UnityPoint Health
Des Moines

Human Research Protection Program Procedures

Version: February 2025

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.

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.

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).

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.

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.

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).

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.

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.

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) [Reserved]

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 can 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 the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects.

(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 and … the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects.

(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 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.

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, or the reasons for denying exempt status. 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 <u>are reports of research</u> 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

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

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.