at a later date. Suspension means that the IRB approval of research is withdrawn in whole, or in part, but the same research protocol could resume at a later date if certain conditions are met.

(2) Time frame for suspension

If a report of an unexpected serious harm to a research subject indicates that there is no immediate risk to other subjects, the chair of the IRB will conduct an investigation and report his findings at a convened meeting of the IRB, which will then determine whether additional action is required. In the case of immediate potential risk to research subjects, the IRB chair may impose a temporary suspension on a protocol (unless the investigator voluntarily suspends or terminates activity). In extreme cases, a protocol may be suspended by either the Director of HRPP or the Vice President for Medical Affairs of UPHDM. In all cases, the IRB will be notified of the suspension as soon as possible and the matter will be discussed at the next convened meeting of the IRB. Suspensions and terminations of IRB approval are reported to OHRP within 30 days.



Suspensions and terminations of IRB approval are reported to the FDA within 30 days.

(3) Suspension of protocol by investigator or sponsor

The investigator must notify the IRB within one working day or as soon as practicable if the investigator or a sponsor suspends or terminates a protocol. The investigator must make adequate arrangements for caring for subjects already enrolled on a protocol, but may not enroll additional subjects. The IRB makes the final determination as to whether to suspend or terminate approval at a convened meeting.

(4) Care of subjects

A decision to suspend or terminate a protocol must include an explicit consideration of the rights and welfare of subjects already enrolled in the study as well as a process to inform current subjects of the termination or suspension of the research. If the suspension or termination is voluntary, then the investigator will be expected to present a plan for continued care or orderly withdrawal of treatment. If the suspension or termination is imposed on an investigator, then the Vice President for Medical Affairs may be consulted about how to continue the care of enrolled subjects. The IRB Chair should be notified of the suspension as soon as possible and the matter will be discussed at the next convened meeting of the IRB.

(5) Unanticipated events after suspension

If a treatment is allowed to continue for safety reasons after a research protocol is formally suspended or terminated, then any unanticipated problems and events that occur will be reported as described in Section IV.G.

(6) Notifying institutional officials, sponsors and regulatory agencies of IRB action

Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported reported within 30 days by the IRB chair to the investigator, Director of HRPP and the Vice President for Medical Affairs, OHRP, FDA (if applicable) and, if applicable, the sponsor of the research.



(7) Time frame for notifying institutional officials, sponsors and regulatory agencies of IRB action

The time frame for notification will depend on the urgency of the matter. Situations presenting immediate, unforeseen risk to subjects will be reported immediately to institutional officials and sponsors.

(8) Notifying subjects of IRB action

Enrolled subjects. Consistent with the organizational Value of Openness, the default presumption is that subjects will always be notified if a protocol in which they are enrolled is suspended. The IRB will determine at a convened meeting how and when such notification will be made. Special consideration will be given to the situation in which a research protocol is suspended, but the experimental treatment should continue for safety reasons. When the IRB permits or requires follow-up of participants for safety reasons, subjects will be so informed. The IRB, together with the Vice President for Medical Affairs, will develop a process for explaining the various options to the participants.

Former subjects. The IRB will consider whether to inform former subjects, i.e. those who are not actively participating in the research. A major consideration in making this determination is whether the reason for terminating the protocol was associated with risks not disclosed during the consent process.

(9) Additional actions taken by IRB

If the IRB suspends or terminates approval of a protocol, it may impose remedial or disciplinary action on the investigator ranging from supplemental education in human subjects protection to suspension of privileges to conduct research on human subjects.

(10) Prompt reporting of suspension and terminations of IRB Approval

The maximum time allowed between the recognition of a reportable event and fulfilling reporting requirements are as follows:

Suspensions and terminations of IRB approval are promptly (no longer than within 30 days) reported to OHRP.

Suspensions and terminations of IRB approval are promptly (no longer than within 30 days) reported to FDA.



O. Local Notification of Initiation of National Cancer Institute Central IRB (NCI-CIRB) studies

If a research study will involve the use of hospital departments (lab, radiology, etc.), the study must go through the following CIRB notification process.

(1) Notification Process for New CIRB Studies

- (a) The investigator/research staff notifies the IRB of their desire to activate a NCI-CIRB approved study.
- (b) The following documents will be submitted to the IRB as a means of notification regarding each particular study:
 - a. Local informed consent with required local modifications
 - b. HIPPA authorization
 - c. Additional documents accessed through NCI-CIRB website: CIRB application, study protocol, NCI-CIRB final approval letter, CIRB final informed consent document
- (c) The HRPP coordinator will submit the NCI-CIRB documents to the IRB chair, or his designee, for review.
- (d) The IRB chair, or his designee, will notify the HRPP Coordinator of the review and will bring forward any local context concerns. Once approved, a copy of the initial review documents will be maintained in the IRB office.
- (e) The Principal Investigator will notify the IRB office of all local events. These include, but are not limited to: SAEs, unanticipated problems that pose a risk to subjects or others, a concerning pattern of protocol deviations, and protocol violations (refer to Section IV.G). The IRB will also be notified of continuing review submissions and changes to previously approved research.

(2) Notification Process for Previously Approved NCI-CIRB Studies

The following documents will be submitted to the IRB as a means of notification regarding amendments to previously approved CIRB studies:

- a. NCI-CIRB amendment approval letter
- b. Local informed consent if language changes due to amendment

P. Central Institutional Review Board Approval of Industry Sponsored Studies

This procedure outlines the process that the UPHDM IRB will follow when an investigator requests oversight by a central IRB (CIRB) rather than the organizational IRB. The UPHDM IRB will only consider deferring oversight of a research study to an IRB that has been accredited through AAHRPP (Association for the Accreditation of Human Research Protection Programs).

If a research study will involve the use of hospital departments (lab, radiology, etc.), the study must go through the following CIRB notification process.

1) Notification Process for New CIRB Studies

(a) The investigator/research staff will submit the following documents to the IRB as a means of notification regarding each particular study previously approved by a CIRB:

- a. Local informed consent with required local modifications
- b. HIPAA authorization
- c. The CIRB application, the approved study protocol, CIRB final approval letter, CIRB final informed consent document

(b) The HRPP coordinator will submit the CIRB documents to the IRB chair, or designee, for review.

(c) The IRB chair will notify the Principal Investigator of the review and will express any local context concerns he has in a written response. The IRB will have authority to either allow CIRB oversight of the study, or to require review and approval by the UnityPoint Health Des Moines IRB. If the Principal Investigator disagrees with the decision of the IRB chair or of the IRB, then they may follow the procedure outlined in IRB Policy and Procedures, IV.F.(14)

(d) A copy of the initial review documents will be maintained in the IRB office.

(e) The Principal Investigator will notify the IRB office of all local events. These include, but are not limited to: SAEs, unanticipated problems that pose a risk to subjects or others, a concerning pattern of protocol deviations, and protocol violations (refer to

Section IV.G). The IRB will also be notified of continuing review submissions and changes to previously approved research.

2) Notification Process for Previously Approved CIRB Studies

The following documents will be submitted to the IRB as a means of notification regarding amendments to previously approved CIRB studies:

- (a) CIRB amendment approval letter
- (b) Local informed consent if language changes due to amendment

Q. Relations with Other IRBs and Other Institutions

[45CFR46.114]

(1) Cooperative Research


Cooperative research projects are those projects covered by 45CFR46 which involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with 45CFR46. A written agreement among the cooperating institutions must describe how their respective IRBs will relate to each other, i.e., whether one IRB will act on behalf of all the others in reviewing and overseeing the research, or whether each institution will have responsibility for local oversight.

(2) Another Institution using an UPHDM IRB as its IRB of Record

An institution may request that a UPHDM IRB function as its IRB of record. A signatory official of the requesting institution must indicate, in writing, whether the request is for a specific project or for all research conducted at the institution and whether the institution has its own internal IRB or uses another board as its IRB of record. The request must be approved by the Institutional Official (Vice President of Medical Affairs).

(3) UPHDM Investigators Conducting Research at Another Institution

An investigator with a formal appointment at UPHDM, or any of its components, wishing to conduct research at another institution, must follow the Policies and Procedures for Protection of Human



Research Subjects at both institutions. If a PI wishes to conduct medical tests, draw labs or see study subjects at locations outside of the normal study location (for convenience of the study subject), the PI/Study coordinator must notify the IRB in writing of this practice prior to conducting any study related activity, preferably when the study is initially approved by the IRB.

If a research subject enrolled in a study not approved by our IRB will be visiting or hospitalized within a UPHDM facility for study related tests, the IRB requests that the physician/medical team notifies the IRB in writing of this practice prior to admission.

(4) Other IRBs

The Chair of the UPHDM IRB may – with consent of the Director of HRPP or the Vice President for Medical Affairs - authorize an investigator to conduct research that has been approved by another IRB, provided that the IRB is accredited by AAHRPP and registered with OHRP/FDA. The responsibility of the other IRB must be documented in a memorandum of understanding signed by the chairs of the two IRBs. In such instances, it will be the responsibility of the investigator to insure that the UPHDM IRB is fully informed of all actions taken by the other IRB. It is anticipated that this option will be exercised very rarely, and only for compelling reasons. The HRPP Director will update the FWA to indicate use of the external IRB.

R. IRB Records

[45CFR46.115]

(1) Documentation of IRB activities

The HRPP Coordinator shall prepare and maintain adequate documentation of IRB activities, including the following:

- a. Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, reports of injuries to subjects, and serious adverse events experienced by subjects.
- b. Minutes of IRB meetings shall be in sufficient detail to show:
 - attendance at the meetings;


- when an alternate member replaces a primary member;
- separate deliberations for each action taken by the IRB;
- the vote on these actions including the number of members voting for, against, abstaining, and recusing;
- the names of IRB members who left the meeting because of a conflicting interest along with the fact that a conflicting interest was the reason for the absence;
- the basis for requiring changes in or disapproving research;
- justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS approved sample consent document;
- determinations required by regulations and protocol specific findings justifying those determinations for: waiver or alteration in the consent process or research involving children;
- assessment of the risk-benefit ratio for research involving children;
- protocol-specific determinations for research involving pregnant women, fetuses, neonates, and adults who lack decision making capacity.
- the rationale for significant risk/non-significant risk device determinations;
- approval period (not to exceed one year);
- and a written summary of the discussion of controverted issues and their resolution. [Consult IRB Office Operations Manual for SOP: Minutes of a Convened Meeting.]

c. Records of continuing review activities.

d. For both initial and continuing review of research approved by the expedited procedure, the records document the following:

- The specific permissible category
- Description of action taken by the reviewer.
- Any findings required under the regulations.

e. For exempt research, IRB records must document the specific category by which research was determined to



be exempt.

- f. Copies of all correspondence between the IRB and the investigators.
- g. A current roster of IRB members
- h. Written procedures for the IRB.
- i. Statements of significant new findings provided to subjects.

(2) Retention of documents

The records required by this policy shall be retained for at least 3 years, and records relating to research which is conducted shall be retained for at least 3 years after completion of the research/final study closure regardless of enrollment. All records shall be accessible for inspection and copying by authorized representatives of the FDA, the IRB and, as applicable, sponsors of the studies, at reasonable times and in a reasonable manner.

(3) Maintenance and storage of records


The HRPP Coordinator shall be responsible for maintaining records and for arranging appropriate and secure storage of records. Once a study goes through final closure with the IRB, the HRPP Coordinator sends the entire study file to offsite storage. If the study file is requested from an investigator or other study personnel, the HRPP Coordinator will request the study file be returned to the IRB Office within 48 hours of receipt of the request. Only the HRPP staff will have access to the stored files.

S. General Requirements for Informed Consent

[45CFR46.116; 45CFR46.117; 21CFR50.20; 21CFR50.23; 21CFR50.25; 21CFR50.27; 21CFR56.111;]

(1) General considerations

Except as provided elsewhere in this document, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the




representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory 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.

(2) Basic elements of informed consent

Except as provided in paragraph (4) or (6) of this section, in seeking informed consent the following information shall be provided to each subject:


- a. a statement that the study involves research, an explanation of the purposes of the research (the statement of purpose must match the statement in the protocol); the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
- b. the approximate number of subjects involved in the study;
- c. a description of any reasonably foreseeable risks or discomforts to the subject (and the description must accurately reflect the description of risks or discomforts in the protocol);
- d. a description of any benefits to the subject or to others which may reasonably be expected from the research;
- e. a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
- f. a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained; (it is to be explicitly stated that records may be inspected by members of the IRB, representatives of the US FDA and sponsors of studies)
- g. for research involving more than minimal risk, an explanation as to whether any compensation will be offered and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of,

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- or where further information may be obtained;
- h. an explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and
 - i. 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;
 - j. a statement that a copy of the consent form will be given to the subject;
 - k. the date on which the consent form was approved by the IRB [21CFR50.27(a)], the expiration date, and if required by the sponsor, the version number of the consent form.

(3) Additional elements of informed consent

When appropriate, one or more of the following elements of information shall also be provided to each subject:

- a. 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;
- b. anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
- c. any additional costs to the subject that may result from participation in the research;
- d. the consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject; and
- e. 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. **Implementation.** If new risks are discovered that may affect subjects' decision to continue participating in a protocol, the IRB may require the investigator to obtain renewed consent from study participants. If the study treatment has been completed but the risk of injury still exists, then the investigator is required to send the study subjects an informational letter describing the new risks;

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- f. a statement that the investigator and/or the institution are being paid to conduct the research;
 - g. a statement that the investigator and/or the institution have a financial interest in the outcome of the research.

(4) Elements of authorization required under the Privacy Rule

The informed consent document may be combined with a document containing the elements of authorization to use and disclose Protected Health Information required under the Privacy Rule.

(5) Research Data Collection

- a. When a subject withdraws from a study, the data collected on the subject to the point of withdrawal remains part of the study database and may not be removed. The consent document cannot give the subject the option of having data removed.
- b. The investigator may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject must distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through noninvasive chart review, and address the maintenance of privacy and confidentiality of the subject's information.
 - The investigator must obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form).
 - The IRB must approve the consent document.
- c. If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the investigator must not access for purposes related to the study, the subject's medical record or other confidential records requiring the subject's consent. However, an investigator may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult

public records, such as those establishing survival status.

(6) Modifications in the consent procedure

The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents in the minutes of a convened meeting that:

- a. the research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs;
- b. the research could not practicably be carried out without the waiver or alteration; and .
- c. the research is not subject to FDA regulation.


(7) Additional circumstances under which the consent procedure may be modified

The IRB may 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 requirements to obtain informed consent provided the IRB finds and documents that:

- a. the research involves no more than minimal risk to the subjects;
- b. the waiver or alteration will not adversely affect the rights and welfare of the subjects;
- c. the research could not practicably be carried out without the waiver or alteration; and
- d. whenever appropriate, the subjects will be provided with additional pertinent information after participation;
- e. The research is not subject to FDA regulation.

(8) Consent in emergency situations

- a. Emergency use of a test article. Emergency use of a test



article may be exempt from the requirement to obtain informed consent under certain circumstances. See Section IV.W(1)(c) of this document and see also policy UPHDM177, “Emergency Use of Drugs/Biologics and Device”

- b. Planned emergency research. The general requirements to obtain informed consent may be waived under certain conditions for planned emergency research. For FDA regulated research, the IRB will make a determination that the consent procedures and the consent document meets FDA regulations. See Section IV.X.

(9) Research involving children

In general, the IRB requires written assent of children older than twelve years of age; an investigator may specifically request that the requirement for assent be waived for a specific protocol, and the decision of the IRB will be noted in the minutes. (See Section VII.H for a more extensive discussion of assent by children to participate in research.)

(10) Iowa law


The informed consent requirements in this policy are not intended to preempt any applicable Federal, State, or local laws which require additional information to be disclosed in order for informed consent to be legally effective.

Implementation. Iowa Code speaks to consent in writing in the context of consent to medical treatment: Consent is presumed valid if in writing, giving nature and purpose of procedure, risks, and provides for answering questions. [Iowa Code 147.137].

Mandatory reporting of child abuse and dependent adult abuse.

Iowa Law requires that health providers report cases of suspected child abuse and dependent adult abuse. [Iowa Code 232.69] Consent documents for research protocols that may elicit information about such abuse must contain a notice that Iowa Law trumps most assurances of confidentiality including federal Certificates of Confidentiality.

Mandatory reporting of communicable diseases. Iowa Law



requires physicians and other health care providers to report various communicable diseases [Iowa Code 641.1]. The policy of the Public Health Service on issuing Certificates of Confidentiality is to defer to state law in this matter.

(11) Emergency medical care

Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable Federal, State, or local law. However, when emergency care is initiated without appropriate informed consent, the patient may not be considered a research subject, and any information obtained in the course of such emergency care may not be considered research data.


(12) Provisions for subjects who cannot understand written or spoken English or are sensory impaired: 45CFR 46.116-117

Subjects who do not speak English should be presented with a consent document written in a language that they understand whenever possible. Alternatively, 46.117(b)(2) permits oral presentation of informed consent information in conjunction with a short-form written document stating that the elements of informed consent have been presented orally, and a written summary of what is presented orally. A witness of the oral presentation is required, and the subject must be given copies of the short-form documentation and the summary.

When this procedure is used with subjects that do not speak English:

- a. the oral presentation and the short form written document should be in a language understandable to the subject and translation must be by a highly trained, qualified medical translator.
- b. the IRB approved English language informed consent document may serve as the summary; and
- c. the witness should be a highly trained, qualified medical translator in the language of the subject.

At the time of consent:

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- a. the short form document should be signed by the subject or the subject's legally authorized representative.
 - b. the summary (i.e., the English language informed consent document) should be signed by the person obtaining consent as authorized under the protocol.
 - c. the short-form document and the summary should be signed by the witness.

The IRB must receive all foreign language versions of the short form document as a condition of approval.

T. Documentation of Informed Consent

[45CFR46.117]


(1) Requirement for written consent

Except as provided in paragraph (3) of this section, informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. A template containing suggested language for a combined consent and authorization form can be downloaded from the IRB web page. A copy of the fully executed document shall be given to the person signing the form.

(2) Alternate formats for written consent

Except as provided in paragraph (3) of this section, the consent form may be either of the following:

- a. a written consent document that embodies the elements of informed consent required by 45CFR46.116. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed; or
- b. a short written consent document stating that the elements of informed consent required by 45CFR46.116 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. For subjects that are non-English speaking, the witness will be conversant in both English and the subject's native



language. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form.

Implementation. In each case (a or b above) the date of initial IRB approval and expiration date (no more than 1 year after most recent approval date) shall be noted on the consent form.

(3) Waiver of requirement for written consent

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


- a. that the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or
- b. that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

FDA regulated research. If the research is subject to FDA regulation, only criterion (b) can be used in considering whether to waive the requirement.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research. In cases in which the IRB requires a written statement regarding the research be given to the participant, the IRB must review this statement prior to approval of research.

(4) Monitoring of the informed consent process

The IRB may determine that the process of obtaining informed consent for a given protocol must be monitored. Such a situation



may arise when the protocol proposes to enroll subjects under unusual conditions or when concerns have been expressed about an investigator's approach to recruiting and obtaining informed consent from subjects. The actions that the IRB may take in such a situation include, but are not limited to, requiring a third party, such as the Research Subject Advocate, to observe or participate in the consent process; interviewing subjects after they have been recruited; and requiring the investigator to record the consent process.


U. Obtaining Consent on Behalf of Adults Who Lack Decision-Making Capacity

(45CFR46.101 (e) (f); 45CFR46.102 (c); 45CFR46.402(d) (e); 21CFR50.3(l); 21CFR50.3(o); 21CFR50.3(s); 21CFR56.103(c))

(1) Conditions to be satisfied

The following conditions must be satisfied when it is anticipated that adults who lack decision-making capacity might be enrolled in a research protocol:

- a. The research should either:
 - Offer the prospect of direct benefit to the research subject; a placebo controlled study may qualify if the IRB is persuaded that there is no generally accepted treatment for the condition being studied; or
 - Offer the prospect of yielding 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 expose the research subject to no greater than minimal risk.
 - The research design provides additional safeguards to protect the rights and welfare of adult subjects unable to consent to research.
- b. Consent must be obtained from a legally authorized representative (see (2) below).
- c. A person not directly involved in the medical care of the subject must participate in the consent process. The role of this person is to assure that the rights of the prospective research subject are protected and reinforce the various



elements of informed consent including, but not limited to, understanding that: the primary purpose of the project is to answer a research question and not treat the patient; participation is voluntary; and declining to participate will not affect any other care the patient may be need or be entitled to receive. This person may be a research nurse, a member of the IRB, a patient advocate, or other person knowledgeable about protection of human research subjects. It is anticipated that details for complying with this requirement will be established during a dialog between the members of the IRB and the investigator and incorporated into the final version of the protocol.


- d. The protocol must be considered at a convened meeting of the IRB, and the IRB's assessment of the risks and benefits of participation in the study will be noted in the minutes of a convened meeting. The IRB may seek advice from the UnityPoint Health System Law Department regarding potential liability issues presented by a protocol.
- e. If the protocol targets individuals who lack decision making capacity at the time of consent, then it will be reviewed at intervals of 6 months or less.
- f. When researchers are likely to approach adults who lack the ability to consent, the IRB evaluates whether:
 - The proposed plan for the assessment of the capacity to consent is adequate.
 - Assent of the participant is a requirement, and, if so, whether the plan for assent is adequate.

(2) Legally authorized representative

Consent for research will be obtained from a person or entity legally authorized to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

Implementation. In Iowa, legally authorized representatives include: Substitute medical decision-making board [Iowa Code 135.29]; guardian for minor or person with impaired decision-making capacity [Iowa Code 633.562, 633.552]; attorney-in-fact, guardian, spouse, adult child, parent, adult sibling [641 Iowa Admin Code 857, Durable power of attorney for health care , Iowa Code 144B.2, 144B.3, 144.B.5].

(3) Assent of subject



When research involves decisionally-impaired persons, the IRB will consider whether the assent of the subject should be sought, when in the judgment of the IRB the subjects are capable of providing assent, and such assent will meaningfully add to the respect of the subjects' autonomy. This judgment may be made for all subjects to be involved in research under a particular protocol, or for each subject, as the IRB deems appropriate.

(4) If a subject regains decisional capacity

A research subject who regains decisional capacity will be fully informed of the nature of the protocol and the conditions under which he or she was enrolled. The subject's continued participation in the protocol will be solicited using the normal process for obtaining informed consent. A subject who objects to participation in the project may request that none of the information obtained about the subject be used for research and such a request will be honored if practicable.

V. Recruitment of Research Subjects


(1) Identification of potential research participants

This section pertains to identification of patients as potential participants in research projects by physicians and caregivers who are treating the patient but are not directly involved in the research. In these situations, the attending physician or caregiver must first ask permission of a patient to inform the researcher about the patient's condition and whether the researcher might discuss the research project with the patient. Members of a research team are not permitted to search medical records of persons who are not their patients in order to identify potential participants without appropriate permission from the IRB (functioning as the Privacy Board). (Necessary forms can be downloaded from the IRB Web Page.)

(2) Who should obtain informed consent

AMA Ethics Opinion 8.0315

The relation between physician and patient is fundamentally different from the relation between researcher and participant in a research project. The IRB recognizes that there is an inherent conflict of interest when an attending physician or health care provider is also a researcher and strongly recommends that a researcher/physician not be solely responsible for obtaining informed consent. Whenever possible and practicable, a person not



directly involved in the medical care of a potential research subject should participate in the consent process.

(3) Payments to research subjects

[FDA Information Sheet]

Payment to research subjects, in the form of money, tokens or vouchers, is permitted. The IRB considers the amount of the payment and the reason for it on a case-by-case basis. The general guidelines are that:

- a. the magnitude and timing of the payment should not be such as to induce persons to assume risks of participating in a protocol if the payment were not offered and
- b. credit for participation should accrue as the study progresses and not be contingent on completion of the study.
- c. for FDA regulated research, compensation for participation in a trial offered by a sponsor cannot include a coupon good for a discount on the purchase price of the product once it has been approved for marketing.

(4) Advertisements

[FDA Information Sheet - Recruiting]

- a. Media advertising The IRB reviews direct advertising for research subjects, i.e., advertising that is intended to be seen or heard by prospective subjects to solicit their participation in a study. Direct advertising includes, but is not necessarily limited to: newspaper, radio, TV, bulletin boards, posters, and flyers that are intended for prospective subjects.
- b. Criteria for reviewing advertisements. Advertisements should be reviewed and approved by the IRB as part of the package for initial review. However, when the clinical investigator decides at a later date to advertise for subjects, the advertising may be considered an amendment to the ongoing study. When such advertisements are easily compared to the approved consent document, the IRB chair or expedited subcommittee member may review and approve by expedited means. When the IRB reviewer has doubts or other complicating issues are involved, the advertising should be reviewed at a convened meeting of



the IRB.

- Advertising should not be unduly coercive and should not promise a certainty of cure beyond what is outlined in the consent and the protocol. Advertising should be limited to the information that prospective participants need to determine eligibility and interest. This is especially critical when a study may involve subjects who are likely to be vulnerable to undue influence.
- The IRB reviews the information contained in the advertisement and the mode of its communication, to determine that the procedure for recruiting subjects is not coercive and does not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol. The IRB must review the final copy of printed advertisements to evaluate the relative size of type used and other visual effects. When advertisements are to be recorded for broadcast, the IRB must review the final recording tape.
- No claims should be made, either explicitly or implicitly, that the drug, biologic or device is safe or effective for the purposes under investigation, or that the test article is known to be equivalent or superior to any other drug, biologic or device.
- Advertising for recruitment into investigational drug, biologic or device studies should not use terms such as "new treatment," "new medication" or "new drug" without explaining that the test article is investigational.
- Advertisements should not promise "free medical treatment," when the intent is only to say subjects will not be charged for taking part in the investigation. For FDA regulated research, advertisements must not 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. Advertisements may state that subjects will be paid, but should not emphasize the payment or the amount to be paid, by

such means as larger or bold type.

- Any advertisement to recruit subjects should be limited to the information the prospective subjects need to determine their eligibility and interest. When appropriately worded, the following items may be included in advertisements.
 - the name and address of the clinical investigator and/or research facility;
 - the condition under study and/or the purpose of the research;
 - in summary form, the criteria that will be used to determine eligibility for the study;
 - a brief list of participation benefits, if any (e.g., a no-cost health examination);
 - the time or other commitment required of the subjects; and
 - the location of the research and the person or office to contact for further information.
 - The advertisement may not contain exculpatory language.


Receptionist scripts. The first contact prospective study subjects make is often with a receptionist who follows a script to determine basic eligibility for the specific study. The procedures followed must adequately protect the rights and welfare of the prospective subjects and that personal and sensitive information is gathered about the individual will be appropriately handled.

W. Use of Investigational Products in Unanticipated Situations

(1) Exemption from IRB approval for “emergency” use of an FDA-regulated test item in a life-threatening situation

[21CFR50.23] (21CFR50.24) (21CFR50.25) (21CFR56.102(d)) (21CFR56.104(c) [21CFR56.104] FDA Information Sheets: Emergency Use of an Investigational Drug or Biologic, Emergency Use of Unapproved Medical Device; Frequently Asked Questions: IRB Procedures,

Emergency use. Use of a test item, i.e. a drug or biologic being investigated in clinical trials under an Investigational New Drug (IND) or a device being investigated in clinical trials under an Investigational Device Exemption (IDE), is exempt from prospective IRB review under the following conditions: (1) there is no standard,



acceptable treatment for a life-threatening condition; and (2) treatment must be initiated before a quorum of the IRB can be convened to review the proposed use.

- a. **Drugs and biologics**. The investigator must obtain permission from the holder of the IND. In some circumstances, the holder of the IND may require an acknowledgement from the IRB of the emergency use request before the drug is released.
- b. **Devices**. An unapproved device, or a device that has not received marketing clearance, may be used in a life-threatening situation if it covered by an Investigational Device exemption (IDE). However, FDA permits use of unapproved devices in emergencies when an IDE does not exist, when the proposed use is not covered under an existing IDE, or the physician or institution is not approved under an IDE. (In these circumstances, the physician must justify to FDA the emergency use.)
- c. **Informed consent**. 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:
 - The human subject is confronted by a life-threatening situation necessitating the use of the test article.
 - Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.
 - Time is not sufficient to obtain consent from the subject's legal representative.
 - There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.
- d. **Independent assessment**. If immediate use of the test article is, in the investigator's opinion, required to preserve the life of the subject, and time is not sufficient to obtain the independent determination required in paragraph (d) of this section in advance of using the test article, the determinations of the clinical investigator shall be made

and, within 5 working days after the use of the article, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

- e. **Notification of IRB.** The physician must notify the IRB as soon as possible, but no later than 5 working days after use of the test item. The letter must document the emergency use and indicate that (1) that a life-threatening situation existed with no standard acceptable treatment; and (2) there was insufficient time to convene a quorum of the IRB to consider the use.
- f. **Evaluation.** The IRB chair will evaluate the letter from the investigator and determine that the qualifying conditions were met. The IRB chair must also determine that the research involving the test article is not subject to DHHS regulations.
- g. **Implementation.** The IRB chair will respond with a letter to the investigator acknowledging notification of the emergency use of the test article, and stating whether the investigator had complied with FDA requirements.
- h. The emergency use exemption may be employed only once for a given test article. If an investigator anticipates that urgent situations justifying use of the test item will arise more than once, then the investigator must submit a full protocol to the IRB.

(2) When a subject enters a second institution

[FDA Guidance]; UPHDM Pharmacy Policy 06-05

If a person enrolled in an approved protocol at another institution requires hospitalization or treatment at one of the constituent entities of UPHDM, that person may, with approval of the UPHDM attending physician, continue to receive treatment under the usual procedures for dealing with drugs prescribed out-of-facility. The physician responsible for the patient (or a representative of the facility) shall verify that protocol treatment with the drug was properly initiated (informed consent, etc.) prior to administration to the patient in this facility. Reasonable effort shall be made to obtain a copy of the signed informed consent from the principal investigator. If obtained, the informed consent shall be placed in the patient chart. In addition, the hospital's Investigational Medication

Administration Waiver shall be signed by the patient and maintained in the patient chart. The pharmacy, in cooperation with the principal investigator, will provide information on the drug to the attending practitioner and those who dispense and administer the drug as needed or requested.

X. Emergency Research Consent Exception


[21CFR50.24; OPRR Report]

Federal regulations permit the general requirements for informed consent at 45 CFR 46.116(a) and (b) [FDA 21CFR50.20] and 46.408 [FDA: 21CFR50.54] to be waived for planned emergency research conducted under strictly limited conditions. In considering a proposal to conduct research involving a waiver of informed consent under this narrow exception, the IRB must first determine whether the research is subject to FDA regulations and then apply the criteria detailed under either (a) or (b) below:

(1) Research subject to FDA regulations


The IRB responsible for the review, approval, and continuing review of the research activity has approved both the activity and a waiver of informed consent and found and documented:

- a. that the research activity is subject to FDA regulations [21CFR50] and will be carried out under an FDA investigational new drug application (IND) or an FDA investigational device exemption (IDE), the application for which has clearly identified the protocols that would include subjects who are unable to consent, and
- b. The IRB with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation finds and documents each of the following:
 - The research activity is subject to regulations codified by the Food and Drug Administration (FDA) 21 CFR 50 and will be carried out under an FDA investigational new drug application (IND) or an FDA investigational device exemption (IDE).
 - The application clearly identifies the protocols that will include participants who are unable to consent.
 - The research participants are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific




evidence, which might include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

- Obtaining consent is not feasible because:
 - The participants will not be able to give their consent as a result of their medical condition.
 - The intervention under investigation must be administered before consent from the participants' legally authorized representatives is feasible.
 - There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.
- Participation in the research holds out the prospect of direct benefit to the participants because:
 - Participants are facing a life-threatening situation that necessitates intervention.
 - Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence supported the potential for the intervention to provide a direct benefit to the individual participants.
 - Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of participants, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.
- The clinical investigation could not practicably be carried out without the waiver.
- The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each participant within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent.
- The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.
- The IRB has reviewed and approved consent procedures and a consent document consistent with 50.25. These procedures and the consent document are to be used with



participants or their legally authorized representatives in situations where use of such procedures and documented is feasible.

- The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a participant's participation in the clinical investigation consistent with the paragraph below.
- Additional protections of the rights and welfare of the participants will be provided, including, at least:
 - Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the participants will be drawn.
 - Public disclosure to the communities in which the clinical investigation will be conducted and from which the participants will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits.
 - Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results.
 - Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation.
 - If obtaining consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the participant's family member who is not a legally authorized representative, and asking whether he or she objects to the participant's participation in the clinical investigation.
 - The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.
 - Procedures are in place to inform, at the earliest feasible opportunity, each participant, or if the participant remains incapacitated, a legally authorized representative of the participant, or if such a representative is not reasonably available, a family member, of the participant's inclusion in the clinical




investigation, the details of the investigation and other information contained in the consent document.

- There is a procedure to inform the participant, or if the participant remains incapacitated, a legally authorized representative of the participant, or if such a representative is not reasonably available, a family member, that he or she might discontinue the participant's participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.
- If a legally authorized representative or family member is told about the clinical investigation and the participant's condition improves, the participant is also to be informed as soon as feasible.
- If a participant is entered into a clinical investigation with waived consent and the participant dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the participant's legally authorized representative or family member, if feasible.
- The protocol is performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identified such protocols as protocols that might include participants who are unable to consent.
- The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists.
- If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly (no longer than within 30 days) in writing to the clinical investigator and to the sponsor of the clinical investigation.


(2) Research not subject to FDA regulations

The IRB responsible for the review, approval, and continuing review of the research has approved both the research and a waiver of informed consent and has found and documented that the research is not subject to regulations codified by the FDA at 21CFR50, and




found and documented and reported to the OHRP that the following conditions have been met relative to the research:

- a. The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
- b. Obtaining informed consent is not feasible because: the subjects will not be able to give their informed consent as a result of their medical condition; the intervention involved in the research must be administered before consent from the subjects' legally authorized representatives is feasible; and there is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research.
- c. Participation in the research holds out the prospect of direct benefit to the subjects because: (i) subjects are facing a life-threatening situation that necessitates intervention; (ii) appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and (iii) risks associated with the research are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.
- d. The research could not practicably be carried out without the waiver.
- e. The proposed research protocol defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact



representatives and make this information available to the IRB at the time of continuing review.

- f. The IRB has reviewed and approved informed consent procedures and an informed consent document in accord with 45CFR46.116 and 46.117. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the research consistent with paragraph (b)(7)(v) of this waiver.
- g. Additional protections of the rights and welfare of the subjects will be provided, including, at least:
 - h. consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the research will be conducted and from which the subjects will be drawn;
 - i. public disclosure to the communities in which the research will be conducted and from which the subjects will be drawn, prior to initiation of the research, of plans for the research and its risks and expected benefits;
 - j. public disclosure of sufficient information following completion of the research to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;
 - k. establishment of an independent data monitoring committee to exercise oversight of the research; and
 - l. if obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the research. The investigator will summarize efforts made to contact family members and



make this information available to the IRB at the time of continuing review.

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

For the purposes of this waiver, "family member" means any one of the following legally competent persons: spouses; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.

Y. Responding to Non-Compliance with Human Research Protection Program Requirements

(1) Corporate Compliance Programs

UnityPoint Health System has established a Corporate Compliance Program for the entire system, which includes UPHDM. Investigators who are not employed by UPHDM may not be subject to the Compliance Programs of UPHDM, but rather to the programs of their employers. However, the procedures described in this section apply to all persons regardless of whether they are subject to a separate corporate compliance program.


(2) Definition/The Spectrum of Non-Compliance


- a. Non-compliance means any action or activity associated with the conduct and oversight of human subjects research that is at variance with this Policy & Procedures and the relevant federal regulations on which they are based. Non-compliant actions may range from minor to serious; they may be unintentional or willful; and they may occur only once or several times.
- b. Serious non-compliance means non-compliance that affects the rights and welfare of participants, or compromises the integrity or validity of the research. Additional considerations of seriousness include compromising the integrity or validity of the research.
- c. Continuing non-compliance means a pattern of non-compliance that indicates a lack of understanding about the regulations or ethical requirements that may affect the rights and welfare of participants, or compromise the integrity or validity of the research. The pattern of non-compliance is assessed by the number of incidents occurring during the course of a protocol, and whether the same noncompliant action was repeated or many different noncompliant events occurred.
- d. The frequency of non-compliance is assessed mainly by the number of incidents occurring during the course of a protocol, and would also take account of whether the same noncompliant action was repeated or many different noncompliant events occurred.

(3) Reporting concerns

Reports of non-compliance in human subjects research may come from many sources including, but not limited to, an investigator (as a self-report); a study monitor, auditor or sponsor; a research subject; or a person not directly involved with the research.

Concerns about any protocol involving human participants may be directed to the Chair or any member of the IRB, the Research Subject Advocate, the Director of HRPP, the Vice President for Medical Affairs or any member of the IRB.


Concerns or complaints may be directed to the Chief Compliance Officer or through the Compliance HelpLine of UPHDM (1-800-548-



8778). Persons raising such concerns are encouraged to express them in writing. However, verbal concerns will be received and should be reduced to writing as soon as possible by the party receiving them.


(4) Responding to concerns

- a. To the extent that an instance of non-compliance may be covered by procedures established by the UnityPoint Health System policies (1.CE.1 and 1.CE.5), any investigation of non-compliance with requirements of the human research protection program conducted by the IRB as well as any remedial action required or recommended by the IRB must be coordinated with the UPHDM Compliance Executive Director. It should be noted that the UPHDM Compliance Executive Director is a voting member of the IRB.
- b. In cases of noncompliance involving investigators subject to other corporate compliance programs, the IRB chair will seek advice from the Law Department and the Compliance Executive Director about how to interact with the corporate compliance officers.
- c. Concerns disclosed to the UPHDM Chief Compliance Officer will be investigated according to procedures described in UPHDM Policy 1.CE.5. The Chief Compliance Officer may refer the matter to the IRB for further investigation.
- d. All concerns disclosed to the chair of the IRB will be disclosed promptly to the Chief Compliance Officer. Unless the Chief Compliance Officer indicates that the matter must be investigated under the guidelines set out in the Corporate Compliance Program (1.CE.1), the IRB chair will initiate an investigation as soon as practicable. In cases of very serious non-compliance, e.g. when a subject's safety has been compromised or when a subject may have been injured due to non-compliance, the investigator's superior may be notified at an early stage of the investigation.
- e. The chair may conduct the investigation personally, delegate the matter to another IRB member who may have particular expertise or insight into the matter, or assemble an ad hoc committee, which may include persons who are not IRB members but have necessary expertise to evaluate the matter.

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- f. If the research is funded by the Public Health Service and there is reason to believe that the non-compliance involves research misconduct, then the procedures described in the UPHDM Policy and Procedures for Ensuring the Responsible Conduct of Research may be activated.
 - g. The time frame for beginning the investigation will generally be determined by the seriousness of the non-compliance, with investigations of the most serious allegations being initiated with greatest urgency. In general, it is to be expected that most investigations should begin within 30 days of being reported to the IRB chair. The IRB Chair – or whoever was designated by the Chief Compliance Director – will communicate the results of the investigation, in writing, to the IRB office and it will be distributed to all members for consideration at the next convened meeting. At the discretion of the IRB Chair, brief reports of continuing investigations may be made verbally at convened meetings and documented in the minutes.

(5) Evaluation


- a. Non-compliance is not serious or not continuing. If an IRB Chair who becomes aware of non-compliance and can determine that (1) the non-compliance was clearly not serious and not continuing, (2) the research staff recognized the non-compliance, and (3) the research staff took appropriate corrective actions, then the Chair will make a decision regarding the appropriate management of the non-compliance. Actions may include a note to the study file, notification of sponsor, notification of any subjects affected by the non-compliance, or notification of appropriate agencies.
- b. Non-compliance is serious or continuing. If the IRB chair determines that non-compliance is likely serious or continuing, then the issue in question of non-compliance must go to the Institutional Review Board at the next convened meeting of the entire IRB for review. Such determination will be made on a case-by-case basis by the IRB chair following the investigation procedures outlined in IV. Y.(4). In general, the seriousness of the non-compliance is gauged by the extent to which research subjects are harmed or put at increased risk. Willful disregard for the



welfare of research subjects would be considered particularly egregious, however, frequent instances of minor non-compliance would also be considered cause for concern. The full IRB will make a final determination about whether the non-compliance was serious or continuing and the appropriate way to remedy the serious or continuing non-compliance during the next scheduled board meeting.

(6) Notifications

- a. IRB staff notes the results of the IRB's determinations in the meeting minutes.
- b. The IRB chair notifies the investigator in writing of the results of the investigation and of any remedial actions required by the IRB. At the discretion of the IRB chair, the report to the investigator might exclude identities of persons who raised concerns or participated in the investigation. The IRB includes in the notification a request for the investigator to respond in writing. The convened IRB will review the response.
- c. After review by the convened IRB, the IRB chair or HRPP Coordinator drafts a report that includes a description of the nature of the event, the findings of the organization, actions taken by the organization or IRB, reasons for the organization's or IRB's actions, and plans for continued investigation or action. The report is approved by the Director of HRPP, signed by the IRB chair, filed in the protocol file and sent to the IRB with the next agenda packet.
- d. If the non-compliance is determined after investigation to be serious or continuing, then copies of the report are sent to:
 - The IRB in the next agenda packet.
 - Chief Compliance Officer.
 - Sponsor, if the IRB determines at a convened meeting that the sponsor of the research should be notified. If the sponsor has already established a reporting policy for the type of event, then those guidelines will be considered.
 - Principal investigator's superior, if the IRB

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- determines at a convened meeting that he or she should be notified.
- OHRP.
 - FDA, if the research is FDA regulated.
 - The maximum time allowed between determination of the event as serious or continuing and reporting of the event will be not more than 30 days.
- e. At the discretion of the Director of HRPP, copies of the report may also be sent to the UPHDM Law Department and the Law Department of the relevant institution.
- f. Consistent with the Corporate Compliance Program of UPHDM, the person who made the initial allegation or reported a concern will be apprised of the results of the investigation.

(7) Protection for whistleblowers

Persons expressing concerns or making allegations about a protocol involving human participants will not be subject to retaliation or disciplinary action if they act in good faith. This protection holds even if the concerns or allegations are found, upon investigation, to be without merit.

(8) Actions that the IRB may take in Responding to Concerns or Allegations of Non-Compliance

Remedial action will be determined by the degree of seriousness of the non-compliance, the willfulness of the action, and the number of times it may have occurred. The following list indicates the range of actions the IRB may take:

- a. No action
- b. Modification of the research protocol
- c. Modification of the information disclosed during the consent process
- d. Additional information provided to past participants
- e. Notification of current participants (required when such information may relate to participants' willingness to continue to take part in the research)
- f. Requirement that current participants re-consent to participation

- g. Modification of the continuing review schedule
- h. Monitoring of the research
- i. Monitoring of the consent
- j. Suspension of the research. (Such action will activate the procedures described in Section IV.N.)
- k. Termination of the research. (Such action will activate the procedures described in Section IV.N.)
- l. Obtaining more information pending a final decision
- m. Referral to other organizational entities (e.g., legal counsel, risk management, institutional official)
- n. Other actions deemed appropriate by the IRB

Z. Use of Protected Health Information for Research

[45CFR164]

UnityPoint Health System Policies 1.MR.9 and 1.MR.13 describe the procedures for complying with requirements of The Health Insurance Portability and Accountability Act of 1996 (“Privacy Rule”) and are hereby incorporated by reference. The following digests are presented here solely for convenience.

(1) Definitions


- a. PHI. Protected health information
- b. Covered entity. A health care provider who transmits any health information in electronic form in connection with a transaction covered by 45CFR164.

(2) Implementation

The UPHDM IRB, along with the Corporate Compliance Office, will function as the Privacy Board for matters relating to research.

(3) Background

The Privacy Rule establishes the conditions under which protected health information (PHI) may be used or disclosed by covered entities for research purposes. A covered entity may always use or disclose for research purposes health information that has been de-identified (in accordance with §§ 164.502(d), 164.514(a)-(c) of the rule) without regard to the provisions below. The Privacy Rule also




defines the means by which individuals/human research subjects are informed of how medical information about them will be used or disclosed and their rights with regard to gaining access to information about themselves, when such information is held by covered entities. Where research is concerned, the Privacy Rule protects the confidentiality of individually identifiable health information, while at the same time, ensuring that researchers continue to have access to medical information necessary to conduct vital research.

(4) Using and disclosing PHI for research without authorization

- a. In the course of conducting research, researchers may create, use, and/ or disclose PHI for research purposes, without the written authorization of the individual, or without providing the individual with an opportunity to agree or object, and regardless of the research funding source, provided that the investigator obtains documentation that an alteration to or waiver of the individual authorization, in whole or in part, has been approved by the IRB and the Chief Compliance Officer.

- b. Documentation of Waiver Approval. The documentation required to show that an alteration to or waiver of the individual's authorization, in whole or in part, has been approved must include the following:
 - A statement identifying the IRB and Chief Compliance Officer and the date on which the alteration or waiver of authorization was approved.
 - A statement that the IRB and Chief Compliance Officer has determined that the alteration or waiver of authorization, in whole or in part, satisfies the following:
 - The use or disclosure of PHI involves no more than minimal risk to the privacy of individuals, based on, at least, the presence of the following elements: [1] An adequate plan to protect the individual's identifying information from improper use and disclosure. [2] An adequate plan to destroy the individual's identifying information at the earliest opportunity consistent with conduct of the Research, unless there is a health or Research justification for retaining the identifiers or such retention is otherwise required by law. [3] Adequate written assurances that the PHI will not be reused or disclosed to any other person or entity, except



as required by law, for authorized oversight of the Research study, or for other Research for which the use or disclosure of PHI would otherwise be permitted.


- The Research could not practicably be conducted without the waiver or alteration.
 - The Research could not practicably be conducted without access to and use of the PHI.
- c. A brief description of the PHI the IRB and Chief Compliance Officer or privacy board have determined must be used or accessed in order to conduct the Research.
- d. A statement that the alteration or waiver of authorization has been reviewed and approved under either normal or expedited review procedures of the IRB.
- e. The documentation of the alteration or waiver of authorization must be signed by the chair or other member, as designated by the chair of the IRB

(5) Reviews Preparatory to Research

- a. When PHI is necessary for reviews preparatory to Research, the Covered Entity must obtain representations from the researcher that include the following:
1. Use or disclosure is sought solely to review PHI as necessary to prepare a Research protocol or for similar purposes preparatory to Research.
 2. No PHI is to be removed from the Covered Entity by the researcher in the course of the review.
 3. The PHI for which use or access is sought is necessary for Research purposes.

(6) Research on Deceased Individual's Information

- a. If the Research involves a deceased individual's PHI, the Covered Entity must obtain from the researcher the following:
1. Representation that the use or disclosure sought is



solely for Research on the PHI of the deceased individual.

2. Documentation, at the request of the Covered Entity, of the death of such individual.
3. Representation that the PHI for which use or disclosure is sought is necessary for Research purposes.

(7) Limited Data Set

A Covered Entity may use and disclose a Limited Data Set for Research purposes, if the Covered Entity enters into a data use agreement with the Limited Data Set recipient.

(8) Research use/disclosure with individual authorization

When a research protocol is combined with a therapeutic intervention, the consent form will contain a statement explicitly requesting the research subject to authorize inspection of the subject's medical record by persons not involved in the subject's treatment. Such persons may include members of the IRB; representatives of the sponsor; and representatives of regulatory agencies. These groups will be specifically itemized on the consent form. The authorization must indicate a specific expiration date or event; in certain circumstances, the notations "no expiration date" or "end of study" are acceptable alternatives to a specific date.

(9) Compound Authorization

An authorization for the use or disclosure of PHI for a Research study may be combined with any other type of written permission for the same Research study, including another authorization for the use or disclosure of PHI for such Research or a consent to participate in such Research.

(10) Covered Entity may condition the provision of Research-related Treatment on the provision of an authorization or the use or disclosure of PHI for such Research under this section.

(11) Restriction of Individual Access to PHI

An individual's access to PHI created or obtained by a Health Care Provider in the course of Research that includes Treatment may be temporarily suspended for as long as the Research is in progress,

provided that the individual has agreed to the denial of access when consenting to participate in the Research that includes Treatment, and the Health Care Provider has informed the individual that the right of access will be reinstated upon completion of the Research.

AA. Conflict of Interest Disclosure

[UPHDM Policy and Procedures for Managing Conflicts of Interest in Research]

All members of the IRB, all investigators, all research study staff, and each consultant used for review of research must complete a “Conflict of Interest Disclosure” form describing any significant financial interest in research. This form is to be submitted to the IRB Office annually, and updated as changing circumstances may warrant, and be readdressed with each new protocol submission by the investigator. Annual disclosures will be evaluated by the Research Conflict of Interest Committee (RCOIC). When appropriate, the RCOIC will suggest ways to manage conflicts. At least one member of the RCOIC will be a voting member of the IRB. The convened IRB is informed of the RCOIC’s determination and proposed management plan. The IRB has the final authority to determine whether or not there is any interest that requires managing. Once the management plan is approved by the full board, a letter explaining the management plan is sent to the investigator/study team member. COI forms from other institutions may be submitted for IRB review. The RCOIC Committee makes the final determination if the form will be accepted in lieu of the UnityPoint Health Des Moines COI form.

BB. Humanitarian Use Devices and Humanitarian Device Exemptions

FDA Guidance Document on HDE

1) Definition

A humanitarian use device (HUD) is a device approved by FDA for marketing without demonstration of efficacy for treating conditions that affect very few people. FDA regulations require that a person seeking to use such a device obtain approval from an IRB even though the use is not in the context of a research protocol or a clinical investigation.

2) Application

A physician applying for approval to use an HUD should submit the



following documents:

- a. A letter to the IRB chair describing: the proposed use; number of patients that might be treated in a given year; and how the physician obtained the training necessary to use the device. The letter must also specify that the HUD will not be used as part of a research project or clinical investigation designed to collect data to support an FDA pre-market approval application.
- b. A statement from the sponsor or manufacturer giving the following information:
 - Generic name and trade name of the device
 - The FDA Humanitarian Device Exemption (HDE) number
 - Date of HUD designation by FDA
 - Indications for use of the device
 - Contraindications, warnings, precautions for use of the device
 - Adverse effects of the device on health
 - Alternative practices and procedures
 - Marketing history
 - Summary of studies using the device
- c. Forms to be used by the physician in reporting usage of the HUD to the sponsor.

3) Conditions of use of the HUD

- i. The IRB may impose conditions on the use of the HUD including, but not limited to specifying the number of patients that may be treated; specifying reporting requirements; the length of time for which the approval is valid.

4) Informed consent

- i. The IRB will consider on a case-by-case basis whether to require a specific consent for use of the HUD.

5) Continuing review

- i. The physician using a HUD will submit an annual report detailing the number of times the device was used and any complications or unanticipated problems encountered. A special HUD Continuing Review form is sent to the investigator prior to the continuing review of the board.



V. Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research (Subpart B)

A. Applicability

[45CFR46.201]

Except as provided in paragraph (2) of this section, this subpart applies to all research involving pregnant women, human fetuses, neonates of uncertain viability, or nonviable neonates conducted or supported by UPHDM.

(1) The exemptions at 45CFR46.101(b) 1-6 are applicable to this subpart.

(2) The provisions of 45CFR46.101(c-i) are applicable to this subpart. Reference to State or local laws in this subpart and in Section III.A(8) [46.101(f)] is intended to include the laws of federally recognized American Indian and Alaska Native Tribal Governments.

(3) The requirements of this subpart are in addition to those imposed under the other subparts of this part.

B. Definitions

[45CFR46.202]


(1) Dead fetus means a fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.

(2) Delivery means complete separation of the fetus from the woman by expulsion or extraction or any other means.

(3) Fetus means the product of conception from implantation until delivery.

(4) Neonate means a newborn.

(5) Nonviable neonate means a neonate after delivery that, although living, is not viable.

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- (6) Pregnancy encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.
 - (7) Secretary means the Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.
 - (8) Viable, as it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. Guidelines published by the Secretary DHHS in the Federal Register will be used in determining whether a neonate is viable for purposes of this subpart. If a neonate is viable then it may be included in research only to the extent permitted and in accordance with the requirements of sections A and D of this chapter.

C. Duties of the IRB in Connection With Research Involving Pregnant Women, Fetuses, and Neonates

[45CFR46.203]


In addition to other responsibilities assigned to the IRB under this part, the IRB shall review research covered by this chapter and approve only research that satisfies the conditions of all applicable sections of this chapter and the other chapters of this document.

Implementation: The “Subpart B” checklist will be used to document that the required determinations have been made when the board reviews research involving pregnant women, fetuses, and neonates. (See Operations Manual for the IRB Office)

D. Research Involving Pregnant Women or Fetuses

[45CFR46.204]

Pregnant women or fetuses may be involved in research if all of the following conditions are met:

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- (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.
 - (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 any 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 a 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, her consent is obtained in accord with the informed consent provisions of subpart A of this part.
 - (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 in accord with the informed consent provisions of subpart A of this part, 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 paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.
 - (7)** For children as defined in [45CFR46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of 45CFR46 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.
- (10) Individuals engaged in the research will have no part in determining the viability of a neonate.

E. Research Involving Neonates

[45CFR46.205]

(1) Neonates of uncertain viability and nonviable neonates


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

- a. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
- b. Each individual providing consent under paragraph (2)(b) or (3)(e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
- c. Individuals engaged in the research will have no part in determining the viability of a neonate.
- d. The requirements of paragraph (2) or (3) of this section have been met as applicable.

(2) Neonates of uncertain viability

Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this subpart unless the following additional conditions have been met:

- a. The IRB determines that: (i) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or (ii) The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and
- b. The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally



authorized representative is obtained in accord with subpart A of this part, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

(3) Nonviable neonates

After delivery, a nonviable neonate may not be involved in research covered by this subpart unless all of the following additional conditions are met:

- a. Vital functions of the neonate will not be artificially maintained;
- b. The research will not terminate the heartbeat or respiration of the neonate;
- c. There will be no added risk to the neonate resulting from the research;
- d. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
- e. The legally effective informed consent of both parents of the neonate is obtained in accord with subpart A of this part, except that the waiver and alteration provisions of [45CFR46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph (3)(e), except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph.

(4) Viable neonates

A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord

with the requirements of Chapters IV and VII.

F. Research Involving, after Delivery, the Placenta, the Dead Fetus or Fetal Material

[45CFR46.206]

- (1) Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable Federal, State, or local laws and regulations regarding such activities.
- (2) If information associated with material described in paragraph (a) of this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of this part are applicable.

G. Research not Otherwise Approvable which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Pregnant Women, Fetuses, or Neonates

[45CFR46.207]

It is not anticipated that research falling in this category will be conducted under the oversight of the UPHDM IRB.

VI. Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects (Subpart C)

A. Definition

"Prisoner" means any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

B. Research prospectively involving prisoners is not allowed

Research involving prisoners will not be allowed at this institution.

C. When a research subject becomes a prisoner

In the event that a person becomes a prisoner after being enrolled in a clinical research protocol, the principal investigator must withdraw the person from the protocol with careful consideration given to the safety of any termination of a test article. This should be done in consultation with the IRB. Any data pertaining to this study subject's participation should be eliminated from the study database.

VII. Protections for Children Participating in Research (Subpart D)

A. Applicability

[45CFR46.401]


- (1) This policy applies to all research involving children as subjects, conducted or supported by the UPHDM.
- (2) Exemptions at 45CFR46.101(b)(1) and (b)(3) through (b)(6) are not generally applicable to this subpart. [See Section IV.A(1).]
- (3) Emancipated minors can consent to medical procedures on their own behalf. Therefore they are not considered children under federal definitions at 45CFR46.402(a) and 21CFR50,3(o), and are not subject to the provisions of this section.

B. Definitions

[45CFR46.402]

The definitions in Section IV.B [§46.102] shall be applicable to this subpart as well. In addition, as used in this subpart:

- (1) Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. In Iowa, the age of majority is 18 years or upon marriage (Iowa Code 234.1).
- (2) Assent means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.
- (3) Permission means the agreement of parent(s) or guardian to the participation of their child or ward in research.

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- (4) Parent means a child's biological or adoptive parent.
 - (5) Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.
 - (6) Emancipated minor is one who is absent from the minor's parents with the consent of the parents, is self-supporting, and has assumed a new relationship inconsistent with being a part of the family of the parents. [Iowa Code 252.16].

C. IRB Duties

[45CFR46.403]

In addition to other responsibilities assigned to the IRB under this part, the IRB shall review research covered by this subpart and approve only research which satisfies the conditions of all applicable sections of this subpart.

D. Research Not Involving Greater than Minimal Risk

[45CFR46.404]

Research found by the IRB to present no greater than minimal risk to children may be conducted, only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in 45CFR46.408. Such a finding must be documented in the minutes of a convened meeting of the IRB.

E. Research Involving Greater than Minimal Risk but Presenting the Prospect of Direct Benefit to the Individual Participants

[45CFR46.405]

The IRB may approve research involving more than minimal risk to children but that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, only if the IRB finds and documents in the minutes of a convened meeting that:

- (1) the risk is justified by the anticipated benefit to the subjects;
- (2) the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
- (3) adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in 45CFR46.408.

F. Research Involving Greater than Minimal Risk and no Prospect of Direct Benefit to Individual Participants, but Likely to Yield Generalizable Knowledge about the Participants' Disorder or Condition

[45CFR46.406]

The IRB may approve research involving greater than minimal risk to children that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject, only if the IRB finds and documents in the minutes of a convened meeting that:

- (1) the risk represents a minor increase over minimal risk;
- (2) 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;
- (3) the intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
- (4) adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth in 45CFR46.408.

G. Research not Otherwise Approvable which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Children


[45CFR46.407]

It is not anticipated that research in this category will be conducted at UPHDM.

H. Requirements for Assent by Children and Permission by Parents

[45CFR46.408]

- (1) Assent by children. In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine that adequate provisions are made for soliciting the assent of the




children, when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that 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 and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with 45CFR46.116.

- (2) Permission of parents. In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine, in accordance with and to the extent that consent is required by 45CFR46.116, that adequate provisions are made for soliciting the permission of each child's parents or guardian unless one parent is dead, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.. When a research protocol presents no more than minimal risk 45CFR46.404 or involves greater than minimal risk with prospect of direct benefit to an individual participants 45CFR46.405, the IRB will determine whether consent will be required from each parent or guardian unless one parent is dead, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child, or whether the permission of one parent is sufficient. The determination of the IRB will be documented on the review checklist.

Implementation. A legal guardian may give consent for a child to participate in research involving greater than minimal risk with prospect of direct benefit to an individual participant (Iowa Code 633.562). The IRB will make determination whether consent of one or both parents is required. The determination will be documented in the minutes and in the notification letter sent to the investigator.

- (3) Waiver of requirement for permission. In addition to the provisions for waiver contained in 45CFR46.116, if the IRB determines that a research protocol is designed for conditions or for a subject



population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with Federal, State, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

- Permission by parents or guardians shall be documented in accordance with and to the extent required by 45CFR46.117.
- When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

Implementation. All research protocols with the potential for inclusion of children 12-17 years of age shall include a signature form for the child's assent unless the IRB determines that the requirement for assent may be waived because the intervention or procedure holds a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research. (See Template for Child's Assent) The IRB allows an investigator the discretion to obtain verbal assent or to forego the assent process completely in individual cases (for example when a child is mentally incapable of understanding the protocol or of giving assent). In this instance, the investigator will write a note on the parental consent form explaining why written assent was not obtained. The investigator may request that the IRB waive the requirement to obtain assent at the time the protocol is presented for approval if the investigator believes that there may be a compelling reason why assent cannot or should not be obtained. Such a waiver of assent will be documented in the minutes of the meeting.

The guiding principle behind this process is respect for the developing decision making capacity of children 12-17. Given this principle, a child's refusal to give assent may not be overridden by parental consent. Just as formal consent of an adult subject should be viewed as a process that continues for the duration of the protocol, so too a child should be given the opportunity to affirm or withdraw assent to participate during the protocol. Waiver or lack of a requirement to obtain assent does not relieve the investigator of the responsibility of explaining the experimental procedures to a child subject in a manner appropriate to the child's developmental stage.



I. Wards

[45CFR46.409]

- (1) Children who are wards of the State, or any other agency, institution, or entity can be included in research approved under 45CFR46.406 only if such research is:
 - a. related to their status as wards; or
 - b. conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

- (2) If the research is approved under paragraph (1) of this section, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.


VIII. HRPP Quality Assessment and Improvement


A. Purpose

The purpose of the HRPP quality assessment and improvement plan is to provide monitoring and internal oversight to assure that all HRPP operations effectively support the UPHDM mandate to protect the rights and welfare of research participants. This includes compliance with institutional policies and procedures, and applicable federal, state, and local laws pertaining to the protection of human subjects in research.

B. Quality assessment and performance measurement:

Performance measurement and quality assessment is an ongoing process and includes the following formal and informal activities:

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- (1) Routine (not for cause) and for-cause reviews of on-site research records provide measures of investigator and research staff understanding of and compliance with laws, regulations, policies governing the conduct of human subject research. These reviews also provide a measure of the effectiveness of investigator and research staff resources, quality and timeliness of Investigator/IRB communication, and access to and awareness of HRPP policies, education and available training opportunities. Routine reviews will be conducted by the UPHDM internal audit department every three years.. Review findings are provided to the IRB for acceptance and/or determination, which may include a corrective action plan and/or a recommendation for additional education and training.
 - (2) **Complaints or Concerns about research.** Everyone involved in the research endeavor-including researchers, staff, residents, students, study participants-is encouraged to communicate their questions, concerns or suggestions regarding the Human Research Protection Program and allegations of coercion or undue influence to the IRB office, the Research Subject Advocate, the Executive Director of Compliance, or anonymously through the compliance helpline. This information is contained in each informed consent document, as well as available on the IRB web page.
 - (3) **Evaluation of volume and type of research reviewed.** At least annually, in conjunction with UPHDM budget process, a review of IRB membership, research reviewed as well as effectiveness of IRB meetings will be discussed and evaluated. A determination will be made at that time regarding continued appropriateness of work volume and IRB membership make-up. A summary of the meeting, along with any concerns raised will be sent to the HRPP Coordinator, the Director of HRPP, and the Vice President of Medical Affairs. Concerns about work volume and type of research may also be raised by any IRB member at any time.
 - (4) Annual review of HRPP Coordinator, chairs and members. Refer to IRB Procedures, IV.D. (3), (11).
 - (5) The Human Subjects Protection Program will undergo an Internal Audit conducted by an auditor from the UnityPoint



Health System Audit Department every 3 years. The Office of Research and the IRB office will undergo separate audits. The audit will evaluate consistency between federal, state, and local laws and regulations and Policy and Procedures; consistency between Policy and Procedures and every day operations within the Human Subjects Protection Program; and review of the evaluation process for IRB chairs and members. The audit will be accomplished through a process that includes record review, Policy and Procedure review as well as interviews with key personnel within the program. The results of the audit will be shared with key personnel within the Program as well as the Vice President for Medical Affairs for UPHDM, the Executive Vice President for Blank Children's Hospital, the Vice President of Medical Education, the Director of Research and the CEO of UPHDM.

C. Continuous Quality Improvement

(1) HRPP QI Group

A working group of the IRB and research nurse coordinators, open to all IRB members and associated research groups, meets periodically to evaluate all aspects of the Program of Human Research Protections and draft proposals for change as needed. At least annually, the working group will conduct an assessment of its outreach activities within the community and plan to make improvements as necessary based on these assessments.


Compliance and quality objectives will be evaluated and developed annually. The annual goals and objective will be kept in a separate document in the HRPP office, and on the IRB SharePoint site.

Minutes will be generated from these meetings and kept in the HRPP office. The HRPP Coordinator will attend regularly and be responsible for the minutes of the meeting. Either the IRB chair or vice-chair will attend. The Director of Research will appoint someone from the Office of Research to attend regularly.

(2) Changes in policy, procedures and forms

Changes in procedures may be considered and adopted by the IRB, subject to review by the Director of HRPP. Changes in IRB forms do not require approval. Changes in policy require the approval of the President/CEO of UPHDM. Revised policy, procedure, or forms will be posted on the IRB webpage within 2 weeks of approval by the IRB.

(3) Communications with investigators



IRB staff and leadership meet periodically with coordinators of the principal research groups to discuss operations, consider suggestions for improvements, and discuss implementation of new procedures. Changes in policy, procedures, or forms will be communicated to investigators - through the research coordinators - within 2 weeks of approval and posted on the IRB website.

D. Revision History

February 2004	Policy and Procedures implemented
March 2004	New Section IV.G Unanticipated Problems and Events New Section IV.N (5) Suspension of protocol by investigator or sponsor
June 2004	Revised Section VIII.B Continuous Quality Improvement New Section IV.C (3) Managing Conflict of Responsibilities of Executive Director of Research Revised Section IV.H (4) Mechanisms of continuing review Revised Section IV.N. (3) Suspension or termination of a protocol by investigator, sponsor or IRB. Revised Section IV.R (4) Monitoring of the informed consent process
September 2004	New Section IV.T (3) Payments to research subjects Clarification in Section D (3) of how the chair and vice chair of the City Wide IRB are elected. Revised Section D(8). Speaks to financial conflict of interest of IRB members. Revised Section F(4) describes how the IRBs review protocols and amendments. Clarification in F(11) of how required changes are communicated to the investigator. Revised Section IV.G clarifies various terms. Revised Section IV.Y describes procedures for obtaining information from IRB members about potential financial conflicts of interest and a change in method for collecting information about potential financial conflicts of interest of investigators.
November 2004	Extensive revision in response to AAHRPP review.
April 2005	Revisions reflect change in organization of the human research protection program.
April 2006	Revisions reflect changes IRB meeting leadership.
October 2006	Revisions reflect changes in review of non-local unanticipated serious events.
May 2007	Reviewed prior to AAHRPP accreditation application.
December 2007	Reviewed and revised following AAHRPP draft site visit report.
August 2008	Revised in accordance with AAHRPP suggested changes following status Pending report. Voted and approved in August 2008.
September 2010	Reviewed and revised prior to AAHRPP accreditation application. Voted and approved, September 2010.
February 2011	Reviewed and revised following AAHRPP step 2 submission approval. Voted and approved, February, 2011.
July 2012	Revisions reflect Quality Improvement initiatives and revised reporting timeframe for unanticipated problems.

	Voted and approved, July 2012
September 2013	Revisions to reflect health system name change, consistency in HRPP Coordinator language, Personnel for Expedited Review Approval, Removed “Certified” medical translator language, typographical errors, removed all references to City Wide IRB, changed name of Conflict of Interest Disclosure Form, added information regarding offsite storage of study files, added information on uploading and removal of board packets to SharePoint website, revised CIRB Facilitated Review Process to Local Notification of Initiation of CIRB studies, added “Contract and Budget” to materials to submit to the IRB for review
October 2013	Revised PHI policy to include all requests for PHI be approved by the IRB and Corporate Compliance Officer
February 2014	Updated website address on cover page; Section G. Unanticipated Problems Involving Risk to Research Participants and Others - Added [45CFR46.103(b)(5) to federal regulation list under; Section G(2) - Added bullet (3) regarding 24 hour SAE notification & changed bullet (n) to bullet (4); Section K(1.c) Additional Materials – Added language to allow investigators to submit other forms of ethics training and COI documentation to IRB for review; Section K(2) Continuing Review – Removed request to include original application under materials to submit to IRB. HRPP Coordinator will include the application from the study file. Added (7) – Current list of study investigators and study personnel and contact information for each person. Revised items to submit to IRB under bullets b. c. & d.; Section O – identified process for (1) notification to IRB for new CIRB studies. Added section (2) for notification of amendments for previously approved CIRB studies; Section Z – Added statement to allow submissions of COI forms from other institutions
May 2014	Inserted New Section “P”, CIRB Approval of Industry Sponsored Studies; reformatted spacing and typo errors; removed asterisks (*) from document
June 2015	Extensive revision in preparation of AAHRPP Re-Accreditation visit
October 2015	Extensive revision following AAHRPP Step 1 Application process
January 2016	Section O & P – Added, “If a research study will involve the use of hospital departments (lab, radiology, etc.), the study must go through the following CIRB notification process.” to both sections.

May 2016	Section G – Added language regarding reporting of events occurring on studies prior to opening at local site; Revised language to include the new Non-Compliance with the Protocol, Board Requirements or Regulations Report Form; Revised language for Evaluation of reported events as all events will be reviewed by full convened IRB
June 2016	Section O – Removed the requirement of submitting the local CIRB abbreviated application (c), revised bullet letters Section P - Removed the requirement of submitting the local CIRB abbreviated application (3), revised bullet numbers to letters to continue formatting of Section O
July 2017	Page 2, Updated Chair/Vice Chair Names; Section G – removal of request to provide external events to the IRB for review, added language relating to non-compliance subcommittee and their duties; Section Q - language added relating to study subjects being seen at local clinic for study visits, tests, labs; language added relating to study subjects who come to UPHDM facilities for study procedures when the research study is not approved through our IRB
August 2017	Page 43 & 45 – Clarification on which events need to be reported to the IRB: UNEXPECTED, RELATED TO THE RESEARCH AND POSES A RISK TO SUBJECTS OR OTHERS. ADVERSE EVENTS THAT ARE EXPECTED AND UNRELATED TO THE RESEARCH DO NOT NEED TO BE REPORTED TO THE IRB. THE IRB WOULD LIKE, HOWEVER, TO BE NOTIFIED OF ALL DEATHS OF HUMAN SUBJECTS THAT OCCUR WITHIN A STUDY.