UnityPoint Health
Des Moines

Human Research Protection Program Procedures

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UnityPoint Health – Des Moines Leadership

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I. Introduction

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

There are two sets of regulations throughout this document: Pre-2018 Regulations and 2018 Regulations. The IRB follows two sets of regulations based on the date of the research study approval date:

Pre-2018 Regulations: Those studies that were approved 1/20/19 or prior.

2018 Regulations: Those that were approved 1/21/19 and after.

The 2018 regulations follow the updated OHRP regulations that are in effect 1/21/19.

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, John Stoddard Cancer Center, and Grinnell Regional Medical Center.

II. Charge

UnityPoint Health – Des Moines (UPHDM) 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 (IRB)** is charged with the responsibility for reviewing and overseeing all research involving human participants conducted within UnityPoint Health – Des Moines.

Jon Rozenfeld, MBA
President and Chief Executive Officer

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 Subject (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 Subject (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. Definitions

A. Pre-2018 Requirement

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 subject 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 subject, 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) for obtaining the information to constitute research involving human subject. 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 subject. 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.

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.

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 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.

19. **Clinical investigation** (according to research regulated by FDA [21CFR50, 56] means any experiment that involves a test article and one or more human subject 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** (according to research regulated by FDA [21CFR50, 56] 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 investigate 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** (according to research regulated by FDA [21CFR50, 56] means an individual who both initiates and 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** (according to research regulated by FDA [21CFR50, 56] 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** (according to research regulated by FDA [21CFR50, 56] 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.

B. 2018 Requirement

1. **Certification** means the official notification by the institution to the supporting Federal department or agency component, in accordance with the requirements of this policy, that a research project or activity involving human subject has been reviewed and approved by an IRB in accordance with an approved assurance.

2. **Clinical trial** means a research study in which one or more human subject are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health related outcomes.

3. **Department or agency head** means the head of any Federal department or agency, for example, the Secretary of HHS, and any other officer or employee of any Federal department or agency to whom the authority provided by these regulations to the department or agency head have been delegated.

4. Electronic signature means:
   a) an electronic sound, symbol, or process attached to, or logically associated with, a record and executed or adopted by a person with the intent to sign the record;
   b) is unique to one individual and shall not be reused by, or reassigned to, anyone else;
   c) is linked to the record to which it pertains to ensure that the signatures cannot be excised, copied, or otherwise transferred to falsify an electronic record.

5. **Federal department or agency** refers to a federal department or agency (the department or agency itself rather than its bureaus, offices, or divisions) that takes appropriate administrative action to make this policy applicable to the research involving human subject it conducts, supports, or otherwise regulates (e.g., the U.S. Department of Health and Human Services, the U.S. Department of Defense, or the Central Intelligence Agency).

6. **Human subject** means a living individual about whom an investigator (whether professional or student) conducting research:
   a) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
   b) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

7. **Intervention** includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

8. **Interaction** includes communication or interpersonal contact between investigator and subject.

9. **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 that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., medical record.

10. **Identifiable private information** is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

11. **Identifiable biospecimen** is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

12. **Institution** means any public or private entity, or department or agency (including federal, state, and other agencies).

13. **IRB** means an Institutional Review Board established in accord with and for the purposes expressed in this policy. The IRB means any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subject. The primary purpose of such review is to assure the protection of the rights and welfare of the human subject.

14. **IRB approval** means the determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and federal requirements.

15. **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. If there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research.

16. **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.

17. **Public health authority** means an agency or authority of the United States, a state, a territory, a political subdivision of a state or territory, an Indian tribe, or a foreign government, or a person or entity acting under a grant of authority from or contract with such public agency, including the employees or agents of such public agency or its contractors or persons or entities to whom it has granted authority, that is responsible for public health matters as part of its official mandate.

18. **Research** means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research:

a) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected. (Not considered generalizable knowledge)

b) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during an event or crisis that threatens public health (including natural or man-made disasters).

c) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

d) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

19. **Written, or in writing**, for purposes of this part, refers to writing on a tangible medium (e.g., paper) or in an electronic format.

V. Basic Procedures for Human Research

A. Scope and Authorities: Exempt Categories, Case Studies, Quality Studies [45CFR46.101]

1. **Research Involving Human Participants** - An activity is defined as research involving human participants if either:

   a) it meets the following definitions of research and human subject as defined in DHHS regulation: Pre-2018 Requirement: 45CFR46.102(d) and 45CFR46 102(f), respectively, 2018 Requirement: 45CFR46.102(e)(1)(i) OR

   b) 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 subject. 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, John Stoddard Cancer Center, and Grinnell Regional Medical 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**: Pre-2018 Requirement:

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

a) **Category (1):**

(1) The research conducted in established or commonly accepted educational settings.

(2) The research involves normal educational practices such as:

(a) Research on regular and special educational instructional strategies.

(b) Research on the effectiveness of the comparison among instructional techniques, curricula, or classroom management methods.

(3) The research does not involve prisoners as participants.

(4) The research is not FDA-regulated.

b) **Category (2):**

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

(1) information obtained is recorded in such a manner that human subject can be identified, directly or through identifiers linked to the subject; and

(2) any disclosure of the human subject' responses outside the research could reasonably place the subject at risk of criminal or civil liability or be damaging to the subject' financial standing, employability, or reputation.

(3) The research is not FDA-regulated.

c) **Category (3):**

Research involving the use of educational tests that is not exempt under paragraph (b)(ii) of this section, if: (i) the human subject is 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. The research is not FDA-regulated.

d) **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 subject cannot be identified, directly or through identifiers linked to the subject. Such research must be in compliance with HIPAA regulations (Section X). The research is not FDA-regulated.

e) **Category (5)**

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

(1) public benefit or service programs;

(2) procedures for obtaining benefits or services under those programs;

(3) possible changes in or alternatives to those programs or procedures; or

(4) possible changes in methods or levels of payment for benefits or services under those programs.

(5) 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).

(6) The research or demonstration project must be conducted pursuant to specific federal statutory authority.

(7) There must be no statutory requirement that the project be reviewed by an IRB.

(8) The project must not involve significant physical invasions or intrusions upon the privacy of participants.

(9) The exemption should have authorization or concurrence by the funding agency.

(10) The research is not FDA-regulated.

f) **Category (6)**

Taste and food quality evaluation and consumer acceptance studies.

4. **Exempt Research Activities**: 2018 Requirement:

a) **Category (1)-** Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods. The research is not FDA-regulated.

b) **Category (2)-** Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

(1) The information obtained is recorded by the investigator in such a manner that the identity of the human subject cannot readily be ascertained, directly or through identifiers linked to the subject;

(2) Any disclosure of the human subject' responses outside the research would not reasonably place the subject at risk of criminal or civil liability or be damaging to the subject' financial standing, employability, educational advancement, or reputation; or

(3) The information obtained is recorded by the investigator in such a manner that the identity of the human subject can readily be ascertained, directly or through identifiers linked to the subject, and an IRB conducts a limited IRB review to make the determination required by §45CFR46.111(a)(7).

(4) The research is not FDA-regulated.

c) **Category (3)-** Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

(1) The information obtained is recorded by the investigator in such a manner that the identity of the human subject cannot readily be ascertained, directly or through identifiers linked to the subject;

(2) Any disclosure of the human subject' responses outside the research would not reasonably place the subject at risk of criminal or civil liability or be damaging to the subject' financial standing, employability, educational advancement, or reputation; or

(3) The information obtained is recorded by the investigator in such a manner that the identity of the human subject can readily be ascertained, directly or through identifiers linked to the subject, and an IRB conducts a limited IRB review to make the determination required by §45CFR46.111(a)(7).

For this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subject, and the investigator has no reason to think the subject will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subject play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

If the research involves deceiving the subject regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

(4) The research is not FDA-regulated.

d) **Category (4)-** Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(1) The identifiable private information or identifiable biospecimens are publicly available;

(2) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subject cannot readily be ascertained directly or through identifiers linked to the subject, the investigator does not contact the subject, and the investigator will not re-identify subject;

(3) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of ''health care operations'' or ''research'' as those terms are defined at 45 CFR 164.501 or for ''public health activities and purposes'' as described under 45 CFR 164.512(b); or

(4) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for non-research activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

(5) The research is not FDA-regulated.

e) **Category (5)-** Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including 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. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

(1) Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal Web site or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subject.

(2) The research is not FDA-regulated.

f) **Category (6)-** Taste and food quality evaluation and consumer acceptance studies:

(1) If wholesome foods without additives are consumed, or

(2) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

g) **Category (7)-** The UPHDM IRB has not implemented the use of broad consent currently. Storage or maintenance for secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determinations required by §45CFR46.111(a)(8).

h) **Category (8)-** The UPHDM IRB has not implemented the use of broad consent currently. Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:

(1) Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with §45CFR46.116(a)(1) through (4), (a)(6), and (d);

(2) Documentation of informed consent or waiver of documentation of consent was obtained in accordance with §45CFR46.117;

(3) An IRB conducts a limited IRB review and makes the determination required by §45CFR46.111(a)(7) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph (d)(8)(i) of this section; and

(4) The investigator does not include returning individual research results to subject as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results.

i) **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.

j) **Application for exemption**. An investigator who believes a project may qualify for exemption should submit a completed an Application for New Protocol within IRBManager including the type of study = exempt. 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. The IRB Chair, or designee, will review the materials to determine if the project meets the criteria for exempt review. If necessary, the IRB Chair, or designee, will seek expert opinion regarding the proposed research and conformity to applicable codes.

k) **Determinations.** Authority to classify research as exempt rests with the Chair of the Institutional Review Board, or designee, and not with an investigator. In deciding 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:

(1) The research holds no more than minimal risk to subject;

(2) Selection of subject is equitable;

(3) If there is recording of identifiable information, there are adequate provisions to maintain the confidentiality of the data;

(4) If there are interactions with subject, there will be a consent process that will disclose such information as:

(a) The activity involves research

(b) A description of the procedures

(c) Participation is voluntary

(d) Name and contact information of the investigator

(e) Provisions to maintain the privacy interests of subject.

l) The "Exemption Checklist" will be used to document the IRB Chair's, or designee's, determination and retained as a record of the application within IRBManager. 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.

m) **Notification.** All requests for exemption are answered promptly by determination letters, signed by the IRB chair or designee, which describe the regulatory basis for granting exempt status as well as any additional requirements that may be imposed to assure protection of the rights and welfare of research subject, 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.

5. Limited Review

It is the policy of the Organization that research which satisfy the criteria for exemption under 45 CFR 46.104(d) (2 or 3) undergo limited IRB review if information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects.

a) **Categories:**

(1) ***Exempt Category 2 section (iii)*** [45 CFR 46.104(d)(2)(iii)]; that is research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if one of the following conditions are met:

(a) If the information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects. If the research involves children, this exemption only applies to educational tests or the observation of public behavior when the researchers do not participate in the activities being observed.

(b) Any disclosure of the participants' responses outside the research would not reasonably place the participants at risk of criminal or civil liability or be damaging to the participants' financial standing, employability, or reputation. If the research involves children, this exemption only applies to educational tests or the observation of public behavior when the researchers do not participate in the activities being observed.

(c) The information obtained is recorded by the researcher in such a manner that the identity of the human participants can readily be ascertained, directly or through identifiers linked to the participants, and an IRB conducts a limited review of research. This condition cannot be applied when the research is subject to Subpart D.

(2) ***Exempt Category 3 section (i)(C)*** [45 CFR 46.104(d)(3)(i)(C)]; that is, research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written

responses (including data entry) or audio-visual recording if the subject prospectively agrees to the intervention and information collection

(a) If the research involves deception of participants regarding the nature or purposes of the research, the participant authorizes the deception through a prospective agreement to participate in the researching circumstances in which the participant is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

(b) The research is not regulated by the US FDA.

(3) ***Exempt Categories 7 & 8 (Broad Consent):*** The Organization does not currently utilize exempt categories 7 and 8 (secondary research for which broad consent is required); therefore, limited IRB review is not used in that context.

b) **Criteria for Approval:**

(1) For research to be approved under exempt category 2 section (iii) or category 3 section (i)(C) limited IRB review must find that there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data [45 CFR 46.111(a)(7)].

(2) Since the adequacy of provisions to maintain confidentiality depend, in part, on the nature of the research, the methods involved, the characteristics of the subject population (including the vulnerability of subjects) and the risks related to the research, limited IRB review will consider all these additional factors.

c) **Restrictions.** Research that meets the federal criteria for limited review 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.

d) **Application for Limited Review**. Research which appears to be eligible for approval under exempt categories 2 section (iii) or 3 section (i)(C) should apply for limited review should submit a completed an Application for New Protocol within IRBManager including the type of study = exempt and must contain enough information to meet the approval criteria as outlined above. Supporting documents demonstrating why the investigator believes the work qualifies for limited review could include surveys, interview scripts, proposed consent forms, recruitment materials and any other pertinent documents to meet the approval criteria.

The investigator must give assurance that the research will be conducted in accordance with any applicable regulations, laws, or codes. The IRB Chair, or designee, will review the materials to determine if the project meets the criteria for limited review. If necessary, the IRB Chair, or designee, will seek expert opinion regarding the proposed research and conformity to applicable codes.

Limited IRB review may be performed by expedited review, as outlined in the Expedited Procedures, Section VII (D). If the expedited reviewer cannot determine that the criteria for approval as defined in this policy are satisfied, then the research will be referred to the convened IRB. The reviewer must document the rationale for this determination and the rationale for review by the convened IRB.

e) **Determinations.** Authority to classify research under limited review rests with the Chair of the Institutional Review Board, or designee, and not with an investigator. In deciding whether to grant limited review approval, the chair, or designee, 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 IRB reviewer of limited review research may not disapprove research. The ethical analysis will include an examination of the following elements:

(1) The research holds no more than minimal risk to subject;
(2) Selection of subject is equitable;
(3) For exemption Categories 2 section (iii) and 3 section (i)(C), there are adequate protections for privacy interests of participants and the confidentiality of the data;
(4) If there are interactions with subject, there will be a consent process that will disclose such information as:
    (a) The activity involves research
    (b) A description of the procedures
    (c) Participation is voluntary
    (d) Name and contact information of the investigator
    (e) Provisions to maintain the privacy interests of subject.

Limited IRB review determinations will be documented on the Exemption Checklist. Research approved by limited IRB review under exempt categories 2 section (iii) or 3 section (i)(C) does not require continuing review unless the expedited reviewer determines that such review would meaningfully protect the rights and welfare of human subjects of research. For limited review studies that are not required to undergo a formal Continuing Review, an Administrative Update Form will be sent to those Principal Investigators/study contacts. The Administrative Update Form will collect information on the status of the study (remain open or close the study), study team members and enrollment status. The Administrative Update Form will be sent to the PI/study contact person via IRBManager approximately 12 months after the study

approval date. The form must be returned to the IRB Office within 30 days, or the research study will be closed. The IRB retains the authority to suspend or terminate IRB approval of research approved with a limited review.

f) **Notification.** All requests for limited review are answered promptly by determination letters, signed by the IRB chair or designee, which describe the regulatory basis for granting limiting review status as well as any additional requirements that may be imposed to assure protection of the rights and welfare of research subject. Limited Review decisions are noted in agendas and minutes of convened meetings and filed in the IRB Office.

6. 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(l):

a) "Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."

b) 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.

7. Case Reports

Case reports, that is, descriptions of unusual or unique presentations of a disease or condition, are <u>not considered reports of research</u> 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:

d) they are presented in a manner that states or implies generalizability;

e) changes were made in the patient's care for the sake of reportability; or

f) 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 case report does or does not qualify as a report of research, investigators must always be sensitive to protecting the privacy and confidentiality of the subject of the reports.

8. Determination about whether an activity qualifies as human research

In most cases, investigators readily understand the definition of human subject research and abide by the provisions of the 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, the Director of HRPP or the IRB Manager, who will explain the definitions and utilize the OHRP decision chart and guidance document. Determinations about whether an activity qualifies as human subject research will be documented in determination letters to the prospective investigator from the IRB Chair or designee. 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 an activity is not human subject research and thus not be subject to the Policy & Procedures or to oversight by the IRB. The IRB Chair, the Director of HRPP and the Medical Director, Medical Staff Office are authorized to make determinations about whether a given project meets the regulatory definitions of DHHS and FDA for human subject research, and which would be subject to these Policy & Procedures. The Medical Director, Medical Staff Office 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 subject 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 Section VII.I

9. **Other laws and regulations**:

Compliance with this policy and procedures requires compliance with pertinent State and Federal laws or regulations, which may provide additional protections for human subject. This policy does not affect any State or local laws or regulations which may otherwise be applicable, and which provide additional protections for human subject.

10. 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 56.105.

11. Research in foreign countries

Research in foreign countries is currently not accepted at this institution.

12. 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 observer. Research that is FDA regulated does not qualify for exemption under Categories 1-5.

13. 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 the requirements of this policy.

B. Assuring Compliance – FWA

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 subject of research conducted at or sponsored by UPHDM, regardless of whether the research is subject to Federal regulation.

   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 subject 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.

3. Implementation. The CEO of UPHDM has authorized the Medical Director, Medical Staff Office, the Director of HRPP and the HRPP Manager to submit, or make changes in, the FWA on behalf of UPHDM.

C. IRB Membership

1. General considerations

a) 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 (professional and competence), and the diversity of the members, including consideration of race, cultural backgrounds, sexual orientation, and gender identity (SOGI), and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subject. 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.

b) 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 subject, viz children; therefore, the IRB shall include one or more individuals who are knowledgeable about and experienced in working with children.

2. Assessment of IRB composition

At least bi-annually, the IRB will review and discuss the current composition of the IRB. Determinations will be made regarding whether the composition is sufficient to review the volume and types of research, has diversity of membership that is reflective of the organization and community, and meets applicable regulatory requirements.

If the IRB determines that there are gaps in composition, then recommendations will be made to correct the misalignment of composition. The IRB chair and the HRPP manager will follow up on the recommendations of the IRB. This bi-annual process will be reflected in the IRB minutes.

3. Appointment to the IRB

a) The Medical Director, Medical Staff Office is authorized by the CEO of UPHDM to appoint regular members, alternate members, and leadership of the IRB.

b) Annually, the HRPP manager will prepare the appointment letters to be sent to the Medical Director, MSO along with the prospective member's curriculum vitae (CV) attached, and the prospective IRB roster. They will review the CV and the roster to determine the professional competence of each member before signing the appointment letter. Competency can be evaluated by degrees held, number of years of service in their professional capacity, or research conducted in a professional capacity.

c) 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.

4. 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 subject 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 subject 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.

c) Evaluation. The HRPP Director or Manager evaluates the IRB Chair and Vice Chair once a year according to the above criteria.

d) The Chair and Vice Chair of the IRB are named by the Medical Director, Medical Staff Office and serve for a calendar year. Appointments may be renewed each year. The Chair or Vice Chair signs all correspondence dealing with decisions and other actions taken by the convened IRB and conducts IRB meetings. The Vice Chair may exercise all functions of the Chair when the Chair is absent or otherwise unavailable. If neither the Chair nor the Vice Chair is available to respond to an urgent matter, the HRPP Director or Manager 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. If neither the Chair nor the Vice Chair is available to conduct the regular meeting, the HRPP Manager will contact an IRB member with at least one year of experience as a voting member of the IRB and formal training in human subject protection to request that they run the scheduled meeting. Neither the Chair, Vice Chair, nor any member may decide individually on behalf of the IRB that is appropriately a matter for determination by the Board as a whole.

5. 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.

6. **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 based on gender.

7. **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 HRPP Manager, Director of HRPP, and the IRB Chair periodically confer 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 V.C.(3). Individuals who are responsible for business development of the organization are prohibited from carrying out day-to-day operations of the review process and are not eligible to serve as IRB members, alternate members, or ex-officio members.

8. 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.

9. 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 subject; informed consent process; treatment of subject 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.

10. 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 Manager 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.

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.

e) 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 subject; informed consent process; treatment of subject 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.

11. Training and Evaluation 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 CITI training modules found at, https://about.citiprogram.org/en/homepage/. Documentation of this training must be verified by 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. CITI training modules for IRB Members must be completed every 3 years.

b) Continuing education of IRB members: UPHDM subscribes to “Medical Ethics Advisor” (previously known as IRB Advisor) and distributes these materials to IRB members via the monthly board meeting packets and are uploaded to the IRB SharePoint website for future reference.

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 IRB Leadership.

d) Periodically, IRB members will be surveyed to illicit their input regarding the focus of continuing education.

e) IRB members are evaluated annually by the IRB Chair, reviewing their meeting attendance, reviews conducted, and overall participation on the board.

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 Medical Director, Medical Staff Office 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 Medical Director, Medical Staff Office in consultation with the IRB Chair, inconsistent with service on the IRB.

D. IRB Functions and Operations

1. **To fulfill the requirements of 45CFR46 and 21CFR56 the IRB shall**:

a) Have access to meeting space and sufficient staff to support the IRB's review and recordkeeping duties;

b) Prepare and maintain a current list of the IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications or licenses sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution, for example, full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid consultant;

c) Establish and written procedures for:

(1) Conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution

(2) 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

(3) 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 subject.

d) Establish and follow written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, department or agency heads, the Office of Human Research Protections, HHS, the Food and Drug Administration of:

(1) any unanticipated problems involving risks to human subject or others or any instance of serious or continuing noncompliance with these regulations or the requirements or determinations of the IRB

(2) any suspension or termination of IRB approval.

e) Except when an expedited review procedure is used, an IRB must review 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 subject must be present to constitute a quorum. The unaffiliated member, the non-scientific member, and the member representing the general perspective of subject may be the same person, two different persons, or three different persons. The HRPP Manager 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.

f) For the research to be approved by the convened IRB, it shall receive the affirmative vote, by voice or polling software, 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.

g) 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 Manager 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 available within IRBManager for viewing by all board members. Documents are also sent to IRB members via secure email and 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 by the HRPP Manager or designee. 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 IRB Chair or IRB Manager, 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. The signed confidentiality statements are filed in the IRB Office with the meeting minutes.

E. IRB Records

[45CFR46.115; 45CFR46.109(f)1]

1. Documentation of IRB activities

The HRPP Manager 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 subject, serious adverse events experienced by subject, and conflict of interest disclosure forms associated with each study are housed within IRBManager.

b) Minutes of IRB meetings shall be in enough detail to show:

(1) attendance at the meetings;

(2) when an alternate member replaces a primary member;

(3) separate deliberations for each action taken by the IRB;

(4) the vote on these actions including the number of members voting for, against, abstaining, and recusing;

(5) 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;

(6) the basis for requiring changes in or disapproving research;

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

(8) determinations required by regulations and protocol specific findings justifying those determinations for: waiver or alteration in the consent process or research involving children;

(9) assessment of the risk-benefit ratio for research involving children;

(10) protocol-specific determinations for research involving pregnant women, fetuses, neonates, and adults who lack decision making capacity.

(11) the rationale for significant risk/non-significant risk device determinations;

(12) approval period (not to exceed one year);

(13) and a written summary of the discussion of controverted issues and their resolution.

c) Continuing review activities:

(1) **Pre-2018 Regulations**: Records of continuing review activities for all open research studies.

(2) **2018 Regulations**: records of continuing review activities, including the rationale for conducting continuing review of research that otherwise would not require continuing review as described below. Unless an IRB determines otherwise, continuing review of research is not required in the following circumstances:

(a) Research eligible for expedited review in accordance with §45CFR46.110;

(b) Research reviewed by the IRB in accordance with the limited IRB review described in §45CFR46.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) or (8);

(c) Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:

(i) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or

(ii) Accessing follow-up clinical data from procedures that subject would undergo as part of clinical care.

d) For both initial and revisions to previously approved research (amendments) approved by the expedited procedure, the records document the following:

(1) The specific permissible category

(2) Description of action taken by the reviewer.

(3) 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 list of IRB members in the same detail as described in 45CFR46.108(a)(2)

h) Written procedures for the IRB in the same detail as described in 45CFR46.116(c)(5).

i) Statements of significant new findings provided to subject.

j) **2018 Regulations:** The rationale for an expedited reviewer's determination under §45CFR46.110(b)(1)(i) that research appearing on the expedited review list described in §45CFR46110(a) is more than minimal risk.

k) Documentation specifying the responsibilities that an institution and an organization operating an IRB each will undertake to ensure compliance with the requirements of 45CFR46.103(e).

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 local completion of the research/final study closure regardless of enrollment.

The records retained will allow a reconstruction of a complete history of IRB actions related to the review and approval of the protocol. The IRB records includes copies of:

a) Recruitment materials
b) Data and safety monitoring board reports.
c) Modifications to previously approved research.
d) Unanticipated problems involving risks to participants and others.
e) Documentation of noncompliance including whether noncompliance is serious or continuing.
f) IRB member work product for each study will be retained and maintained in the study file within the IRB electronic system including any worksheets or checklist. The IRB members will upload the worksheet, or any other study related materials to the electronic system prior to the meeting.

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 Manager 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 Manager will either send the entire paper study file to offsite storage or scan in the study file to the electronic study file. If the study file is requested from investigator or other study personnel, the HRPP Manager 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. Once finished with the study file, the file will be returned to offsite storage or destroyed if printed from the electronic study file.

F. Electronic Records and Signatures

[21CFR11]

1. **Contents: Title 21 Code of Federal Regulations (21 CFR Part 11)**
Electronic Records; Electronic Signatures came into effect on August 20, 1997, and sets forth criteria under which the agency considers electronic records, electronic signatures, and handwritten signatures executed to electronic records to be trustworthy, reliable, and generally equivalent to paper records and handwritten signatures executed on paper. People using electronic signatures must certify to the agency that the electronic signature in their system is intended to be the legally binding equivalent of traditional handwritten signatures.

2. Electronic Records

UnityPoint Health Des Moines IRB utilizes IRBManager software for its online records management. IRBManager is considered an open system complying with 21 CFR 11.10 & 21 CFR 11.30. A copy of the IRBManager validation statement is available upon request by contacting the HRPP/IRB office. UnityPoint Health Des Moines IRB is solely responsible for the following:

a) Limiting system access to authorized individuals [21 CFR 11.10d]

The access to the system used for electronic IRB submissions and reviews (IRBManager) will be limited to authorized users. Each IRBManager user must have a registered account with a unique username and password and a specified level of system access. Only designated IRB administrators are authorized to enable log-in of authorized users. Users are responsible for maintaining the confidentiality of their Username and Passwords.

b) Determination that persons who develop, maintain, or use the electronic record/electronic signature systems have the education, training, and experience to perform their assigned tasks [21 CFR 11.10i]

All users are provided a copy of the UnityPoint Health Des Moines IRBManager User's Manual along with the ability to access it online from the UnityPoint Health Des Moines IRB webpage under the forms tab: Institutional Review Board (IRB) - UnityPoint Health - Iowa Methodist Medical Center. Users can also receive a one-on-one training with the HRPP/IRB Manager upon request.

c) Establishment of written policies that hold individuals responsible and accountable for actions initiated under their electronic signatures [21 CFR 11.10j]

Policies outlining accountability of actions are outlined within the HRPP Policy and Procedures Manual, as well as the IRB Investigator Handbook. Both documents are accessible on the UnityPoint Health Des Moines IRB webpage: Institutional Review Board (IRB) - UnityPoint Health - Iowa Methodist Medical Center.

3. Electronic Signatures [21 CFR 11.50, 11.100, 11.200, 11.300]

a) Users accessing the IRBManager system require a unique username and password with each sign on to the system. Each individual user is accountable and responsible for actions initiated under their electronic signature. Each user is accountable and responsible for maintaining confidentiality of their username and password and must not disclose their username and password to anyone else.

b) Users are responsible for notifying the IRB office if their password has been compromised for the purposes of establish a new password. Users who are leaving the organization should notify the IRB to deactivate their username or password. If the IRB office becomes aware of a user no longer working for the organization, their account will automatically be deactivated.

c) All electronic signatures within IRBManager include the name of the signer, date, and time the signature was executed, and the reason for the signature.

d) An audit trail of all actions, including signing, that occur within the system is maintained by IRBManager.

G. Principal Investigator Responsibilities

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 Subject Protection prior to the initiation of research approved by the IRB. This training must be repeated or enhanced with additional training at least every 3 years. The training completion must be verified by the HRPP Manager 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 Subject Protection prior to the initiation of research approved by the IRB. This training must be repeated or enhanced with additional training at least every 3 years. UPHDM subscribes to the CITI training program. Any person involved in the endeavor of research has access to this training through UPHDM. GCP training, or its equivalent will also be considered. The training completion must be verified by the HRPP Manager before the study is processed for review.

f) A new principal investigator must complete a current "Conflict of Interest Disclosure Form" and completed the CITI Conflict of Interest education modules prior to the review of research by the IRB.

g) The principal investigator is responsible for ensuring that all members of the Research Staff complete a current "Conflict of Interest Disclosure Form," and complete the CITI Conflict of Interest education modules prior to the review of research by the IRB. If the conflict of interest requirements are revised in a manner that changes researcher requirements**,** researchers must be re-educated.

h) Records related to disclosures and management of financial conflicts of interest will be retained for at least three years from completion of the research.

i) If researchers are noncompliant with the requirements for conflict of interest the following sanctions could occur:

(1) Additional conflict of interest education
(2) Suspension or termination of research
(3) Other actions deemed appropriate by the IRB

(4) Information regarding travel will be collected on travel disclosures including the following:

(a) The purpose of the trip

(b) The identity of the sponsor or organizer

(c) The destination

(d) The duration

j) 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 Subject," 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 Subject 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 subject protection education and conflict of interest reporting requirements will be the responsibility of the HRPP Manager. Monitoring will be performed before the initiation of a new protocol and yearly thereafter during continuing review (Pre-2018 Regulations) or during the administrative review (2018 Regulations).

H. Conflict of Interest Disclosure

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

To ensure that reporting requirements for funding or regulatory agencies are met, all members of the IRB, all investigators, all research study staff, and each consultant used for review of research (covered entities) must review the educational material attached to the “Conflict of Interest Disclosure” form and complete the 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. Conflict of Interest education is required at least every 4 years. Additional education will be required if a researcher or other covered entity is non-compliant with the UPHDM IRB conflict of interest policy and procedures.

A completed and signed COI form will indicate review and understanding of the attached educational material.

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 there is any interest that requires managing. Management of a potential conflict of interest might include, but is not limited to:

a) While study activity takes place, suspension of educational or consulting services that are provided by the investigator and paid for by the sponsor of the research.
b) While study activity takes place, funds incurred by the covered individual from the study sponsor for services rendered may be required to be donated to a foundation or contributed to the general operating fund of the covered entities business or practice.
c) Recusal from voting by an IRB member that has financial or other interest in a study reviewed by the IRB.
d) When a financial interest is disclosed but no current conflict exists, the party will be asked to report any future involvement with the particular entity.

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.

The following are definitions of different types of potential conflict to interests:

e) A **conflict of interest** may exist when an individual has an interest that may compromise or have the appearance of compromising the professional judgment of the individual. For example, a conflict of interest could affect the oversight of research, choice of research protocols, the enrollment of human subject, the collection and interpretation of data, or the reporting of results. A conflict of interest may result from interests that are either financial or associational in nature (collectively, an "Interest").

f) A **financial interest** is an interest that stems from an individual's or entity's financial relationship with another individual or entity. A financial interest may arise from a compensation arrangement or an ownership arrangement.

g) An **associational interest** is an interest that stems from a covered individual's or entity's formal or informal participation in or involvement with (directly or indirectly such as through a family member) an organization or entity that, in turn, has a financial or economic stake in an industry entity engaged in research activities. A covered individual means any person covered by this policy, namely all persons who perform, regulate, or oversee research conducted under the auspices of UnityPoint Health Des Moines or an Institutional Review Board of this organization. Neither the IRB reviewer nor their immediate family may have financial interests related to the research. Immediate family means spouse, and any family member who is dependent of the covered individual or whom the covered individual is dependent upon. A potential conflict of interest may arise when the party holding the financial interest is related to the employee in ways other than spouse and dependent children. Financial interests held by this party should be disclosed by the covered individual to the best of his or her knowledge.

Conflicts may be most likely to occur or appear to occur regarding Interests in relation to financially interested persons or entities. A **financially interested person or entity** is a person or entity which would reasonably appear to affect or be affected by the conduct or outcome of a research project at a UnityPoint Health Des Moines facility. This term includes: (1) the manufacturer or distributor (including business partners and affiliates) of any drug, device or other process being used in the research; (2) any entity acting as the agent of the sponsor of the clinical research or other company with an Interest (e.g. a contracted research organization); and (3) a company that provides direct or primary competition for the investigational product if the investigator actually knows the

financial interests of the company would reasonably appear to affect or be affected by the research (each a “Financially Interested Entity”).

I. HRPP Quality Assessment and Improvement

1. **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 subject in research.

2. **Quality assessment and performance measurement:** Performance measurement and quality assessment is an ongoing process and includes the following formal and informal activities:

   a) 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. The results of the internal audit will be provided in a report outlining the findings of the audit.

   b) **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 Resources Needed to Support the HRPP.** At least annually, in conjunction with UPHDM budget process, HRPP leadership will review and evaluate the following resources:

a) Administrative support, space allotment, and human resources dedicated to the HRPP.

b) IRB membership is sufficient to manage the type and volume of research

c) IRB meetings are effective and sufficient to manage required responsibilities of the IRB.

d) HRPP educational program is sufficient to meet the needs of the organization and external partners. A brief survey will be conducted to assess the adequacy of HRPP education and assess for gaps that may need attention. This survey will be conducted every two years.

e) Legal counsel is available to the IRB and other component parts of the HRPP and able to respond in a timely manner. Tracking will occur if response from legal counsel takes 48 business hours or more, or more than 2 inquiries. This metric will be discussed with the UPH legal department at least annually, or as needed.

f) Conflict of Interest assessment process can be managed in a thorough and timely manner including conflict of interest management plans. Compliance with our organizational policies and various regulations will be evaluated as part of our intermittent internal audit process. This will occur every 3-5 years.

g) Community Outreach activities have sufficient resources so that outreach can take place in a variety of settings and methods. This will be assessed through a brief survey of our research partners regarding outreach activity and resources at least every 2 years.

h) Concerns about availability of resources may be brought forward by any member of the HRPP and will be addressed by HRPP leadership at that time. If HRPP leadership determines a deficit of resources devoted to the HRPP in any of these areas, a written request for additional resources will be submitted to the Vice President of Medical Affairs/Institutional Official:

(1) Annual review of HRPP Manager, chairs, and members. Refer to IRB Procedures, V.C. (4c), (11c).

(2) The Human Subject Protection Program will undergo an Internal Audit conducted by an auditor from the UnityPoint Health System Audit Department periodically. 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. 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 Medical Director,

Medical Staff Office for UPHDM, and the CEO of UPHDM.

4. Continuous Quality Improvement

a) **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 assess its outreach activities within the community and plan to make improvements as necessary based on these assessments. The agenda and meeting notes are created by the group organizer and sent via email to members prior to each meeting.

b) **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.

c) **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.

VI. External IRB Procedures

A. IRB Notification of Intent to Conduct (NCI-CIRB) studies

This procedure outlines the process that the UPHDM IRB will follow when an investigator requests oversight by the National Cancer Institute Central IRB (NCI-CIRB) rather than the organizational IRB.

The following procedure should be followed for all research taking place within UPHDM, and for any research occurring where UPHDM is the IRB of record for that organization.

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 NCI-CIRB Studies**

a) The principal investigator/research staff notifies the IRB of their desire to activate an NCI-CIRB approved study.

b) The following documents will be submitted via IRBManager to the IRB as a means of notification regarding each study:

(1) Local informed consent with required local modifications (i.e., local contact information)

(2) Assent or Patient Participation Statement (the local IRB defers to the CIRB age of assent if different than the local IRB policy of 12-17 years of age)

(3) HIPPA authorization

(4) CIRB application

(5) Study protocol

(6) NCI-CIRB final approval letter

(7) CIRB final informed consent document

(8) Pharmacy Utilization Form- For any study utilizing the UPHDSM pharmacy department, this form must accompany the application. This form is available on the IRB website.

(9) Current Conflict of Interest forms for all members of study team

(10) CITI completion certificates for all members of study team if not completed through the UPHDM CITI link. Other forms of human research protection education modules may be accepted in lieu of CITI training (i.e., GCP Training, sponsor training, etc.). Please check with the IRB Office prior to submission of materials to ensure the education modules will be accepted. Researcher Training is required every 3 years. Conflict of Interest training is required every 4 years.

c) The HRPP Manager 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 Manager 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:

(1) SAEs

(2) unanticipated problems that pose a risk to subject or others

(3) a concerning pattern of protocol deviations

(4) protocol violations (refer to Section IV.G).

2. Notification Process for Previously Approved NCI-CIRB Studies

The following documents will be submitted to the local IRB as a means of notification of activity occurring within the study:

a) Amendments to previously approved research including the following:
   (1) CIRB Amendment approval letter
   (2) Local informed consent if language changes due to amendment

b) Continuing reviews:
   (1) CIRB continuing review approval letter
   (2) Approved informed consent when applicable

c) All reports or notification letters relating to the study including:
   (1) Enrollment status including suspension and closure
   (2) DMSB/DMC reports
   (3) Annual study reports
   (4) Any local subject death that occurs within the study

B. Request for reliance on an External IRB

This procedure outlines the process that the UPHDM IRB will follow when an investigator requests oversight by an external IRB rather than the organizational IRB. The UPHDM IRB will only consider deferring oversight of a non-exempt research study to an IRB that has been accredited through AAHRPP (Association for the Accreditation of Human Research Protection Programs), registered with OHRP/FDA, and when an IRB Authorization Agreement (IAA) exists with the external IRB. Refer to HRPP Procedures IV.C. for the IAA process steps.

The following procedure should be followed for all research taking place within UPHDM, and for any research occurring where UPHDM is the IRB of record for that organization.

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

Materials submitted to the IRB for review through IRBManager are processed on a first come, first served basis. The average turnaround time for local review once all required documents have been received is less than 2 weeks, pending availability of the IRB Chair or designee.

⇨ ***Local enrollment cannot begin until the local IRB has provided an acceptance letter that cedes oversight to the external IRB.***

1. Notification Review Process for Externally Approved Studies

a) **Step 1 – Submission of Local IRB Documents**
Once the IAA is in place, the investigator/research staff will submit the following documents to the UPHDM IRB for review. All submissions should be made through IRBManager:

(1) Local informed consent with required local modifications (i.e., local contact information)

(2) HIPPA authorization

(3) Approved study protocol

(4) Current Conflict of Interest forms for all members of study team

(5) Pharmacy Utilization Form- For any study utilizing the UPHDSM pharmacy department, this form must accompany the application. This form is available on the IRB website.

(6) CITI completion certificates for all members of study team if not completed through the UPHDM CITI link. Other forms of human research protection education modules may be accepted in lieu of CITI training (i.e., GCP Training, sponsor training, etc.). Please check with the IRB Office prior to submission of materials to ensure the education modules will be accepted. Researcher Training is required every 3 years. Conflict of Interest training is required every 4 years.

(7) IRB Authorization Agreement if not already on record in the IRB office. If this is a new IAA, the HRPP Director or HRPP Manager will update the organization's FWA on the OHRP website.

(8) Billing information for IRB review, including contact name, phone number and email address

b) **Review:** The HRPP staff will submit the study documents to the IRB chair, or designee, for review and consideration.

c) **Notification of Review:** The IRB staff will notify the Principal Investigator/research staff of the review and will express any local context concerns in a written response. Once the IRB Chair or designee has reviewed the study materials and agrees to cede oversight of the study to the external IRB, the Principal Investigator/research staff will be notified by sending a letter to the study contact email address.

The IRB has the authority to allow or disallow external oversight of the study. If external oversight of the study is not allowed, in certain cases, the Principal Investigator may pursue application to the UPHDM 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, VII.B.(14)(15)

d) **Step 2 – Submission of finalized External IRB Documents**

Once the UPHDM IRB has agreed to cede oversight of the study to the external IRB, the Principal Investigator will submit the following documents as soon as they become available:

(1) External IRB application

(2) External IRB final approval letter

(3) Any additional reviews conducted by the external IRB, including, but not limited to, biosafety review, radiation safety review, recombinant DNA research review, human stem cell research review, and conflict of interest review.

(4) Informed Consent document with final external IRB approval

(5) A copy of the initial review documents and the letter that cedes oversight to the external IRB will be maintained in the IRB office.

(6) The Principal Investigator/research staff will notify the IRB Office through IRBManager of all local events. These include, but are not limited to:

(a) SAEs

(b) unanticipated problems that pose a risk to subject or others.

(c) a concerning pattern of protocol deviations

(d) protocol violations (refer to Section VII.H).

2. Continued Reporting to the UPHDM IRB

The following documents will be submitted to the UPHDM IRB through IRBManager using the External IRB Modifications form as a means of continued reporting of activity occurring within the study. Approval letters are not provided for these items. The PI/research team will receive stamped IRB receipts of each document:

a) Amendments to previously approved research including the following:

(1) External IRB Amendment approval letter
(2) Local informed consent if language changes due to amendment
(3) Study protocol if language changes due to amendment
(4) Any other study documents if language changes due to the amendment

b) Continuing reviews:

(1) External IRB continuing review approval letter
(2) Approved informed consent when applicable
(3) Approved study protocol when applicable
(4) Any other study documents, including above, if current documents are not on file with the IRB

c) All reports or notification letters relating to the study including:
   (1) Enrollment status including suspension and closure
   (2) DMSB/DMC reports
   (3) Annual study reports

C. Relations with Other IRBs and Other Institutions

[45CFR46.114]

1. IRB Authorization Agreement (IAA) Process

An IRB Authorization Agreement, also referred to as a Collaborative Agreement or a Reliance Agreement, may be used when a non-exempt human subjects study has external collaborators. The IAA is used both when UPHDM IRB is serving as the IRB of Record with an external collaborator or is ceding oversight to an external IRB and will describe how the two organizations will relate to each other. UPHDM investigators should not initiate an IAA with another institution without first checking with the UPHDM IRB at IRBsubmissions@unitypoint.org to:

a) Verify that the collaborator's research activity meets the definition of "engaged" in research.
b) Identify the appropriate type of IRB agreement.
c) Facilitate the signing of the agreement by the UPHDM Institutional Official, as applicable. At UPHDM, signatory responsibility is delegated to the Vice President of Medical Affairs.
d) Implement and Manage the Agreement.

When following NIH policy on single IRB review, the IAA will include the following:

e) A description of the process for documenting respective roles, responsibilities, and communication between the reviewing IRB and the relying organization.
f) A description of the process used by the awardee organization to ensure that the IAA is in place and that documentation is in place.
g) A description of which organization is responsible for meeting additional certification requirements such as Certificates of Confidentiality or the NIH Genomic Data Sharing Policy.
h) A description of the process to document the rationale for not relying upon a single IRB review in accordance with NIH policy on exceptions from single IRB review.

2. Cooperative Research

a) Cooperative research projects are those projects covered by 45CFR46 which involve more than one institution. In the conduct of cooperative research, each institution is responsible for safeguarding the rights and welfare of human

subject and for complying with 45CFR46.

b) When sharing oversight of research, the IAA signed by the two organizations will describe the respective responsibilities of each organization. These delineated responsibilities include, but may not be limited to:

(1) Provision of education to researchers and research staff

(2) Conducting scientific review.

(3) Ensuring concordance between any applicable grant and the IRB application.

(4) Reviewing potential noncompliance, including complaints, protocol deviations, and results of audits. The agreement will identify which organization is responsible for deciding whether allegations of noncompliance have a basis in fact. The agreement will identify which organization's process is used to decide whether each incident of noncompliance is serious or continuing.

(5) Management of conflicts of interest related to research. The agreement will identify who will develop and approve management plans and how those will be shared with the other organization for both individual and institutional conflicts of interest.

(6) A statement that should the termination of the authorization agreement occur, one of the parties is clearly responsible for continued oversight of active studies until the closure or a mutually agreed upon transfer of the studies occurs.

c) When following DHHS and FDA requirements, the IAA must define the responsibilities of the relying organization and the reviewing IRB, including, but not limited to:

(1) Determining whether the relying organization applies its FWA to some or all research and ensuring the IRB review is consistent with the requirements in the relying organization's FWA.

(2) Determining which organization is responsible for obtaining any additional approvals from DHS when the research involves pregnant women, fetuses, neonates, or children.

(3) Determining which organization is responsible for reporting serious or continuing noncompliance; unanticipated problems involving risks to participants or others; and suspension or termination of IRB approval.

3. Another Institution relying on UPHDM IRB as its IRB of Record

An institution may request that a UPHDM IRB function as its IRB of record. UPHDM will determine on a case-by-case basis whether it is appropriate to execute an IAA in which an external organization relies on the authority of the UPHDM IRB. 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 UPHDM Institutional Official. Once the IAA is in place, the principal investigator follows UPHDM IRB procedures to submit a new study application within IRBManager. This includes all relevant study documents, conflict of interest disclosure form and verification of education, and documentation of CITI training.

In general, the executed IAA delineates roles and responsibilities for the UPHDM IRB, the external organization, and the principal investigator including the following:

a) The process for evaluating and managing potential conflicts of interest in research both individual and institutional.
b) Reporting requirements and timelines for possible unanticipated problems, participant complaints, protocol deviations, and other events.
c) The process for making a request to add additional research sites to previously approved protocols. UPHDM IRB will review those requests as protocol modifications and determine whether the addition of a site qualifies as a minor modification by reevaluating the risk profile of the protocol with the additional site.
d) The process for UPHDM IRB to communicate suspension or termination of the research to the principal investigator and the investigator's organization.
e) The process for making available to the principal investigator and the investigator's organization relevant IRB records, including but not limited to IRB minutes, approved protocols, consent documents, and other records that document the IRB's determinations upon request.
f) The process for communicating relevant policies to the relying organization, the principal investigator, and the research staff. This includes the process for notification regarding revision in relevant policies.
g) The process for contacting the IRB.

4. 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 Subject at both institutions. If a PI wishes to conduct medical tests, draw labs, or see study subject 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.

VII. IRB Submission & Review Procedures

A. Information to be Submitted for Review by the IRB

1. Initial Review

a) Application form. Investigators will submit study documents using the form "Application for New Protocol" within IRBManager. 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 will receive a notification from IRBManager to review the content of the form prior to signing and submission. All elements of the form must be specifically addressed. 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:

(1) Complete protocol

(2) Pharmacy Utilization Form- For any study utilizing the UPHDSM pharmacy department, this form must accompany the application. This form is available on the IRB website.

(3) Investigator's Brochure (if one exists)

(4) Grant Application (if one exists)

(5) For Industry sponsored Clinical Trials:

(6) Copy of the Final Contract and budget, if available.

(7) Copy of a "good faith" preliminary Contract, if final contract not available at the time of submission.

(8) Contact information for IRB billing purposes

(9) Validation of IND or IDE as indicated in the Application form.

(10) Documentation of Completion of the CITI human subject research training found at, https://about.citiprogram.org/en/homepage/ if not already on file in the IRB office. Other forms of ethics training completed within the last 3 years may be submitted for IRB review (i.e., GCP Training), but acceptance of other forms of training is up to the discretion of IRB Leadership. Human subject training completion is required for all parties listed on the IRB Application form.

(11) Documentation of Completion of the CITI conflict of interest training found at, https://about.citiprogram.org/en/homepage/ if not already on file in the IRB office. Other forms of COI training completed within the last 4 years may be submitted for IRB review, but acceptance of other forms of training is up to the discretion of IRB Leadership. Conflict of Interest

training completion is required for all parties listed on the IRB Application form.

(12) Updated “Conflict of Interest Disclosure” form from all parties listed on the IRB Application form

(13) For DHHS-supported multicenter clinical trials:

(14) DHHS-approved sample informed consent document (if one exists)

(15) Complete DHHS-approved protocol (if one exists)

d) Protocol. Much of the information needed to address the criteria listed in Section I will usually be presented in a formal protocol written by the principal investigator or by the study sponsor. A suggested format for a protocol is available on the IRB website.

e) Advertisements and other materials. All materials that will be presented to research subject or potential subject 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 subject 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 an amendment as explained in Section G (3).

Primary reviewers receive all materials, but all board members can access the materials via IRBManager agenda.

The HRPP Manager 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 type 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) Current protocol incorporating all approved amendments and changes

(5) Statements or reports from safety monitor or data safety monitoring board (if available)

(6) Current list of study investigators and study personnel and contact information for each person.

b) Studies open to enrollment. Board members including primary reviewers receive all documents listed above.

c) Studies closed to enrollment but with continuing treatment or active follow up. All board members including primary reviewers receive (1), (4), (5), (6).

d) Pre-2018 Requirements: Studies closed to enrollment and treatment; follow up continues annually. All members receive (1), (5) and (6). These studies may be reviewed using the expedited procedure.

e) 2018 Requirements: Continuing review of minimal risk studies are not required. If the IRB decides to conduct a continuing review of such studies, the rationale for conducting a continuing review must be documented and filed with the study documents in the IRB Office.

B. Initial Review of Research by IRB

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

1. Functions and authority of the IRB

a) Pre-2018 Regulations: The IRB shall review and have sole authority to approve, require modifications in (to secure approval), or disapprove all research activities involving human subject conducted at UPHDM, including exempt research activities under 45CFR46.104 for which limited IRB review is a condition of exemption.

The CEO of UPHDM, or their 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 the requirements of this policy.

Research involving prisoners is not contemplated currently.

b) 2018 Regulations: The IRB shall review and have sole authority to approve, require modifications in (to secure approval), or disapprove all research activities involving human subject conducted at UPHDM, including exempt research activities under 45CFR46.104 for which limited IRB review is a condition of exemption. The IRB retains the authority to suspend or terminate IRB approval of research approved by a limited review.

The CEO of UPHDM, or their 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 the requirements of this policy.

Research involving prisoners is not contemplated currently.

2. Format for submitting applications to the IRB

Investigators are expected to use the "Application for New Protocol" within IRBManager 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 convened IRB and be available to answer questions. Investigators are excused after their presentation and 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 website (Guide for Oral Presentation to IRB).

4. Procedure for evaluating protocols

a) The HRPP Manager will assign a board member as primary reviewer (scientific member) and a secondary reviewer (non-scientific member) to conduct an in-depth review of the protocol. Four reviewers, usually two physicians and two non-physicians, are assigned to serve each month.

b) The HRPP Manager, in consultation with the IRB Chair, will determine for each protocol application whether it involves subject likely to be vulnerable or subject to coercion. If this is the case, then the HRPP Manager will ensure that at least one IRB member knowledgeable about or experienced in working with such subject will be present at the meeting.

c) Each primary reviewer receives copies of all new protocols or protocol amendments, protocol applications, consent documents, study progress reports, safety monitoring reports and recruitment materials.

d) (A copy of the final contract with the industry sponsor will be submitted for each new protocol to be reviewed. The HRPP Manager 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 a board member serving as community legal representative on the IRB for:

(1) Consistency regarding provisions for medical care or other care or services for research-related injury;

(2) to ensure that it indicated who would provide care and who was responsible to pay for it;

(3) 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.

(4) Board members who are not primary reviewers may access the submitted materials through the agenda links provided within IRBManager.

(5) 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 subject 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 VIII.A of the IRB Procedures.

6. Research involving children:
For research involving children, the convened 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 VIII.E. of the IRB Procedures.

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:

(1) Exemption #1:

(a) 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;

(b) 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;

(c) 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;

(d) 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

(e) The investigation is conducted in compliance with the requirements of 21CFR 312.7 (Promotion and charging for investigational drugs).

(2) Exemption #2:

(a) The clinical investigation is for an in vitro diagnostic biological product that involves one or more of the following:

(i) Blood grouping serum

(ii) Reagent red blood cells

(iii) Anti-human globulin

(3) Exemption #3:

(a) 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.

(b) The diagnostic test is shipped in compliance with 21CFR312.160.

(4) 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:

a) 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 Manager: (the Investigator Brochure may not be used for this purpose)

(1) Sponsor protocol imprinted with the IDE number.

(2) Written communication from the sponsor documenting the IDE number.

(3) Written communication from the FDA documenting the IDE number. (Required if the investigator holds the IDE.)

b) The device meets the requirements for an abbreviated IDE:

(1) The device is not banned

(2) The device is not a significant risk device;

(3) The sponsor (or investigator) will label the device in accordance with 21 CFR 812.5;

(4) The sponsor (or investigator) will comply with the requirements of 21 CFR 812.46 with respect to monitoring investigations;

(5) 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);

(6) 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 12 CFR 812.150 (a) (1), (2), (5), and (7)

(7) The sponsor (or investigator) will comply with the prohibitions in 21 CFR 812.7 against promotion and other practices.

(8) 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.

(9) 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.

c) The device falls into one of the categories of exemption from an IDE:

(1) Exemption #1

(a) Is not a transitional device.

(b) Has been in commercial distribution immediately before May 28, 1976

(c) Is being used or investigated in accordance with the indications in labeling in effect at the time.

(2) Exemption #2

(a) Is not a transitional device

(b) Was introduced into commercial distribution on or after May 28, 1976

(c) The FDA has determined it to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976

(d) 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.

(3) Exemption #3

(a) Is a diagnostic device

(b) The sponsor will comply with applicable requirements in 21 CFR 809.10.

(c) The testing:

(i) Is noninvasive

(ii) Does not require an invasive sampling procedure that represents significant risk.

(iii) Does not by design or intention introduce energy into a subject.

(iv) Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

(4) Exemption #4

(a) 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 subject at risk.

(b) 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 procedures in section VIII.B [§45CFR46.117].

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. If 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 HRPP Manager 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. If the IRB approves research with conditions that require IRB board chair approval, then the approval date is the date that the conditions were determined to be met.

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 Manager 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 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 Medical Director, Medical Staff Office/Institutional Official (IO), the IRB Chair and the Director of HRPP for review. The IO and the IRB Chair sign the minutes once the convened IRB has approved the minutes.

C. Continuing Review and Amendments of Research by the IRB

[45CFR46.109]

1. Frequency of Review:

a) Pre-2018 Regulations:

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 if 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.

b) 2018 Regulations:

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. Unless an IRB determines otherwise, continuing review of research is not required in the following circumstances:

(1) Research eligible for expedited review in accordance with §45CFR46.110;

(2) Research reviewed by the IRB in accordance with the limited IRB review described in §45CFR46.104(d)(2)(iii) (d)(3)(i)(C), or (d)(7) or (8);

(3) Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:

(a) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or

(b) Accessing follow-up clinical data from procedures that subject would undergo as part of clinical care.

When the IRB is not required to conduct continuing review, a recorded rationale must be provided for any decisions to conduct continuing review of research otherwise eligible for review using the expedited procedure.

For those minimal risk studies that are not required to undergo a formal Continuing Review, an Administrative Update Form will be sent via IRBManager to Principal Investigators/study contacts. The Administrative Update Form will collect information on the current status of the study (remain open or close the study), study team members and enrollment status. The Administrative Update Form will be sent via IRBManager to the PI/study contact person approximately 60 and 30 days prior to the study expiration. The form must be submitted through IRBManager prior to the expiration date, or the research study will be closed.

When the IRB is not required to conduct continuing review, records must provide a rationale for any decisions to conduct continuing review of research otherwise eligible for review using the expedited procedure.

2. Timing of Continuing Review:

a) Pre-2018 Regulations:

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, or an administrative review will be conducted.

b) 2018 Regulations:

If a protocol that is deemed greater than minimal risk is initially approved for one year and the investigator wishes to continue the research, then the IRB will review the research 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, or an administrative review will be conducted.

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 subject. Requests for changes in approved protocols or consent forms must be submitted through the amendment form within IRBManager. A copy of the protocol with proposed changes is to be attached to the form. 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 to eliminate immediate hazard to subject, is an Unanticipated Problem and the investigator is required to follow the procedures described in Section VII.H. If it is necessary to terminate or suspend a protocol, the investigator must follow procedures described in Section VII.K. 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 within 60 and 30 days before an application to Continue Research on Human Subject is due. The HRPP Manager 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, or the study is closed to enrollment and no study subject are receiving treatment in which the expedited review procedure is followed. All members of the board receive copies of the continuation application, currently approved consent document, and all reports from the sponsor. At least one member also receives a copy of the complete protocol. Furthermore, all IRB members have access to the complete IRB protocol file and relevant IRB minutes prior to or during the convened IRB meeting by accessing them within IRBManager.

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 subject; 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:

a) radiopharmaceuticals
b) modification in procedure for informed consent
c) subject lacking decision-making capacity
d) research conducted under the emergency research consent exemption
e) expanded access use

6. Criteria for approval of research undergoing Continuing Review

The regulatory criteria for initial approval of research are also used for the continuing review of research. 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. This checklist can be found on the IRB SharePoint site. Both the primary and secondary reviewers complete the checklist within IRBManager when making their reviewer recommendations.

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 subject 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 validity 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 subject or others, or of serious continuing noncompliance, then the matter will be considered at a convened meeting of the IRB. In such instance consideration may be given to suspending or terminating an approved protocol. (See Section VII.K for provisions regarding suspension or termination of a protocol.)

Such matters will be reported promptly and in writing by the IRB chair to the Medical Director, Medical Staff Office 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 continuing review form used by investigators to submit reports for continuing review by the IRB can be found within IRBManager.

a) For research undergoing full board continuing review, the following documents will be required:
   1) Full Board continuing review form within IRBManager
   2) Current approved protocol
   3) Current approved informed consent
   4) Current approved HIPAA (if applicable)
   5) Last signed informed consent
   6) Last signed HIPAA (if applicable)
   7) Any other applicable documents such as updated brochures, materials, updated conflict of interest forms and/or CITI trainings, etc.
   8) Reports- this may include relevant multi-center trial reports, DSMB reports, demographic reports, or any other reports related to the research being conducted or its outcomes.

b) For research undergoing expedited continuing review, the following documents will be required:
   1) Expedited continuing review form within IRBManager
   2) Current approved protocol
   3) Current approved informed consent
   4) Any other applicable documents such as updated brochures, materials, updated conflict of interest forms and/or CITI trainings, etc.
   5) Reports- this may include relevant multi-center trial reports, DSMB reports, demographic reports, or any other reports related to the research being conducted or its outcomes.

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:

a) All activities stop, including recruitment, advertising, screening, enrollment, consent, interventions, interactions, and collection of private identifiable information.
b) 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.
c) Will be set to expired within IRBManager and can be administratively closed by the HRPP Manager if sufficient notices have been given to the principal investigator.

D. Expedited Review Procedures Involving No More than Minimal Risk

[45CFR46.110]

1. Applicability Criteria

a) The IRB may use the expedited review procedure to review the following research activities that:

(1) present no more than minimal risk to human subject, 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 subject.

b) The expedited review procedure may not be used where identification of the subject and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subject' 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 subject.

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.

(1) Research on drugs for which an investigational new drug application (21CFR312) is not required.

(2) 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:

(1) 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

(2) from other adults and children, considering the age, weight, and health of the subject, 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:

(1) where the research is permanently closed to the enrollment of new subject; all subjects have completed all research-related interventions; and the research remains active only for long-term follow-up of subject; or

(2) where no subject has been enrolled and no additional risks have been identified; or

(3) (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 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 Manager who reviews new submissions, amendments, and applicable continuing reviews for complete paperwork. The HRPP Manager may also sit on the expedited review subcommittee.

a) The HRPP Manager ensures that CITI Training Certificates and current 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 Manager 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 reviewer completes the checklist as part of their review within IRBManager. The checklist is associated with the reviewer within the study profile and cannot be altered by the PI or another IRB member.

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 checklist is only completed for those studies open to

enrollment. The checklist is completed by the subcommittee member and filed in the study file within IRBManager.

e) When the subcommittee member has reviewed and approved the submission by completing the expedited checklist, the approval letter is received, sign and returned within IRBManager.

f) For expedited continuing review of research, the subcommittee may exercise all 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 within IRBManager. The completed Expedited Review Checklist is 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, continuing reviews 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 the type of review for each protocol.

E. Criteria for IRB Approval of Research

[45CFR46.111; 21CFR56.111]

1. For the IRB to approve research, the IRB shall determine that the

following requirements to be satisfied:

a) Risks to subject are minimized

(1) Physical, psychological, social, legal, and economic risks to participants are minimized by using procedures that are consistent with sound research design and that do not unnecessarily expose participants to risk.

(2) Physical, psychological, social, legal, and economic risks to participants are minimized whenever appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes.

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

c) Selection of Participants is equitable. In making this assessment the IRB should consider the purposes of the research and the setting in which the research will be conducted. The IRB should be particularly cognizant of the special problems of research that involves a category of subject who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.

d) 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 VIII.A.(2e) – (2f).

e) Informed consent will be appropriately documented or appropriately waived, in writing, in accordance with the regulations. The requirement for written documentation may be waived or altered under specific circumstances. See Section VIII.B.(2).

f) Research involving no greater than minimal risk does not require a Data Safety Monitoring Board.

g) 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:

(1) Studies that involve a greater than minimal risk to subject

(2) Research with a particularly large study population.

(3) Research conducted at multiple sites.
(4) Research involving dangerous procedures.
(5) Research with a high chance of study termination.

(a) There are adequate provisions to protect the privacy of participants.
(b) There are adequate provisions to protect the confidentiality of the data.
(c) 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.

h) For purposes of conducting the limited IRB review required by §45CFR46.104(d)(7)), the IRB has made the determination that the requirement of broad consent will not be implemented at UPHDM.

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]

F. Humanitarian Use Devices and Exemptions

1. Definition

A humanitarian use device (HUD) is a device approved by the 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 a HUD should complete the "Application for New Protocol" within IRBManager, selecting Humanitarian Use Device as the type of study. The physician should attach the following documents to the application:

a) A letter to the IRB chair describing: the proposed use; number of patients that might be treated each 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:
   (1) Generic name and trade name of the device
   (2) The FDA Humanitarian Device Exemption (HDE) number
   (3) Date of HUD designation by FDA
   (4) Indications for use of the devise
   (5) Contraindications, warnings, precautions for use of the device
   (6) Adverse effects of the device on health
   (7) Alternative practices and procedures
   (8) Marketing history
   (9) 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

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

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

5. Continuing review

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 HUD Continuing Review form is sent via IRBManager to the investigator for completion prior to the

continuing review by either full board or the board chair.

G. Emergency Use Authorization: Investigational Products in Unanticipated Situations

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

1. Emergency use

a) 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.

b) **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.

c) **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.)

d) **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 the following:

(1) The human subject is confronted by a life-threatening situation necessitating the use of the test article.

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

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

(4) 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.

e) **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 (a) 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.

f) 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.

g) **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.

h) **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.

i) 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.

H. Unanticipated Problems Involving Risks to Research Subject or Others

[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.

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 subject or others. Adverse events that are expected and unrelated to the research do not need to be reported to the IRB.
   (1) An adverse event is “unexpected” when its specificity and severity are not accurately reflected in the informed consent document.
   (2) 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 than 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:
   (1) 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.
   (2) 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.

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 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 subject.)

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 subject 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 Manager and/or a designated non-compliance subcommittee. The manager or subcommittee will review each event and, if necessary, gather additional information from the PI/study coordinator. Events that are unexpected, related to the research and increases harm to subject or others will be put on the agenda for the next convened IRB meeting for review/discussion where the board will decide on the event. If the subcommittee reviews an event, they will make a recommended determination

to the full convened IRB at the next convened board meeting.

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:
   (1) if the event meets the definition of serious non-compliance
   (2) if the event meets the definition of continuing non-compliance.
   (3) if the event increases the risk of harm to subject or others
   (4) Whether the event represents an unanticipated problem involving risks to subject or others (as defined above)
   (5) Whether any further actions should take place.

c) If the convened IRB determines that a problem is NOT an unanticipated problem relating to the research that increases 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:

   (1) No action
   (2) Requiring a modification of the research protocol
   (3) Requiring a modification of the information disclosed during the consent process
   (4) Requiring additional information be provided to past participants
   (5) Requiring notification of current participants (required when such information may relate to participants' willingness to continue to take part in the research)
   (6) Requiring that current participants re-consent to participation
   (7) Modifying the continuing review schedule
   (8) Monitoring of the research; monitoring the consent process
   (9) Suspending or terminating the research; (which would activate procedures described in Section VII.K)
   (10) Seeking additional information pending a final decision; referring the matter to other organizational entities (e.g., Law Department)
   (11) If the evaluation indicates that non-compliance occurred, then the procedures described in Section VII.I(5-6) are activated.

e) If the convened IRB determines that there is insufficient information to decide whether an event is an unanticipated problem involving risks to participants or others, the event will be tabled and the HRPP Manager 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) If the IRB determines that the event was not an unanticipated problem relating to the research, involving risks to participants or others, no further reporting is required.

b) In all cases when the IRB determines that there is an unanticipated problem relating to the research, involving risks to participants or others, the IRB will report its findings and actions to the investigator. In addition, the following reporting steps will be followed and completed within 30 days following the IRB's final determination.

c) The HRPP Manager will prepare a report of the event describing:
   (1) The nature of the event.
   (2) The findings of the organization.
   (3) Actions taken by the organization or IRB.
   (4) Reasons for the organizations or IRB's actions.
   (5) Plans for continued investigation or action.

d) The report will be reviewed and approved by the HRPP Director and the IRB chair.

e) The IRB Manager will provide a copy of the report to:
   (1) The IRB in the next agenda packet.
   (2) The Director of HRPP
   (3) OHRP
   (4) FDA, if the research is subject to FDA regulations
   (5) Other federal agencies that have regulatory oversight
   (6) Vice President of Medical Affairs
   (7) The sponsor
   (8) The Principal Investigator
   (9) The study file

I. Noncompliance Response 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 subject 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 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 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 subject 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 Medical Director, Medical Staff Office or any member of the IRB.

Concerns or complaints may be directed to the Regional Hospital 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 Regional Hospital Compliance Officer.

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 Regional Hospital Compliance Officer about how to interact with the corporate compliance officers.

c) Concerns disclosed to the UPHDM Regional Hospital Compliance Officer will be investigated according to procedures described in UPHDM Policy 1.CE.5. The Regional Hospital 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 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.

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

Regional Hospital Compliance Officer – 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 decide the appropriate management of the non-compliance. Actions may include a note to the study file, notification of sponsor, notification of any subject 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. In general, the seriousness of the non-compliance is gauged by the extent to which research subject are harmed or put at increased risk. Willful disregard for the welfare of research subject 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 staff 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 organizations 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:
   (1) The IRB in the next agenda packet.
   (2) Regional Hospital Compliance Officer.
   (3) 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.
   (4) Principal investigator's superior, if the IRB determines at a convened meeting that he or she should be notified.
   (5) OHRP (if applicable, see (g) below.
   (6) FDA, if the research is FDA regulated.
   (7) 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.

g) When research is not covered by DHHS regulations, reports of unanticipated problems involving risks to participants or others are not to be reported to OHRP.

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 VII.K.)
k) Termination of the research. (Such action will activate the procedures described in Section VII.K.) Obtaining more information pending a final decision
l) Referral to other organizational entities (e.g., legal counsel, risk management, institutional official)
m) Other actions deemed appropriate by the IRB

J. 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 subject. 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 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 Medical Director, Medical Staff Office 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 subject.

K. 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 subject.

a) Termination means that the IRB approval of research is withdrawn permanently, and the same research protocol cannot resume later.

b) Suspension means that the IRB approval of research is withdrawn in whole, or in part, but the same research protocol could resume later 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 subject, the chair of the IRB will investigate 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 subject, the IRB Chair may impose a temporary suspension, in whole or in part, 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 Medical Director, Medical Staff Office 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 subject already enrolled on a protocol but may not enroll additional subject. The IRB makes the final determination as to whether to suspend or terminate approval at a convened meeting.

4. Care of subject

A decision to suspend or terminate a protocol must include an explicit consideration of the rights and welfare of subject already enrolled in the study as well as a process to inform current subject 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 Medical Director, Medical Staff Office may be consulted about how to continue the care of enrolled subject. 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 within 30 days by the IRB Chair or HRPP Manager to the investigator, Director of HRPP and the Medical Director, Medical Staff Office, 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 subject will be reported immediately to institutional officials and sponsors.

8. Notifying subject of IRB action

a) Enrolled subject. Consistent with the organizational Value of Openness, the default presumption is that subject 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, subject will be so informed. The IRB, together with the Medical Director, Medical Staff Office, will develop a process for explaining the various options to the participants.

b) Former subject. The IRB will consider whether to inform former subject, 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 subject protection to suspension of privileges to conduct research on human subject.

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 (within 30 calendar days) reported to OHRP.

Suspensions and terminations of IRB approval are promptly (within 30 calendar days) reported to FDA.

VIII. Informed Consent Procedures

A. General Requirements for Informed Consent

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

1. Pre-2018 Requirements

a) 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 enough opportunity to consider whether 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.

b) 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:

(1) 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;

(2) the approximate number of subjects involved in the study;

(3) 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);

(4) a description of any benefits to the subject or to others which may reasonably be expected from the research;

(5) a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(6) 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). See Section VIII.H. “Certificate of Confidentiality” for additional procedures.

(7) 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, or where further information may be obtained;

(8) an explanation of whom to contact for answers to pertinent questions about the research and research subject' rights, and whom to contact in the event of a research-related injury to the subject; and

(9) 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;

(10) a statement that a copy of the consent form will be given to the subject;

(11) 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.

c) Additional elements of informed consent

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

(1) a statement that the treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;

(2) anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

(3) any additional costs to the subject that may result from participation in the research;

(4) the consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject; and

(5) a statement that significant new findings developed during 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 subject' 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 subject an informational letter describing the new risks;

(6) a statement that the investigator and/or the institution are being paid to conduct the research;

(7) a statement that the investigator and/or the institution have a financial interest in the outcome of the research.

d) 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.

e) Research Data Collection

(1) 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.

(2) The investigator may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection

after 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.

(a) 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).

(b) The IRB must approve the consent document.

(3) 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.

f) Modifications in the consent procedure

The IRB may approve a consent procedure which does not include, or which alters, some or all 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:

(1) the research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:

(a) public benefit or service programs;

(b) procedures for obtaining benefits or services under those programs;

(c) 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;

(2) the research could not practicably be carried out without the waiver or alteration; and

(3) the research is not subject to FDA regulation.

g) 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 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:

(1) the research involves no more than minimal risk to the subject;

(2) the waiver or alteration will not adversely affect the rights and welfare of the subject;

(3) the research could not practicably be carried out without the waiver or alteration; and

(4) whenever appropriate, the subject will be provided with additional pertinent information after participation;

(5) The research is not subject to FDA regulation.

h) Consent in emergency situations

(1) 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 VIII.D of this document and see also policy UPHDM177, “Emergency Use of Drugs/Biologics and Device”

(2) 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 decide whether the consent procedures and the consent document meets FDA regulations. See Section IV.X.

i) 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 IX.C. for a more extensive discussion of assent by children to participate in research.)

j) 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 for informed consent to be legally effective.

(1) 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].

(2) 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.

(3) 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.

k) 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 during such emergency care may not be considered research data.

l) Provisions for subject who cannot understand written or spoken English or are sensory impaired: [45CFR 46.116-117]

Subject who does 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.

(1) When this procedure is used with subject 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.

(2) At the time of consent:

(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.

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

2. 2018 Regulations

a) General Requirements for Informed Consent (45CFR46.116)
General requirements for informed consent, whether written or oral, are set forth in this paragraph and apply to consent obtained in accordance with the requirements set forth in paragraphs (b) through (d) of this section. Waiver or alteration of consent in research involving public benefit and service programs conducted by or subject to the approval of state or local officials is described in paragraph (e) of this section. General waiver or alteration of informed consent is described in paragraph (f) of this section. Except as provided elsewhere in this policy:

(1) Before involving a human subject in research covered by this policy, an investigator shall obtain the legally effective informed consent of the subject or the subject's legally authorized representative.

(2) An investigator shall seek informed consent only under circumstances that provide the prospective subject or the legally authorized representative enough opportunity to discuss and consider whether to participate and that minimize the possibility of coercion or undue influence.

(3) The information that is given to the subject or the legally authorized representative shall be in language understandable to the subject or the legally authorized representative.

(4) The prospective subject or the legally authorized representative must be provided with the information that a reasonable person would want to have to make an informed decision about whether to participate, and an opportunity to discuss that information.

(5) Except for broad consent obtained in accordance with paragraph (d) of this section:

(a) Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to

participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.

(b) Informed consent must present information in enough detail relating to the research and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or legally authorized representative's understanding of the reasons why one might or might not want to participate.

(6) No informed consent may include any exculpatory language through which the subject or the legally authorized 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.

b) Basic elements of informed consent. Except as provided in paragraph (d), (e), or (f) of this section, in seeking informed consent the following information shall be provided to each subject or the legally authorized representative:

(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures that are experimental;

(2) A description of any reasonably foreseeable risks or discomforts to the subject;

(3) A description of any benefits to the subject or to others that may reasonably be expected from the research;

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained; see IV. T "Certificate of Confidentiality" for additional procedures.

(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

(7) An explanation of whom to contact for answers to pertinent questions

about the research and research subject' rights, and whom to contact in the event of a research-related injury to the subject;

(8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled; and

(9) One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

(a) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or

(b) A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used, or distributed for future research studies.

c) Additional elements of informed consent.

Except as provided in paragraph (d), (e), or (f) of this section, one or more of the following elements of information, when appropriate, shall also be provided to each subject or the legally authorized representative:

(1) A statement that the treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) that are currently unforeseeable;

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's or the legally authorized representative's consent;

(3) Any additional costs to the subject that may result from participation in the research;

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

(5) A statement that significant new findings developed during the research that may relate to the subject's willingness to continue participation will be provided to the subject;

(6) The approximate number of subjects involved in the study;

(7) A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;

(8) A statement regarding whether clinically relevant research results,

including individual research results, will be disclosed to subject, and if so, under what conditions; and

(9) For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (*i.e.,* sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

d) Elements of broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens. UPHDM has chosen not to implement the use of broad consent currently.

e) Waiver or alteration of consent in research involving public benefit and service programs conducted by or subject to the approval of state or local officials. *The provisions for waiver of informed consent do not apply to Food and Drug Administration (FDA) regulated research involving human subjects pertaining to sections e, f, & g below.

(1) Waiver. An IRB may waive the requirement to obtain informed consent for research under paragraphs (a) through (c) of this section, provided the IRB satisfies the requirements of paragraph (e)(3) of this section. If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements at paragraph (d) of this section, and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

(2) Alteration. An IRB may approve a consent procedure that omits some, or alters some or all, of the elements of informed consent set forth in paragraphs (b) and (c) of this section provided the IRB satisfies the requirements of paragraph (e)(3) of this section. An IRB may not omit or alter any of the requirements described in paragraph (a) of this section.

(3) Requirements for waiver and alteration. For an IRB to waive or alter consent as described in this subsection, the IRB must find and document 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:

- *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; and*

(b) The research could not practicably be carried out without the waiver or alteration.

f) General waiver or alteration of consent

(1) Waiver. An IRB may waive the requirement to obtain informed consent for research under paragraphs (a) through (c) of this section, provided the IRB satisfies the requirements of paragraph (f)(3) of this section. If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements at paragraph (d) of this section, and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

(2) Alteration. An IRB may approve a consent procedure that omits some, or alters some or all, of the elements of informed consent set forth in paragraphs (b) and (c) of this section provided the IRB satisfies the requirements of paragraph (f)(3) of this section. An IRB may not omit or alter any of the requirements described in paragraph (a) of this section. If a broad consent procedure is used, an IRB may not omit or alter any of the elements required under paragraph (d) of this section.

(3) Requirements for waiver and alteration. For an IRB to waive or alter consent as described in this subsection, the IRB must find and document that:

(a) *The research involves no more than minimal risk to the subject;*

(b) *The research could not practicably be carried out without the requested waiver or alteration*

(c) *If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;*

(d) *The waiver or alteration will not adversely affect the rights and welfare of the subject; and*

(e) *Whenever appropriate, the subject or legally authorized representatives will be provided with additional pertinent information after participation.*

g) Screening, recruiting, or determining eligibility.
An IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subject without the informed consent of the prospective subject or the subject's legally authorized representative, if either of the following conditions are met:

(1) The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or

(2) The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

h) Posting of clinical trial consent form.

(1) For each clinical trial conducted or supported by a federal department or agency, one IRB approved informed consent form used to enroll subject must be posted by the awardee or the Federal department or agency component conducting the trial on a publicly available Federal Web site that will be established as a repository for such informed consent forms.

(2) If the Federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a Federal Web site (*e.g.,* confidential commercial information), such Federal department or agency may permit or require redactions to the information posted.

(3) The informed consent form must be posted on the Federal Web site after the clinical trial is closed to recruitment and no later than 60 days after the last study visit by any subject, as required by the protocol.

(4) The regulation allows for certain confidential information to be redacted at the time of posting. For example, certain confidential commercial information. Note that the regulation does not allow for exceptions to the requirement for posting, only permitted, or required redaction of certain confidential information by the agency.

i) Preemption. The informed consent requirements in this policy are not intended to preempt any applicable Federal, state, or local laws (including tribal laws passed by the official governing body of an American Indian or Alaska Native tribe) that require additional information to be disclosed for informed consent to be legally effective.

j) 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 (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe).

B. 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 using a written informed consent form approved by the IRB and signed (including in an electronic format) 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 (www.unitypoint.org/irb). A copy of the fully executed document shall be given to the person signing the informed consent form.

2. Alternate formats for written consent

a) Pre-2018 Requirements:

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

(1) 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

(2) a short form written informed consent form 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. The short form includes required disclosures when the research involves private identifiable information or identifiable biospecimens. When this method is used, there shall be a witness to the oral presentation. For subject 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 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.

b) 2018 Requirements:

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

(1) A written informed consent form that meets the requirements of

45CFR46.116. The investigator shall give either the subject or the subject's legally authorized representative adequate opportunity to read the informed consent form before it is signed; alternatively, this form may be read to the subject or the subject's legally authorized representative.

(2) A short form written informed consent form 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, and that the key information required by 45CFR46.116(a)(5)(i) was presented first to the subject, before other information, if any, was provided. The short form includes required disclosures when the research involves private identifiable information or identifiable biospecimens. The IRB shall approve a written summary of what is to be said to the subject or the legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Only the short form itself is to be signed by the subject or the subject's legally authorized representative. However, the witness shall sign both the short form and a copy of the summary, and the person obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the subject's legally authorized representative, in addition to a copy of the short form.

(3) An IRB may waive the requirement for the investigator to obtain a signed informed consent form for some or all subject if it is not regulated by the US FDA and meets criteria outlined in section 3 below.

3. Waiver of requirement for written consent

The provisions for waiver of informed consent do not apply to Food and Drug Administration (FDA) regulated research involving human subjects pertaining to sections a-c below. For research regulated by the US FDA, see section d below.

The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subject 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 subject and involves no procedures for which written consent is normally required outside of the research context.

c) 2018 Requirement

(1) If the subject or legally authorized representatives are members of a

distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subject and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained. The oral or written information provided to the participants must include all required and appropriate additional elements of consent disclosure.

(2) In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subject or legally authorized representatives with a written statement regarding the research.

(3) In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subject 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) In cases where the research involves children and waiver of informed consent is considered:
(a) The IRB is allowed to waive or alter the consent process by determining that the regulatory criteria for waivers or alterations of parental permission are met.
(b) The IRB is allowed to waive the requirement to document the parental permission by determining that the regulatory criteria for waivers are met.

d) Research regulated by the US FDA must meet the five criteria below to qualify for waiver of informed consent:

(1) The research involves no more than minimal risk to the subject;

(2) The research could not practicably be carried out without the requested waiver or alteration;

(3) If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;

(4) The waiver or alteration will not adversely affect the rights and welfare of the subject; and

(5) Whenever appropriate, the subject or legally authorized representatives will be provided with additional pertinent information after participation.

e) The IRB reviewer utilizes the expedited or the exempt checklist to document their findings justifying the waiver or alteration.

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 subject under unusual conditions or when concerns have been expressed about an investigator's approach to recruiting and obtaining informed consent from subject. 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 subject after they have been recruited; and requiring the investigator to record the consent process.

C. Electronic Consent (eIC) in Human Subjects Research

1. Purpose

This procedure establishes the informed consent process and documentation that may be conducted utilizing an electronic platform and/or media in human subjects research.

eIC employs the use of electronic systems and processes, whether remotely or in-person, to convey information to a participant and/or document research consent. The electronic media can vary depending on the type of system utilized and can include the use of applications, videos, graphics, interactive text, etc.

eIC may be used in several different methods and time-points during the eIC process. For example:

a) This process can take place at the research study site where both the investigator (or other authorized member of the research team) and the subject/legally authorized representative are at the same location (“In-Person e-IC”);

b) Remotely where the subject reviews the consent information in the absence of the investigator/research team member (“Remote e-IC”).

2. Policy

IRB must approve the eIC process and forms used during the informed consent process prior to implementation in the study. The methods to be utilized in the eIC process must be submitted to IRB in a format that facilitates this review and includes a sufficient description of the eIC process and the platforms, systems, and/or media employed. EIC employs the use of electronic systems and processes, whether remotely or in-person, to convey information to a participant and/or document research consent. The electronic media can vary depending on the type of system utilized and can include the use of applications, videos, graphics, interactive text, etc.

Any subsequent changes to the eIC process also requires IRB approval prior to implementation, unless the proposed alteration is required to eliminate an immediate hazard to participants or staff.

If requested, or required, the subject/legally authorized representative must have the option to use paper-based forms completely or partially.

The subject/legally authorized representative must be provided a copy of the fully executed, signed informed consent/assent form either in hard copy or as an electronic file that can be stored on their own personal device of choice.

3. Requirements During eIC and Guiding Principles

It is not the intention of the IRB to limit eIC use to specific electronic platforms or methods.

The eIC platform/application must comply with the regulations outlined in 21CFR Part 11. For FDA regulated studies, it is the researcher' responsibility to provide documentation to the IRB that the proposed eIC complies with all applicable requirements under 21 CFR Part 11.

The principles that govern in-person informed consent still apply during an eIC process. Refer to procedures in IV.S. of the IRB Procedures.

An eIC process may also be utilized when the IRB has waived the requirement to obtain a signature on a consent form. With this waiver, the eIC process still includes an information sheet that is provided to the subject/legally authorized representative in its entirety. A checkbox response that states “I agree to participate” should be used to verify/confirm consent prior to initiating study procedures.

4. eIC and Privacy

Privacy measures require extra consideration during a remote eIC process. If during the eIC process the person obtaining consent is remotely located (i.e., the consent process is conducted via a call, video conferencing, or other e-messaging method) the subject should be reminded to find a private location to help ensure privacy of this discussion.

The system that supports e-IC must be secure, utilize restricted access (e.g., unique users and password protection) and store records of the subject’s identity, study participation and personal information, so that subject confidentiality is protected.

Special attention is needed when vulnerable or special populations are included and there should be an adequate plan in place to obtain eIC for the needs of these populations.

5. Electronic Signature

Ensures compliance with the definition of electronic signature as defined in Section IV(d).

The platform for the eIC is to include a method to ensure that the person electronically signing the informed consent document, or providing their consent, is the subject who will be participating in the research study or is the subject's legally authorized representative.

For studies in which HIPAA Authorization is required, this may be obtained utilizing an eIC platform to obtain an electronic signature. The HIPAA regulations also include that the subject/legally authorized representative's typed name is equivalent to an electronic signature.

6. eIC and Vulnerable Populations

a) Non-English speaking subjects:

Investigators are to incorporate an interpreter into the eIC process. Refer to procedures in VIII.B. of the IRB Procedures.

Special attention is required when there is a need for a short form in an eIC process. This may apply when the eIC process is conducted "in-person" or "remotely". At the time of consent, the investigator or designated study team member, are to be aware of this need for the addition of a translated short form to the eIC process/platform and include an interpreter for the non-English speaking subject.

b) Legally Authorized Representatives (LAR) for Adults:

If a legally authorized representative is to provide consent for an adult subject, the principles for obtaining informed consent via the eIC platform still apply. Refer to procedures in VIII.B. of the IRB Procedures.

When possible, the eIC application/process should accommodate the special needs for adults that are visually or hearing impaired, or illiterate.

The IRB may also make determinations that assent from the adult subject is needed. In these cases, this adult assent process is also to be incorporated into the eIC process.

The IRB may also make determinations that assent from the adult subject is needed. In these cases, this adult assent process is also to be incorporated into the eIC process.

c) Children:

When children are to be enrolled, the investigator will need to incorporate the IRB approved assent process in the eIC procedures/platform. If needed,

assent can be obtained in the same way the parental permission was obtained. Refer to procedures in IX.C. of the IRB Procedures.

D. 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 subject 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:

(1) 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).

(2) The application clearly identifies the protocols that will include participants who are unable to consent.

(3) 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 interventions.

(4) Obtaining consent is not feasible because:

(a) The participants will not be able to give their consent because of their medical condition.

(b) The intervention under investigation must be administered before consent from the participants' legally authorized representatives is feasible.

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

(5) Participation in the research holds out the prospect of direct benefit to the participants because:

(a) Participants are facing a life-threatening situation that necessitates intervention.

(b) 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.

(c) 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.

(6) The clinical investigation could not practicably be carried out without the waiver.

(7) 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.

(8) 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.

(9) The IRB has reviewed and approved consent procedures and a consent document consistent with 21CFR50.25. 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.

(10) 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.

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

(a) 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.

(b) 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.

(c) Public disclosure of enough 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.

(d) Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation.

(e) 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.

(f) The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

(g) 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.

(h) 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.

(i) 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.

(j) 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.

(k) 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.

(l) 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.

(m) 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 interventions.

b) Obtaining informed consent is not feasible because: the subject will not be able to give their informed consent because of their medical condition; the intervention involved in the research must be administered before consent from the subject' 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 subject because: (i) subject 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 subject; and (iii) risks associated with the research are reasonable in relation to what is known about the medical condition of the potential class of subject, 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 subject 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 VIII.A.(f3), (g5), (h1) of this waiver.

g) Additional protections of the rights and welfare of the subject will be provided, including, at least:

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

(2) public disclosure to the communities in which the research will be conducted and from which the subject will be drawn, prior to initiation of the research, of plans for the research and its risks and expected benefits;

(3) public disclosure of enough 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;

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

(5) 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.

h) 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.

i) 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.

E. 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:

(1) 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

(2) 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.

(3) The research design provides additional safeguards to protect the rights and welfare of adult subject 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 subject. 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 may 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:
   (1) The proposed plan for the assessment of the capacity to consent is adequate.
   (2) 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 a person who has a decisional impairment, the

IRB will consider whether the assent of the subject should be sought, when in the judgment of the IRB the subject are capable of providing assent, and such assent will meaningfully add to the respect of the subject' autonomy. This judgment may be made for all subject to be involved in research under a 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.

F. Recruitment of Research Subject

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 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.)

UnityPoint Health Des Moines Oncology programs follow the standard of the Commission on Cancer Clinical Trials, including Standard 9.1 which requires they have a screening policy to identify eligible clinical research participants along with how to provide the clinical trial information to those participants. This is to aid in the assessment of identifying and addressing barriers to enrollment and participation. Per this standard, the Clinical Trials policy was created for the John Stoddard Cancer Center. As the IRB of record for UnityPoint Health Des Moines, the IRB supports the Clinical Trials policy for identifying potential research participants from within the community.

Additionally, the IRB provides consultation to researchers to assist with

recruiting challenges. Together with the researcher, they may collaborate to locate resources pertaining to their recruitment obstacles and/or education that may be required to identify potential participants within their community.

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 subject [FDA Information Sheet]

Payment to research subject, 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 subject, i.e., advertising that is intended to be seen or heard by prospective subject 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 subject.

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 later to advertise for subject, 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.

c) 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 subject who are likely to be vulnerable to undue influence.

d) The IRB reviews the information contained in the advertisement and the mode of its communication, to determine that the procedure for recruiting subject 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.

e) 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.

f) 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.

g) Advertisements should not promise "free medical treatment," when the intent is only to say subject 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 subject will be paid but should not emphasize the payment or the amount to be paid, by such means as larger or bold type.

h) Any advertisement to recruit subject should be limited to the information the prospective subject need to determine their eligibility and interest. When appropriately worded, the following items may be included in advertisements.

(1) the name and address of the clinical investigator and/or research facility;
(2) the condition under study and/or the purpose of the research;
(3) in summary form, the criteria that will be used to determine eligibility for the study;
(4) a brief list of participation benefits, if any (e.g., a no-cost health examination);
(5) the time or other commitment required of the subject; and
(6) the location of the research and the person or office to contact for further information.
(7) The advertisement may not contain exculpatory language.

i) Receptionist scripts. The first contact prospective study subject 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 subject and that personal and sensitive information is gathered about the individual will be appropriately handled.

G. 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 how individuals/human research subject are informed of how medical information about them will be used or disclosed and their rights about 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 Regional Hospital 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:

(1) A statement identifying the IRB and Regional Hospital Compliance Officer and the date on which the alteration or waiver of authorization was approved.

(2) A statement that the IRB and Regional Hospital Compliance Officer has determined that the alteration or waiver of authorization, in whole or in part, satisfies the following:

(a) 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.

(b) The research could not practicably be conducted without the waiver or alteration.

(c) 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 Regional Hospital Compliance Officer or privacy board have determined must be used or accessed 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

When PHI is necessary for reviews preparatory to research, the Covered Entity must obtain representations from the researcher that include the following:

a) Use or disclosure is sought solely to review PHI as necessary to prepare a research protocol or for similar purposes preparatory to research.
b) No PHI is to be removed from the Covered Entity by the researcher during the review.
c) The PHI for which use, or access is sought is necessary for research purposes.

6. Research on Deceased Individual's Information

If the research involves a deceased individual's PHI, the Covered Entity must obtain from the researcher the following:

a) Representation that the use or disclosure sought is solely for research on the PHI of the deceased individual.
b) Documentation, at the request of the Covered Entity, of the death of such individual.
c) 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.

H. Requirements for Obtaining a Certificate of Confidentiality

1. Definitions

a) Certificate of Confidentiality (Certificate) protects the privacy of research participants enrolled in biomedical, behavioral, clinical, or other types of health-related research that collect or use identifiable, sensitive information. With limited exceptions, researcher may not disclose names or any information, documents or biospecimens containing identifiable, sensitive information. The Certificate prohibits disclosure in response to legal demands, such as a subpoena.

b) Identifiable, sensitive information: The statute that governs Certificates of Confidentiality broadened the meaning of sensitive, identifiable information and focuses more directly on identifiability. Identifiable, sensitive information is information about an individual, gathered or used during biomedical, behavioral, clinical, or other research, through which the individual is identified, or there is at least a very small risk that some combination of the information, a request for information, and other available data sources could be used to determine the identity of an individual. This includes, but is not limited to name, address, social security, or other identifying number; and fingerprints, voiceprints, photographs genetic information, tissue samples, or data fields, that when used in combination with other information may lead to identification of an individual.

2. **NIH funded research**

NIH funded research is automatically covered by a Certificate of Confidentiality. Examples of research automatically covered by a certificate of confidentiality are:

a) Biomedical, behavioral, clinical, or other research including exempt research, except where the information obtained is recorded in such a manner that human participants cannot be identified or the identity of the human participants cannot be readily ascertained, directly or through identifiers linked to the participants.

b) The collection or use of biospecimens that are identifiable to an individual or for which there is at least a very small risk that some combination of the biospecimen, a request for the biospecimen, and other available data sources could be used to deduce the identity of an individual.

c) The generation of individual level, human genomic data, from biospecimens, or the use of such data, regardless of whether the data is recorded in such a manner that human participants can be identified, or the identity of the human participants can be readily ascertained.

d) Any other research that involves information about an individual for which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

3. Researchers may also apply for a Certificate of Confidentiality for non-federally funded research.

4. When research is covered by a Certificate of Confidentiality, Researchers:

a) May not disclose or provide, in any federal, state, or local civil, criminal, administrative, legislative, or other proceeding, the name of such individual or any such information, document, or biospecimen that contains identifiable, sensitive information about the individual and that was created or complied for purposes of the research, unless such disclosure or use is made with the consent of the individual to whom the information, document, or biospecimen pertains; or,

b) May not disclose or provide to any other person not connected with the research the name of such an individual or any information, document, or biospecimen that contains identifiable, sensitive information about such an individual and that was created or compiled for purposes of the research.

5. When research is covered by a Certificate of Confidentiality, researchers may disclose information only when:

a) Required by federal, state, or local laws (e.g., as required by the Federal

Food, Drug, and Cosmetic Act, or state laws requiring the reporting of communicable diseases to state and local health departments), excluding instances of disclosure in any federal, state, or local civil, criminal, administrative, legislative, or other proceeding; or,

b) Necessary for the medical treatment of the individual to whom the information, document, or biospecimen pertains and made with the consent of such individual; or,

c) Made with the consent of the individual to whom the information, document, or biospecimen pertains; or,

d) Made for the purposes of other scientific research that follows applicable federal regulations governing the protection of the human participants in research.

6. When research is covered by a Certificate of Confidentiality, researchers must inform participants (for example, in the consent document) of the protections and limitations of the Certificate of Confidentiality:

   a) For studies that were previously issued a Certificate of Confidentiality, and participants were notified of the protections provided by that Certificate, NIH does not expect participants to be notified that the protections afforded by the Certificate have changed, although the UPHDM IRB may determine that it is appropriate to notify participants.

   b) If part of the study cohort was recruited prior to issuance of the Certificate, but are no longer actively participating int eh study, NIH does not expect participants consented prior to the change in authority, or prior to the issuance of the Certificate, to be notified that the protections afforded by the Certificate have changed, or that participants who were previously consented to be re-contacted to be informed of the Certificate, although the UPHDM IRB may determine that is is appropriate to inform participants.

7. Researchers conduction research covered by a Certificate of Confidentiality, whether funded by NIH or not federally funded, must ensure that if identifiable, sensitive information is provided to other researchers or organizations, the other researchers or organization must comply with applicable requirements when research is covered by a certificate of confidentiality.

IX. Vulnerable Populations

[45CFR46: Subparts B, C, D]

A. Subpart B: Protections for Pregnant Women, Human Fetuses, & Neonates

1. Applicability [45CFR46.201]

Except as provided in paragraph (b) 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.

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

b) 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.

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

2. Definitions [45CFR46.202]

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

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

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

d) Neonate means a newborn.

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

f) 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.

g) 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.

h) 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.

3. 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)

a) Research Involving Pregnant Women or Fetuses [45CFR46.204]
Pregnant women or fetuses may be involved in research if all the following conditions are met:

(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.

4. Research Involving Neonates [45CFR46.205]

a) Neonates of uncertain viability and nonviable neonates

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

(1) Where scientifically appropriate, preclinical, and clinical studies have been conducted and provide data for assessing potential risks to neonates.

(2) Each individual providing consent under paragraph (2)(b) or (3)(e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

(3) Individuals engaged in the research will have no part in determining the viability of a neonate.

(4) The requirements of paragraph (2) or (3) of this section have been met as applicable.

b) Neonates of uncertain viability

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

(1) The IRB determines that:

(a) (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

(b) (ii) The purpose of the research is the development of important

biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and

(2) The legally effective informed consent of either parent of the neonate or, if neither parent can 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.

c) Nonviable neonates

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

(1) Vital functions of the neonate will not be artificially maintained;

(2) The research will not terminate the heartbeat or respiration of the neonate;

(3) There will be no added risk to the neonate resulting from the research;

(4) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and

(5) The legally effective informed consent of both parents of the neonate is obtained 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 parents of a nonviable neonate will not suffice *to meet the requirements of this paragraph.*

d) 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 V and IX.C.

5. Research Involving, after Delivery, the Placenta, the Dead Fetus or Fetal Material [45CFR46.206]

a) 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.

b) 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 subject, and all pertinent subparts of this part are applicable.

6. 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.

B. Subpart C: Protections involving Prisoners as Subjects

1. 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.

2. Research prospectively involving prisoners is not allowed

Research involving prisoners will not be allowed at this institution.

3. When a research subject becomes a prisoner

If 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. Any data pertaining to this study subject's participation should be eliminated from the study database starting on the date of incarceration and thereafter.

C. Subpart D: Protections for Children Participating in Research

1. Applicability [45CFR46.401]

a) This policy applies to all research involving children as subject, conducted, or

supported by UPHDM.

b) Exemptions at 45CFR46.101(b)(1) and (b)(3) through (b)(6) are not generally applicable to this subpart. [See Section V.A.]

c) 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.

2. Definitions [45CFR46.402]

The definitions in Section IV [§45CFR46.102] shall be applicable to this subpart as well. In addition, as used in this subpart:

a) 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).

b) Assent means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

c) Permission means the agreement of parent(s) or guardian to the participation of their child or ward in research.

d) Parent means a child's biological or adoptive parent.

e) Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

f) 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].

3. 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.

4. 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.

5. 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:

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

6. 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:

a) the risk represents a minor increase over minimal risk;
b) the intervention or procedure presents experiences to subject that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
c) the intervention or procedure is likely to yield generalizable knowledge about the subject' disorder or condition which is of vital importance for the understanding or amelioration of the subject' disorder or condition; and
d) adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth in 45CFR46.408.

7. 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.

8. Requirements for Assent by Children and Permission by Parents[45CFR46.408]

a) 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 can provide assent. In determining whether children are capable of assenting, the IRB shall consider 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 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 when consent may be waived in accord with 45CFR46.116.

b) 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.

c) 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 subject (for example, neglected or abused children), it may waive the consent requirements provided an appropriate mechanism for protecting the children who will participate as subject 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 subject, and their age, maturity, status, and condition.

(1) Permission by parents or guardians shall be documented in accordance with and to the extent required by 45CFR46.117.

(2) When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

d) Implementation & Waiver of Assent. 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. A template of the Child's Assent can be found on the IRB website. 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.

e) The guiding principle behind this process is respect for the developing decision-making capacity of children 12-17 years of age. 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.

9. Wards [45CFR46.409]

a) 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:

(1) related to their status as wards; or

(2) conducted in schools, camps, hospitals, institutions, or similar settings in which most children involved as subject are not wards.

b) 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.

10. Adopted Children Enrolled in a Research Study (UPHDM Legal Counsel)

If a child is enrolled in a research study, then later adopted, the adoptive parent(s) have full responsibility for decision making for the child. Therefore, if the adoptive parent(s) want to continue the trial, the informed consent form would need to be completed by the new adoptive parent who is the decision maker.

X. IRB Procedure 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
	Revised Section VIII.B Continuous Quality Improvement
June 2004	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

	New Section IV.T (3) Payments to research subject
September 2004	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 subject being seen at local clinic for

	study visits, tests, labs; language added relating to study subject 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 subject 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 subject that occur within a study.
January 2019	Revisions to multiple areas of procedure document to reflect changes to Common Rule, in effect 1/21/19. Reformatted all procedures for online document. The IRB reversed its decision regarding reporting of study subject deaths. Only deaths of local subject that occur within a study need to be reported to the IRB.
September 2020	Minor revisions to multiple sections of procedure in preparation for AAHRPP Step 1 submission. Revisions made to accurately reflect current procedural practice.
January 2021	Several revisions through AAHRPP Step 1 review.
May 2022	Revisions to External IRB procedures to align with current practice.
August 2023	Revisions to multiple areas of procedure document to reflect submission changes to new software platform, IRBManager. Added sections V.F & VIII.C, updated definitions to match new sections. Reorganized and reformatted all procedures for consistency and efficiency.
February 2025	Updates to change Institutional or Signatory Official from VPMA to Medical Director, Medical Staff Office
September 2025	Several revisions through AAHRPP Step 1 review.