

HUMAN SUBJECTS RESEARCH INVESTIGATOR GUIDE

for the protection of human subjects in research

This guide assists Montana State University Billings investigators who may be uncertain if their research involves human subjects. Human subjects research and Institutional Review Board regulations are federally governed by the Health and Human Services Code of Federal Regulations Title 45: Public Welfare Part 46-Protection of Human Subjects (45 CFR 46)¹ and the Food and Drug Administration Code of Federal Regulations Title 21: Food and Drugs Part 56-Institutional Review Boards (21 CFR 56)².

HUMAN SUBJECTS RESEARCH

Research projects involving human subjects require review and approval by the MSU Billings Institutional Review Board (IRB) prior to subject recruitment and data collection.

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

Human Subjects are living individuals about whom an investigator conducting research obtains:

1. Data through intervention or interaction with the individual:
 - a. Intervention includes both physical procedures and manipulations of the subject or the subject's environment that are performed for research purposes.
 - b. Interaction includes communication or interpersonal contact between investigator and subject.
2. Identifiable private information:
 - a. 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. 45 CFR 46.102(f)

The IRB is charged with the responsibility of overseeing all human subjects research that is:

- Sponsored by MSUB
- Conducted by or under the direction of any employee, faculty, staff, or student of MSUB in connection with their institutional responsibilities
- Conducted by or under the direction of any employee, faculty, staff, or student of MSUB using any property or facility of the institution
- Involves the use of MSUB's non-public information to identify or contact human research subjects or prospective subjects

Applications are submitted to the Office of Research Compliance for processing and are transmitted to the IRB Chair, who determines whether the study requires exempt, expedited, or full board review.

Exempt - low-risk human subjects research. In order to qualify for exemption, a research study must fall entirely within one or more of the following six categories; it cannot place subjects at greater than minimal risk and cannot use high risk subjects.

Exemption status does not excuse the researcher from meeting the ethical intent of the Belmont Report³ and Common Rule⁴ or from obtaining informed consent for research participation.

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices.
2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, unless:

- a. Information obtained is recorded in such a manner that human participants can be identified, directly or through identifiers linked to them;
 - b. Any disclosure of the human participant's responses outside the research could reasonably place the participant at risk of criminal or civil liability or be damaging to the participant's financial standing, employability, or reputation.
3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (2) of this section, if:
 - a. The participants are elected or appointed public officials or candidates for public office;
 - b. Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information be maintained throughout the research and thereafter.
4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the researcher in such a manner that participants cannot be identified, directly or through identifiers linked to them.
5. Research and demonstration projects conducted by or subject to the approval of Federal department or agency heads and designed to study, evaluate, or otherwise examine public health benefit or service programs (only available to the Federal government).
6. Taste and food-quality evaluation and consumer acceptance studies. 45 CFR 46.101(b)

These exemptions do not apply to research involving prisoners, fetuses, pregnant women, or newborns. Further, the exemption in item 2 above does not apply to children, except in research involving educational tests or observation of public behavior where the investigators do not participate in the activity being observed

Examples of exempt projects include:

- Data collection for internal departmental, school, or other University administrative purposes; e.g., teaching evaluations, customer service surveys
- Service surveys issued or completed by University personnel for the intent and purposes of improving services and programs of the University or for developing new services or programs for students, employees, or alumni, as long as the privacy of the subjects is protected and the confidentiality of individual responses are maintained
- Information-gathering interviews where questions focus on things, products, or policies rather than people or their thoughts regarding themselves
- Course-related activities designed specifically for educational or teaching purposes, where data is collected from and about human subjects as part of a class exercise or assignment, but are not intended for use outside of the classroom
- Biography or oral history research involving a living individual that is not generalizable beyond that individual
- Quality improvement projects are generally not considered research unless there is a clear intent to contribute to generalizable knowledge and use the data derived from the project to improve or alter the quality of care or the efficiency of an institutional practice
- Case histories which are published and/or presented at national or regional meetings are not considered research if the case is limited to a description of the clinical features and/or outcome of a single patient and do not contribute to generalizable knowledge
- Publicly available data, e.g., census data, labor statistics
- Coded private information that was not collected for the currently proposed projects as long as the investigator cannot link the coded data/specimens back to individual subjects

Expedited - human subjects research involving no more than minimal risk, and for minor changes or amendments to approved research; the IRB Chair reviews the proposed research rather than the entire IRB. It cannot be assumed that research poses minimal risk because it involves only interview or survey data collection. Sensitive questions may lead to distress that exposes participants to greater than minimal risk. Loss of confidentiality can cause harm to participants, their relatives, and others.

Applicability

- A. Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may qualify for an 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.
- B. The categories in this list apply regardless of the age of subjects, except as noted.
- C. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
- D. The expedited review procedure may not be used for classified research involving human subjects.
- E. IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review.
- F. Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

Categories

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
 - a. Research on drugs for which an investigational new drug application (21 CFR 312)⁵ is not required.
 - b. Research on medical devices for which (i) an investigational device exemption application (21 CFR 812)⁶ is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
 - a. From healthy, nonpregnant adults who weigh at least 110 pounds; 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
 - b. From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected; 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.
3. Prospective collection of biological specimens for research purposes by noninvasive means.
4. Collection of data through noninvasive procedures 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.)
5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

6. Collection of data from voice, video, digital, or image recordings made for research purposes.
7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.
8. Continuing review of research previously approved by the IRB as follows:
 - a. Where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
 - b. Where no subjects have been enrolled and no additional risks have been identified; or
 - c. Where the remaining research activities are limited to data analysis.
9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

For more examples see <http://www.hhs.gov/ohrp/policy/expressed98.html>.

Full Board - human subjects research deemed to involve more than minimal risk or for which a wider range of expertise is required for review. In addition, full board review is required for all research activities involving vulnerable subject populations including, but not limited to, pregnant women and fetuses, children (except for normal educational practice in school settings), international research, prisoners and cognitively impaired/psychiatric patients.

The research proposal is presented and discussed at a meeting at which a quorum of IRB members is present. For the research to be approved, it must receive the approval of a majority of those voting members present.

Non-Human Subjects Research - projects not defined as human subjects research and do not require IRB approval. Projects that are not defined as human subjects research, market research for the purpose of refining or improving the quality of a service and oral history where the story teller is aware that the story is being recorded for publication are examples research that does not fit the definition of human subjects research.

Any investigator unsure of whether their project constitutes human subjects research should contact the Office of Research Compliance at 406-657-2364 irb@msubillings.edu.

INVESTIGATOR RESPONSIBILITIES

Investigators have certain responsibilities regarding the ethical treatment of human subjects including:

- Obtaining IRB approval before beginning a human subjects research study
- Providing the IRB with sufficient information and related materials about the research
- Following institutional policies and procedures for IRB review
- Obtaining and maintaining the informed consent of subjects (or subjects' legally authorized representative) prior to participation in the research
- Providing a copy of the informed consent document to each research subject (or subject's legally authorized representative)
- Obtaining prior approval from the IRB to modify previously approved protocols
- Ensuring that requests for continuing review and approval are submitted to the IRB

- In certain circumstances, investigators are also responsible for meeting the following additional regulatory requirements:
 - providing to the IRB prompt reports of any unanticipated problems involving risks to subjects or others
 - providing to the IRB prompt reports of serious or continuing noncompliance with the regulations, requirements, or determinations of the IRB
 - keeping certain records as required by the HHS regulations for at least three years after completion of the study

INSTITUTIONAL REVIEW BOARD (IRB)

IRBs must consist of at least five members of varying backgrounds to promote complete and adequate review of research activities. MSUB's Board consists of:

- One faculty member of the College of Liberal Arts and Social Sciences
- One faculty member of the College of Health Professions and Science
- One faculty member of the College of Education
- One faculty member of the College of Business
- One faculty member of City College
- One member whose primary concerns are in scientific areas
- One member whose primary concerns are in nonscientific areas
- One member who is not otherwise affiliated with the institution and is not part of the immediate family of a person who is affiliated with the institution

Please consult the ORC website for current board members and to view the IRB bylaws <http://www.msubillings.edu/orc/board.htm>.

OFFICE OF RESEARCH COMPLIANCE (ORC)

The ORC provides administrative assistance to the IRB and maintains copies of all applications and documentation, which includes the protocol, consent forms, modifications, adverse event or unexpected problem reports, status forms, approvals, protocol violation or exception reports, and any written communication regarding the protocol.

REVIEW PROCESS

1. Investigators submit a completed Human Subjects Research application, <http://www.msubillings.edu/orc/application.htm> to the Office of Research Compliance
 - a. Applications must be submitted through DocuSign using the IRB cover page.
 - b. Investigators are encouraged to reach out to irb@msubillings.edu for guidance if they are having difficulties with DocuSign.
2. ORC circulates the application to the IRB Chair
3. Review of the application may take up to 10 working days
4. The IRB Chair notifies the ORC of its decision, who then notifies the investigator in writing of the status of the proposal
5. When approved, a project may begin immediately
6. If the IRB decides to disapprove 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/correct in person or in writing.

Approved protocols are valid for one (1) year from the date of the approval. Amendments or modifications of a protocol require additional IRB review and approval. PIs may apply for renewal prior to the expiration date of the approved protocol; however, if the approval expires, data collection must cease immediately and PIs must submit a new application. The IRB has the authority to approve, require modifications, or disapprove all research activities.

FOR INSTRUCTORS

This checklist is intended to assist MSUB Instructors in assessing whether classroom research projects may be excluded from review and approval by the MSUB Institutional Review Board (IRB). **All items below must be satisfied for classroom projects to proceed outside of IRB review.**

- The research project is to be performed by students enrolled in an undergraduate or graduate course at MSUB as a requirement for completion of the course.
- The overriding and primary purpose of the project is as a learning experience in the methods and procedures of research.
- The instructor is fully aware of all aspects of the research project and will take responsibility for overseeing the project and assuring that ethical principles are adhered to in the conduct of the activities.
- The project involves minimal risk to subjects; i.e., the risk of harm is not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
- The project does not involve sensitive topics or confidential information that could place a participant at risk if disclosed; e.g., sexual health, abuse, and illegal behavior.
- The project does not involve persons from vulnerable populations as participants; e.g., pregnant women, children, and prisoners.
- The project involves the voluntary participation of individuals without any coercion or pressure being placed upon them.

FAQs, 45 CFR 46:

Q1: Who are “investigators”?

A: An “investigator” is any individual who is involved in conducting human subjects research studies. Such involvement would include:

- obtaining information about living individuals by intervening or interacting with them for research purposes;
- obtaining identifiable private information about living individuals for research purposes;
- obtaining the voluntary informed consent of individuals to be subjects in research; and
- studying, interpreting, or analyzing identifiable private information or data for research purposes.

Some research studies are conducted by more than one investigator, and usually one investigator is designated the “principal investigator” with overall responsibilities for the study.

Q2: Must investigators obtain IRB approval before involving human subjects in nonexempt research?

A: Yes, investigators are responsible for obtaining IRB approval before beginning any nonexempt human subjects research. Investigators are responsible for providing the IRB with sufficient information and related materials about the research (e.g., grant applications, research protocols, sample consent documents) so that the IRB can fulfill its regulatory obligations. Investigators should follow institutional policies and procedures for IRB review that are required by HHS regulations.

Q3: Are investigators responsible for obtaining and documenting informed consent?

A: Yes, investigators are responsible for obtaining and documenting the informed consent of research subjects or their legally authorized representatives. Investigators must give a copy of the informed consent document to each research subject (or the subject’s legally authorized representative), and keep the signed original or a copy of it for their records. For information about parental permission and assent see, 45 CFR 46(d).

Q4: What should investigators do if they want to revise an IRB-approved research study?

A: If investigators wish to modify an ongoing IRB-approved research study, they must submit a request to the IRB and receive IRB approval before implementing the proposed modification, unless the change is designed to eliminate an apparent immediate hazard to subjects. If the investigators change the research in order to eliminate apparent immediate hazards to subjects without prior IRB approval, they should report those changes promptly to the IRB. The HHS protection of human subjects regulations allow for expedited review and approval of requests for minor changes in previously approved studies.

Q5: Are investigators responsible for obtaining continuing review of research?

A: Yes, investigators are responsible for fulfilling requirements associated with continuing review in time for the IRB to carry out review prior to the expiration date of the current IRB approval. Continuing review of research and approval of research studies is required so long as the research study is ongoing, that is, until research-related interactions and interventions with human subjects or the obtaining and analysis of identifiable private information described in the IRB-approved research plan have been completed. Investigators are responsible for submitting sufficient materials and information for the IRB to meet its regulatory obligations, and should follow the institutional policies and procedures for continuing IRB review of research that are required by HHS regulations and referenced in the institution's OHRP- approved Federalwide assurance.

Q6: What should investigators do if IRB approval expires?

A: If IRB approval of a specific study expires before continuing review and approval occur, investigators must stop all research activities involving human subjects related to that study. Investigators may resume the human subjects research activity once continuing review and approval by the IRB has occurred.

Q7: What are investigators' responsibilities once a study is completed?

A: If all research-related interventions or interactions with human subjects have been completed, and all data collection and analysis of identifiable private information described in the IRB- approved research plan have been finished, then the human subjects research study has been completed. Once a study has been completed, investigators may keep the data they collected if consistent with the IRB-approved research plan. Investigators should continue to honor any confidentiality protections of the data and any other commitments that were agreed to as part of the approved research.

Q8: What records should investigators keep, and for how long?

A: The HHS protection of human subjects regulations require institutions to retain records of IRB activities and certain other records frequently held by investigators for at least three years after completion of the research. In addition, other regulations may apply and require retention of these records for a longer period of time. Documentation of the informed consent of the subjects are records related to conducted research that are typically held by investigators and must be retained for at least three years after completion of the research.

Q9: Must investigators obtain training in the protection of human subjects?

A: Regulations for the protection of human subjects do not require investigators to obtain training in the protection of human subjects in research. However, an institution holding an OHRP-approved Federalwide Assurance (FWA) is responsible for ensuring that its investigators conducting HHS-conducted or -supported human subjects research understand and act in accordance with the requirements of the HHS regulations for the protection of human subjects. In some cases, other federal requirements regarding training for investigators must be met, such as the National Institute of Health's (NIH) requirement for the training of key personnel in NIH-sponsored or -conducted human subjects research.

RESOURCES

1. Office for Human Research Protections (OHRP) <http://www.hhs.gov/ohrp/> provides leadership in the protection of the rights, welfare, and wellbeing of subjects involved in research and policies and guidance <http://www.hhs.gov/ohrp/policy/>
Code of Federal Regulations Title 45 Part 46: <http://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&SID=6697a385565f7b4b172c327044972f79&rgn=div5&view=text&node=45:1.0.1.1.25&idno=45>
2. Food & Drug Administration (FDA) <http://www.fda.gov/> regulates clinical investigations of products under its jurisdiction, such as drugs, biological products, and medical devices.
Code of Federal Regulations Title 21 Part 56: <http://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&SID=431d49ba7bc85737ae31c0b4aeb53794&rgn=div5&view=text&node=21:1.0.1.1.22&idno=21>
3. <http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html>
4. <http://www.hhs.gov/ohrp/humansubjects/commonrule/>
5. <http://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&SID=c09ce7128811030e3f73ff0eddc90b40&rgn=div5&view=text&node=21:5.0.1.1.3&idno=21>
6. <http://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&SID=c09ce7128811030e3f73ff0eddc90b40&rgn=div5&view=text&node=21:8.0.1.1.9&idno=21>
7. National Institutes of Health (NIH) <http://www.nih.gov/> provides resources for the protection of human subjects in research <http://grants.nih.gov/grants/policy/hs/index.htm> and tutorials on [Protecting Human Research Participants](#); also available in Spanish.
8. Risks and Wrongs in Social Science Research: An Evaluator's Guide to the IRB, J. Michael Oakes, <http://www.irb.umn.edu/documents/EvaluatorsGuidetoIRB.pdf>