

Part 6 - Roles and Responsibilities of Investigators and Research Staff (July 2009)

Every person involved in human research plays a critical role in protecting the rights and welfare of research participants. This section describes the roles and responsibilities of investigators and research staff engaged in University research.

I. ELIGIBILITY TO PERFORM RESEARCH AT THE UNIVERSITY OF MICHIGAN

A. Who May Apply to Serve as Principal Investigator on IRB Applications

The following individuals are eligible to serve as PI on University research projects and submit applications to University IRBs and other oversight committees:

- Non-temporary members of the University's faculty and staff.
- Trainees, including undergraduates, graduates, medical students, residents/interns, clinical and postdoctoral fellows – but only if an eligible mentor sponsors the application and accepts all of the responsibilities of a PI.
- Other individuals whose applications are sponsored by University faculty or staff members who accept all of the responsibilities of a PI.

Exceptions to these requirements are at the discretion of the Vice President for Research or designee.

B. Other Key Personnel

Key personnel include the principal investigator, co-investigators, and other individuals who contribute to the scientific development or execution of a study in a substantive, measurable way. Typically, these individuals have doctoral or other professional degrees, although individuals at the masters or baccalaureate level are sometimes considered key personnel depending on their involvement in a project. Research fellows, residents, associates and consultants may be key personnel.

Co-Investigators (Co-Is) are a subset of key personnel and have special responsibilities on research projects. While the PI has ultimate responsibility for the conduct of a research project, Co-Is also are obligated to ensure the project is designed and conducted in compliance with applicable laws and regulations and institutional policy governing the conduct of human subjects research. The Co-I must be qualified by training and experience to conduct his or her responsibilities on the research project. Only the following individuals may serve as co-investigators on IRB applications:

- University faculty and staff, including those with temporary UM appointments, such as visiting professors
- Trainees, including undergraduates, graduates, medical students, residents/interns, clinical and postdoctoral fellows
- Individuals who are not UM faculty, trainees or staff, provided they meet the other qualifications defined above

Exceptions to these requirements are at the discretion of the Vice President for Research or designee.

All Co-Is must be listed in IRB applications. Each must explicitly acknowledge to the IRB their participation as a Co-I on the study and will be asked to acknowledge their addition to or deletion from any existing IRB-approved study. Co-Is will be notified of, but will not be required to acknowledge, communications from the PI to the IRB such as amendments, adverse event reports, scheduled continuation reviews, and terminations.

II. ROLES AND RESPONSIBILITIES OF INVESTIGATORS AND RESEARCH STAFF

A. Generally

The Principal Investigator (PI) has primary responsibility for protecting the rights and welfare of human research subjects. The safeguarding of human subjects must at all times take precedence over the goals and requirements of any research endeavor. Detailed discussion on HRPP requirements for research participant protection is provided in [Part 7](#) of this Operations Manual.

The PI and any co-investigators, key personnel and other research staff (together referred to as “researchers” or the “research team”) are expected to be knowledgeable about and comply with the requirements of the [Common Rule](#) and other federal research laws and regulations, applicable state law, the University’s [federalwide assurance](#), [institutional policies and procedures](#) for the protection of human subjects and reporting and managing conflicts of interest, the terms and conditions of any research agreements (with government or private sponsors) and the basic [ethical principles](#) that guide human subjects research. Researchers must complete any educational training required by the University, the relevant IRB, and other review units prior to initiating research. Researchers should not undertake responsibility for human subjects studies unless they understand these requirements and are willing to be held accountable for complying with the relevant standards and protecting the rights and welfare of research participants; nor until they can assure adequate resources (e.g., through internal or external funding) to fulfill these commitments.

Following are descriptions of some of a researcher’s central obligations when conducting studies involving human subjects. They are intended only as a general guide and do not contain a comprehensive description of all of a researcher’s responsibilities. Some of the laws and regulations that most directly and routinely impact the conduct of human subjects research studies are described in [Part 11](#) of this Operations Manual. Institutional policies and procedures include this Operations Manual as well as policies and procedures maintained by the academic units to which researchers and research staff are appointed, IRB policies and procedures, and the policies and procedures of other research review units with relevant oversight responsibilities, such as the Investigational Drug Service or the Radiation Safety Committee.

1. *Minimizing Risks to Subjects and Protecting Subject Rights and Welfare*

Federal regulations, institutional policy and guiding ethical standards all require that human subjects research be designed to minimize risks to participants. This is accomplished in a number of ways. For example, researchers are expected to design and implement protocols that comply, at a minimum, with applicable regulatory and institutional policy requirements, as well as the principles of the Belmont Report (i.e., respect for persons, beneficence, justice). All research must use procedures that are consistent with sound research design. In other words, the research must be reasonably expected to answer its proposed question and the knowledge reasonably expected to result from the research must be sufficiently important to justify the undertaking. Thus, for example, a quantitative research study proposal submitted to an IRB generally must include a plan to recruit sufficient numbers of subjects to result in a statistically valid sample; if inadequate subjects will be recruited, the research likely cannot answer its proposed question. This rule would not apply to feasibility studies, pilot projects and the like, where the activity is intended to help frame future study, rather than to answer an ultimate research question. A descriptive, qualitative study or a pilot study need not achieve statistical validity (and, therefore, may not require a specific number of subjects) but still must be designed to achieve its stated scientific objective. No project should be pursued if the research question already has been fully answered by others. In that case, any risks to subjects cannot be justified by the knowledge to be gained by the study.

In addition to properly designing studies, researchers must take other steps to minimize risk and protect subject rights and welfare. For example:

- Recruitment and enrollment plans should promote equitable subject selection (*i.e.*, subjects should equitably bear the burdens and enjoy the benefits of participation in research),
- Whenever appropriate, researchers should use procedures already being performed on subjects for diagnostic and treatment purposes,
- Researchers responsible for multi-site research should evaluate the resources (facilities, equipment, supplies, personnel) available at each site where the research will be conducted,
- When appropriate, research plans should make adequate provision for monitoring subjects to promptly detect any adverse events and for reviewing data collected to ensure subject safety, for example through weekly PI-led team meetings, independent monitors, or external data safety monitoring boards,
- Research plans must contain adequate provisions to protect the privacy of subjects and confidentiality of data collected,
- If some or all of the participants in a study are likely to be vulnerable to coercion or undue influence (*e.g.*, children, prisoners, pregnant women, mentally disabled individuals, or economically or educationally disadvantaged people), the research plan should provide for additional safeguards, as appropriate, to protect their rights and welfare.

2. Compliance With IRB and Other Review Unit Requirements

Investigators are encouraged to consult with the appropriate UM IRB or Institutional Official or designee to ensure that activities that meet the definition of human subjects research (including pre-research activities such as access to databases containing private information and screening data for possible recruitment and enrollment) undergo IRB review and approval before they are initiated, or are certified to be exempt from IRB oversight (see [Part 4](#) of this Operations Manual for additional details).

Researchers must at all times cooperate with the IRB in fulfilling its responsibility for initial and continuing review, monitoring, record keeping, and reporting. To this end, they must provide all information requested by the IRB in a timely fashion. Investigators and research teams must conduct their research as specified in their IRB-approved protocols and must comply with all IRB determinations, including directives to terminate participation in designated research activities. Any proposed changes in the research, no matter how minor, must be approved *in advance* by the IRB unless necessary to eliminate apparent immediate hazards to subjects. Similar requirements apply for other review units (such as the General Clinical Research Center and the Conflict of Interest Review Committees) responsible for monitoring the research activities.

Note: A physician may provide emergency medical care to a patient without prior IRB review and approval, as permitted by applicable laws and regulations. For example, if the eligibility criteria for a study of an experimental surgical procedure for critical care patients limit enrollment to those age 18-50, and a 52-year-old who might benefit from the procedure and has no other options presents to the researchers for clinical treatment, the researchers may provide the experimental treatment off-study. However, they may be required to report the off-study treatment to the IRB. In addition, emergency care may not be considered research nor may the data obtained be used in support of research, except to the extent required under FDA regulations. When emergency care involves use of investigational drugs, biologics or devices, special FDA requirements must be satisfied. These are discussed in [Part 8](#) of this Operations Manual.

Investigators are responsible for the content of all submissions (e.g., initial review, continuing review, adverse events, progress reports) to the IRB and other review units and for ensuring that those documents are submitted in a timely manner, as required by the IRB or other review unit. For example, investigators must promptly report to the IRB any unanticipated problems involving risks to subjects or others. An unanticipated problem involving risks to subjects or others may be an adverse event or some other problem such as exposure of a member of the research team to a harmful substance.

Investigators also must report any potentially serious or continuing noncompliance with applicable laws or regulations or IRB requirements, whether by investigators, research staff, or others. This requirement applies even if the potentially serious or continuing noncompliance was unintentional or was discovered in the course of quality assurance or quality improvement activities.

3. *Obtaining and Documenting Informed Consent*

Informed consent refers to the voluntary choice of an individual to participate in research based on a complete and accurate understanding of the study including its purposes, procedures, risks, potential benefits, alternatives, and other factors that may affect the person's decision to participate. Informed consent is not a single event or document, but an ongoing process that takes place between the investigator (or other key personnel, as appropriate) and the research subject. At its core, the process of informed consent requires full disclosure of the nature of the research and the subject's participation, adequate understanding on the part of the subject (or subject's legally authorized representative), and the subject's voluntary choice to participate.

Investigators are responsible for obtaining and documenting the informed consent of each prospective research subject (or the subject's legally authorized representative) before the research begins (including any related eligibility testing not conducted solely for clinical purposes), unless the appropriate IRB has waived this requirement. The principal investigator is responsible for ensuring that each potential subject understands the nature of the research and participation in the project (even if the PI has delegated responsibility for part or all of the consent process to co-investigators or research staff). For example, verbal and written information must be conveyed in language that is understandable to the subject or the subject's legally authorized representative.

Investigators must ensure that consent is sought only under circumstances that minimize the possibility of coercion or undue influence. For example, subjects must be given a sufficient opportunity to determine whether or not to participate in the study. It is therefore desirable to allow some time between initial discussion of the opportunity to participate in the research and the final decision, as recorded in the consent document. Moreover, subjects must be specifically informed that participation in a project is on a voluntary basis; that they may discontinue participation at any time; and that no penalty will be imposed and no rights to which they would otherwise be entitled will be waived as a result of refusal to participate or later withdrawal.

Informed consent must be documented on a form approved in advance by the IRB, unless the IRB approves a waiver or alteration of consent, or waiver of documentation, as described in [Part 3](#) of this Operations Manual. Some IRBs require their own templates to be used and may or may not permit departures from those templates in special cases. The form must contain at least the information specified in a "[checklist](#)" published by the Office for Human Research Protections (OHRP). The information provided during conversations and in the informed consent document must make clear that the activity involves research. It must explain any procedures the subject will undergo, specifying which are experimental (e.g., a new drug, extra tests, non-standard methods of management such as randomizing the subject to a treatment or placebo arm). It must describe how much time the subject can

expect to devote to the study (e.g., how long will study visits or research-related procedures take, what is the total expected length of participation after enrollment).

Note: A “short form” stating that the elements of informed consent normally required have been presented orally to the subject or subject’s legally authorized representative may be used in limited circumstances e.g., for illiterate subjects. When this method is used, a witness must be present at the oral presentation. The IRB must approve a written summary of what is to be said to the subject or representative. The witness must sign both the short form and a copy of the summary. The person obtaining consent must sign a copy of the summary. Copies of both the short form and the summary must be provided to the subject or representative. A short form is intended to be used infrequently and requires more work on the part of the research team than does a standard consent.

The consent process and form also must describe any reasonably foreseeable risks, discomforts, inconveniences, and harms associated with the research activities. These risks should not be understated nor glossed over. If additional risks are identified during the course of the research project, the IRB must be informed. The IRB may require consent process and documentation revisions, and may require subjects previously consented to be re-contacted and informed about the new risks. (The IRB must approve any protocol or consent revisions and any proposed communication to subjects.) Subjects also must be provided with information about any benefits that may reasonably be expected from the research, either to them individually or to society at large. If there is no reasonable expectation of direct benefit, the subject must be informed. Payments for participation may never be listed as benefits of the research.

To ensure subjects can make an informed choice about participation in the research, appropriate alternatives to participation that might be advantageous to subjects must be described, where applicable. For example, in a drug study, the medications being studied may be available outside the research study from a physician without the need to participate in the research. Investigators should be reasonably specific about describing the nature and type of available alternatives. It generally is not sufficient simply to state that “the researcher will discuss alternative treatments” with the subject.

Subjects must be told the extent, if any, to which confidentiality of research records that may identify them will be maintained, and who has access to those records. For example, sponsors, funding agencies, regulatory agencies and IRBs and other institutional officials may review research records. If a study involves the collection, use or disclosure of protected health information, it will be regulated not only by the Common Rule but also by privacy regulations promulgated under the [Health Insurance Portability and Accountability Act of 1996 \(HIPAA\)](#) as well as special policies and standards required by the covered entity (e.g., health care provider, health plan, or clearinghouse) where the information originated.

For research involving more than minimal risk, the consent process must provide an explanation as to whether any compensation or treatment will be provided to an injured subject (injury in this context refers both to physical injuries and to less tangible injuries, such as injury to reputation or legal rights). If so, the compensation and treatment should be described, or the subject should be told where to find additional information. In no event may the consent process or the documentation of consent include exculpatory language (e.g., requiring subjects to give up legal rights to which they otherwise would be entitled, such as the right to sue in case of an adverse response to a study intervention).

Subjects must be informed about whom to contact for answers to pertinent questions or concerns about the research or their rights as research subjects, as well as whom to contact in the event of a research-related injury, if injuries are foreseeable. Specifically, they should be told how to contact the researchers and whom they can contact if they cannot reach or do

not want to speak with the researchers. They also should be told how to lodge a complaint (e.g., by contacting the IRB office or the Vice President for Research or, in the case of a privacy concern, the Privacy Official).

Each subject (or a subject's legally authorized representative) must be provided with a copy of the consent document at the time of consent, unless the IRB specifically has waived this requirement. Investigators are responsible to ensure that original signed consents are retained for at least three (3) years after completion of the research (six years if protected health information will be used or disclosed in connection with the study in accordance with HIPAA requirements), or longer as required by institutional policy or applicable sponsor agreements or regulations. Investigators conducting research in health care settings are encouraged to retain original duplicates of informed consent documents in both the research record and the regular medical record to ensure compliance with the health care organization's and research documentation requirements. Depending on the circumstances of the study, they may also be required to maintain documentation of HIPAA-compliant authorization.

Summaries of informed consent requirements and drafting aids are available on the [HRPP portal](#).

4. *Conflict of Interest Disclosures*

A conflict of interest may take many forms, but arises when a faculty or staff member, in relationship to an outside organization, is in a position to influence the university's business, research, or other decisions in ways that could lead directly or indirectly to financial gain for the faculty or staff member or his or her family, or give improper advantage to others to the detriment of the University. Detailed information about University policy on conflicts of interest and conflicts of commitment is available at http://www.drda.umich.edu/policies/um/conflict_of_interest.html; see also <http://www.med.umich.edu/medschool/orgs/ResearchPolicies/ConflictofInterest.html> (Medical School faculty) and http://www.drda.umich.edu/policies/um/conflict_procedures.html - procedures (general procedures).

Financial conflicts of interest are not inherently wrong and should always be disclosed in the research context. For example, scholars may benefit financially from scholarly publications and are presumably motivated in part by those financial benefits. The 1980 Bayh-Dole act strongly encouraged researchers to seek ways to put their ideas to use for the benefit of the public and allowed them and their institutions to profit from what is commonly called technology transfer. As long as conflicts are openly reported and appropriately managed or resolved, they do not distort and can benefit the research process. It is therefore in a researcher's best interest to follow one simple rule: *when in doubt, disclose*.

The University and individual academic units have established mechanisms to identify and manage potential conflicts, including annual disclosure requirements, research and sponsored project application questions, and informal communications. An investigator who believes he or she – or other members of the research team – may have a conflict that has not otherwise been disclosed should consult with the appropriate conflict of interest committee for guidance to determine whether the conflict is reportable and, if so, how it might be managed (see Part 9 of this Operations Manual for additional information).

5. *Accountability and Additional Administrative Requirements*

To fulfill their obligations with respect to the conduct of human subjects research, investigators must personally perform or delegate to qualified co-investigators or research staff all of the necessary tasks to carry out their studies. These include securing any necessary departmental, institutional, and regulatory approvals in advance of the research, obtaining informed consent prior to enrollment of subjects into studies, ensuring continuing

review at least annually or more frequently as required by the IRB, informing the IRB of any disapprovals, suspensions, or terminations of the project by any University or non-University review units or agencies (e.g., the IDS or IBC, or the IRB at another performance site, or a regulatory agency such as the National Institutes of Health, Food and Drug Administration, or National Science Foundation), completion of required paperwork, and creation and secure maintenance of accurate records. Even when specific tasks are delegated, the principal investigator remains ultimately responsible for proper conduct of the study and fulfillment of all associated obligations. To fulfill his or her oversight and accountability responsibilities, the PI must provide members of the research team with sufficient information and training to facilitate appropriate safety procedures and protocol adherence.

Note: If IRB approval for a study lapses for any reason, even if the investigator submitted an application for review in a timely manner and promptly responded to any requests for clarifications or changes, the research must stop (and applicable charges against many grants, including all government-funded grants, must be suspended) until the IRB issues its formal approval or determines that it is in the best interest of individual subjects to continue participating in the research interventions or interactions.

Investigators and research staff must inform subjects participating in their studies how to contact the research team with requests for information or complaints related to the studies. Typically this is accomplished through informed consent documents. Complaints should be professionally and appropriately handled.

Investigators and research staff are expected to cooperate with evaluations, inspections, and audits performed by authorized internal oversight authorities, including the [IRBs](#), the [Office for Human Research Compliance Review](#), and the [Office of University Audits](#). Cooperation is also expected for external reviews (e.g., by industry sponsors or government agencies such as the FDA or NIH Office of Research Integrity). Any external investigation, inspection or other external review and its outcome must be reported to the IRB responsible for the research in question. Researchers should consult with their administrators, CACR, the IRBs, as appropriate, OVPR, and/or the Office of the Vice President and General Counsel for assistance and representation.

Investigators and research staff may contact the institutional Official, the Deputy Institutional Official or General Counsel to obtain answer to questions, express concerns or conveys suggestions regarding the human research protection program.

B. Studies Regulated By the Food and Drug Administration

[Part 8](#) of this Operations Manual describes in detail the circumstances under which human subjects research studies become subject to [FDA regulations](#). In conducting research involving FDA-regulated products, researchers must comply with all applicable FDA regulations and fulfill all investigator responsibilities (or all sponsor-investigator responsibilities, as applicable). These include, at a minimum:

1. *Investigator Responsibilities*

An investigator must personally conduct or supervise the study as specified in the signed investigator statement, the investigational plan, any applicable sponsor agreement, and the IRB-approved protocol. Before initiating a study, the investigator must read and understand the information in the investigator's brochure or similar documentation, including the risks and potential benefits of the investigational drug or device.

The investigator must ensure that a University IRB will be responsible for the initial and continuing review of the study. Changes may be made to a protocol only after notifying the sponsor and receiving approval from the IRB, except when necessary to eliminate apparent

immediate hazards to subjects. Informed consent must be obtained from all prospective subjects prior to enrollment in the study, as further described in Section II (A) above.

During the study, the principal investigator is responsible for all aspects of protocol implementation. These include:

- Proper receipt, storage, use and disposal of the investigational drug or device. The principal investigator is asked through eResearch for his or her plans to assure that test articles are used only in approved protocols and under the direction of approved investigators. Deviations from these plans are permitted only in emergency circumstances, consistent with FDA requirements and University policies on emergency use. An IRB may not approve a proposed project that does not include satisfactory plans for test article accountability. Additional information on emergency use is provided in [Part 8](#) of this Operations Manual; at the IRBMED website (<http://www.med.umich.edu/irbmed/guidance/emerguide.htm>); and on the FDA website (<http://www.fda.gov/oc/ohrt/irbs/drugsbiologics.html#emergency> for drugs or biologics and http://www.fda.gov/oc/ohrt/irbs/irbreview/pdf_for_devices).
- Timely reporting of adverse events and other unanticipated problems involving risks to subjects or others to the sponsor and the IRB. More information on adverse event and other reporting requirements is available in IRB Standard Operating Procedures, on the IRBMED website http://www.med.umich.edu/irbmed/ae_orio/.
- Creating and maintaining complete and accurate records, such as informed consent documents, case report forms, correspondence files, and other relevant information for recordkeeping purposes and possible inspection by institutional officials, outside sponsors, and regulatory agencies. Principal investigators must provide to the IRB promptly after receipt copies of any audit or inspection reports, warning letters, debarment notices or similar documents generated internally or created by sponsors, government regulators (such as the FDA or NIH) or others with oversight responsibilities.

The principal investigator is responsible for ensuring that all co-investigators and other research team members assisting in the conduct of the study are informed about their obligations in meeting these commitments and are adequately trained to do so competently and appropriately.

Investigator responsibilities are described in further detail at [21 CFR §§ 312.60-312.69](#) (drugs and biologics); and [21 CFR §§ 812.100-812.110](#) (devices). See also <http://www.fda.gov/cdrh/devadvice/ide/responsibilities.shtml> (regarding investigational devices).

2. Sponsor-Investigator

A sponsor-investigator is a person who both initiates and conducts an FDA-regulated study; that is, an individual who (i) holds an IND or IDE; and (ii) serves as the principal investigator in one or more studies conducted under that IND or IDE. A sponsor-investigator is responsible for fulfilling all of the investigator obligations described above.

In addition to fulfilling the obligations of an investigator, the sponsor-investigator is responsible for drafting and submitting to the FDA all required documentation for a study, including the IND or IDE application, required amendments and progress reports, safety reports, annual reports, and so forth. The sponsor-investigator also is responsible for selecting other qualified investigators, as appropriate, providing them with the information they need to conduct the studies properly, ensuring proper monitoring of the studies, ensuring the studies are conducted in accordance with the general investigational plan and

protocols contained in the IND or IDE application, maintaining an effective IND or IDE with respect to the investigations, and ensuring that FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the investigational agent. The FDA has published guidance on appropriate monitoring procedures, available at http://www.fda.gov/ora/compliance_ref/bimo/clinguid.html. While compliance with this guidance is not mandatory, failure to implement similar procedures or alternative procedures approved by FDA may be deemed inadequate monitoring.

FDA regulations and an increasing number of peer reviewed publications mandate public registration of certain clinical trials. Failure to register may result in administrative sanctions and civil penalties, in addition to refusal by journals to publish. See [Part 11](#) of this Operations Manual for additional information about clinical trials registries.

A sponsor may transfer some or all of these obligations to a contract research organization under a written agreement, but at all times remains ultimately accountable for their fulfillment.

Under FDA regulations, the responsibilities of a sponsor do not vary depending on the sponsor's affiliation. Thus, for example, a multinational pharmaceutical manufacturer has precisely the same obligations under the regulations, as does an academic sponsor-investigator. The responsibilities of a sponsor are described further at [21 CFR §§ 312.50-312.59](#) and [812.40-812.47](#). See also FDA, Guideline for Monitoring Clinical Trials, at http://www.fda.gov/ora/compliance_ref/bimo/clinguid.html; and FDA, Responsibilities of Sponsors for Significant Risk Device Studies, <http://www.fda.gov/cdrh/devadvice/ide/responsibilities.shtml>.

3. *Manufacturers*

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III. EDUCATION

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