Marshfield Clinic

Determining Engagement in Research

1. SCOPE

1.1. System Wide

2. DEFINITIONS & EXPLANATIONS OF TERMS

2.1 Generalizable Knowledge

- Investigations designed to develop or contribute to generalizable knowledge are those designed to draw general conclusions (i.e., knowledge gained from a study may be applied to populations outside the specific study population), to inform policy, or to provide general, applicable conclusions.

2.2 Individually identifiable private information

- "Private information" is information provided for a specific purpose by an individual, and the individual can readily expect will not be made public.
- "Individually identifiable" means the identity of living individuals is, or may readily be, ascertained by the investigator or associated with the information.
  - ◊ At a minimum, data containing an individual's name, street address, social security number or phone number would be considered individually identifiable
  - ◊ Also includes circumstances where private information or specimens can be linked to specific individuals by the investigator, either directly or indirectly through coding systems (e.g., medical history number or other code linked to a legend including a direct identifier, such as name). However, OHRP does not ordinarily consider information to be individually identifiable if: (1) the investigator and the holder of individually identifying information sign an agreement prohibiting the release of individually identifying information to the investigator under any circumstances, or (2) there are other legal requirements prohibiting the release of the link to the investigator.

2.2. Institution

- For purposes of this document, any public or private entity or agency, including federal, state, or other agencies.
- For purposes of this document, an institution's "employees" or "agents" include all who act on behalf of the institution, exercise institutional authority or responsibility, or perform institutionally designated activities. Employees and agents can include staff, students, contractors, and volunteers, regardless of whether they are receiving compensation.

2.3 Research

- A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

2.4 Systematic Investigation

- An activity that involves a prospective plan that incorporates data collection, either quantitative or qualitative, and data analysis to answer a question.

  Activities are not research if they do not involve a systematic approach involving a predetermined method for studying a specific topic, answering a specific question, testing a specific hypothesis, or developing theory

3. RESOURCE GUIDE BODY

This document is intended to assist Marshfield Clinic investigators, research staff, the Marshfield Clinic Research Foundation Institutional Review Board (MCRF IRB), and the Office of Research Integrity & Protections (ORIP) to determine whether Marshfield Clinic, or any outside individual or site, is considered to be "engaged" in human subjects research. The U.S. Department of Health & Human Services (DHHS) requires institutions engaged in non-exempt human subjects research conducted or supported by DHHS to file a Federal Wide Assurance ("FWA") with its Office of Human Research Protections (OHRP). A FWA is a documented commitment from the institution that when it engages in human subjects research, it will comply with the terms of the assurance and the human subjects protection requirements of 45 CFR 46, which includes requiring institutional review board review and approval of research projects. Marshfield Clinic has filed a FWA with OHRP, but it must consider what activities at Marshfield Clinic constitute engagement, as well as whether outside institutions or individuals cooperating in, or performing certain aspects of, research projects are considered engaged. **Investigators are encouraged to contact ORIP for interpreting this information in terms of specific research activities, as needed.**

3.1. Federal Guidance

a. In 2008, OHRP issued a guidance document, "Research Guidance on Engagement of Institutions in Human Subjects Research." While it is primarily aimed at helping institutions decide whether they are required to file a FWA, it can also assist institutions, investigators, and IRBs determine whether an individual or institution is considered "engaged" in a particular research project. The guidance confirms that institutions and individuals may work on certain aspects of a research project without being considered engaged. It also provides examples of when an institution is, and is not, engaged.

3.2. Instances of Engagement

a. As a general rule, an institution is considered engaged in human subjects research when its employees or agents, for purposes of a research project, obtain:

   - Data about living individuals through intervention or interaction with them;
   - Individually identifiable private information about living individuals; or
   - The informed consent of human subjects for the research.

b. More specifically, Marshfield Clinic or any other institution is generally considered engaged when:

   - It has received an award from DHHS for a research project, even when all activities involving research subjects are carried out by another institution;

- Its employees or agents intervene with any subject by performing invasive or noninvasive procedures, such as drawing blood, collecting swab samples, administering drugs, or taking measurements;
- Its employees or agents intervene with any subject by manipulating the environment, such as presenting sensory stimuli or coordinating interactions;
- Its employees or agents interact with any subject for research purposes, such as making interpersonal contact dictated by the protocol, asking subjects to provide specimens, or administering questionnaires;
- Its employees or agents obtain informed consent of subjects for the research; or
- Its employees or agents obtain identifiable private information or specimens from any source for research purposes, even without direct interaction or intervention with subjects.
  - This includes observing or recording private behavior, using or analyzing identifiable private information or specimens provided by another institution for research; or using or analyzing identifiable private information or specimens already in the possession of the institution or its investigators for research.

3.3. Exceptions to Engagement

a. An institution's employees and agents can be involved with human subjects research without being engaged. In these situations, the institution does not need to hold a FWA, and no IRB is required to review the actions of the employees of agents of the institution.

- Activities Performed As Commercial or Other Service
  - An institution is not considered engaged when its employees or agents perform commercial or other services, provided that:

    The services do not merit professional recognition or publication privileges;

    The institution typically performs the services for non-research purposes; and

    Its employees or agents do not administer any study intervention being tested or evaluated as part of the research.
  - Examples include where a laboratory performs routine sample analyses, or where a facility collects blood or urine, or performs x-rays, each as a commercial service.
- Clinical Trial-Related Medical Services Not Involving A Study Intervention Being Evaluated and Normally Performed For Clinical Purposes
  - An institution is not considered engaged when it is not a selected research site, but provides clinical trial-related medical services dictated by the protocol that would normally be performed as part of routine clinical monitoring or follow-up by clinical trial investigators, provided that:

It does not administer the study intervention being tested or evaluated;

It typically provides the medical services for clinical purposes;

Its employees or agents do not enroll subjects or obtain informed consent for the research; and

Investigators from the engaged institution retain responsibility for overseeing protocol-related activities, and for ensuring reporting of protocol-related data to investigators at the engaged institution, including of safety monitoring data and adverse events.

- One-Time or Short-Term Administration of Study Intervention
  - An institution is not considered engaged when it was not initially a selected research site, but its employees or agents administer a study intervention being tested or evaluated as part of the research project, limited to a one-time or short-term basis, provided that:

    An investigator from the engaged institution determines it is in the subject's best interest to receive the intervention;

    Employees or agents of the institution administering the intervention do not enroll the subject in, or obtain informed consent for, the research;

    The investigators from the engaged institution retain responsibility for overseeing protocol-related activities, which includes ensuring that interventions are administered according to the protocol; ensuring reporting of protocol-related data to investigators at the engaged institution, including of safety monitoring data and adverse events; and ensuring that the engaged institution's IRB is informed that the intervention was administered at a site not selected as a research site.
  - An example of this would be a Marshfield Clinic physician administering one-time or short-term chemotherapy to a subject enrolled in a study at another institution because the subject is unexpectedly went out of town, or is unexpectedly hospitalized. Marshfield Clinic would not be engaged in the research if all of the above requirements are met.
- Providing Research-Related Information Only
  - An institution is not considered engaged when the activities of its employees or agents are limited to:

    Informing prospective subjects about the availability of research, or providing them with information about the research, which can include the informed consent document, but do not seek or obtain informed consent, or act as investigator representatives;

    Providing prospective subjects with information about contacting investigators for information or enrollment; and/or

Seeking or obtaining prospective subjects' permission for investigators to contact them.

- Providing Facilities Only
  - An institution is not considered engaged when it allows the use of its facilities for intervention or interaction with subjects by investigators from another institution.
  - Examples include a school permitting investigators from a different institution to distribute a survey, or a business permitting another institution to recruit subjects, or to draw a blood sample at a work site.
- Releasing Identifiable Private Information or Specimens Only
  - An institution is not considered engaged when its employees or agents only release identifiable private information or identifiable biological specimens pertaining to research subjects to investigators at another institution.
  - The release cannot violate the informed consent provided by the subjects to whom the information or biological specimens pertain, or if the IRB waived informed consent, the release must be consistent with the IRB's determinations permitting the waiver. See the document, "Sharing and Transferring Research Data and Materials" for guidance.
- Obtaining Coded Private Information or Specimens
  - An institution is not considered engaged when its employees or agents:

    Obtain coded private information or human biological specimens from another institution involved in the research that retains a link to individually identifying information such as name or social security number, but are unable to readily ascertain the identity of the subjects to whom the coded information or specimens pertain.

    "Coded" means that identifying information that would enable the investigator to readily ascertain the identity of an individual has been replaced by a number, letter, symbol, and/or combination thereof.
  - An example of this circumstance would be where Marshfield Clinic received health data from an outside institution that has been coded, but Marshfield Clinic enters into an agreement with the outside institution prohibiting the release of the key to any Marshfield Clinic employees or agents.
- Visiting Investigators, Employees, or Agents
  - An institution is not considered engaged when its employees or agents access or utilize individually identifiable private information only while visiting an institution engaged in the research, provided that the research activities of those employees or agents are overseen by the IRB of the institution engaged in the research. An example would be if an outside collaborating individual from an institution without a OHRP-approved FWA had his or her activities reviewed by MCRF IRB and

comes to Marshfield Clinic to access or utilize the individually identifiable private information of research subjects as part of his or her IRB-approved activities. Marshfield Clinic normally requires an agreement to be in place in these circumstances. See the document, "Sharing and Transferring Research Data and Materials."

- An "agency physician or practitioner" is one who contracts with Marshfield Clinic for a limited time period, or is in a teaching program and providing contract services outside of that program. If these agency physicians are in a position to treat subjects on a research protocol, they can provide clinical care without being added as a co-investigator. However, the agency physician is considered "engaged" in the research if he or she is (1) conducting protocol-dictated interactions or interviews with subjects, or collecting patient data, beyond what is called for in clinical care; (2) obtaining informed consent for the research from the subjects; or (3) named on study publications. He or she should be added as a co-investigator when planning to enroll a known potential subject, or when there is no specific subject in mind but the study is known to have a high potential for accrual, but not to every open study in the department, or under a particular research base.

- Auditors
  - An institution is not considered engaged in research when the activities of its employees or agents are limited to accessing and reviewing identifiable private information for purposes of study auditing.
- FDA Reporting
  - An institution is not considered engaged when its employees or agents receive identifiable private information for purposes of satisfying FDA reporting requirements.
- Authorship
  - An institution is not engaged when activities of its employees or agents are limited to authoring a paper, journal article, or presentation describing a human subjects research study. However, if other aspects of engagement led to the publication, the engagement definition is met.

3.4. Cooperative Research and Engagement In Research

a. Marshfield Clinic often engages in non-exempt human subjects research projects by collaborating with other institutions. OHRP has stated that in cooperative research projects, institutions may enter into joint review arrangements, rely upon the review of another qualified IRB, or make arrangements to avoid duplication of effort, in accordance with HHS regulations at 45 CFR 46.114. See the documents "Deferring Review of Marshfield Clinic Studies to an External IRB" and "Marshfield Clinic Research Foundation as IRB of Record" for further information.

b. When Marshfield Clinic is engaged in only part of a cooperative research project (see 3.2.(b) for examples of such engagement), MCRF IRB, designated

under its FWA, must review and approve the parts of the research in which Marshfield Clinic employees and agents are engaged. OHRP has also stated that when an institution is engaged in only part of a cooperative research project, its IRB may decide to review the entire project, even if information about the entire project is not necessary to approve the institution's part.

c. A OHRP document, "Assurance Process – FAQs," also clarifies that an institution can extend its FWA to cover a "collaborating individual investigator" or "collaborating institutional investigator" engaged in research under an individual investigator agreement.

- In order for an institution to extend its FWA to a "collaborating independent investigator," the investigator must:
  - not be an employee or agent of the assured institution;
  - be conducting collaborative research outside the facilities of the assured institution; and
  - not be acting as an employee of any institution with respect to his or her involvement in the research.
- A collaborating institutional investigator must:
  - not be an employee or agent of the assured institution;
  - be conducting collaborative research activities outside the facilities of the assured institution; and
  - be acting as an employee or agent of an institution that does not hold an OHRP-approved FDA with respect to his or her involvement in the research being conducted by the assured institution; and
  - be employed by, or acting as an agent of, an institution that does not hold an OHRP-approved FWA, and does not routinely conduct human subjects research.

4. ADDITIONAL RESOURCES

4.1. References:
- Deferring Review of Marshfield Clinic Studies to an External IRB
- Marshfield Clinic Research Foundation as IRB of Record
- http://srdweb1.srd.local/attachments/4291-0-Ownership_Management_and_Sharing_of_Research_Data_and_Materials.pdfSharing and Transferring Research Data and Materials

4.2. Supporting Documents Available:
- None

5. DOCUMENT HISTORY

Version No.	Revision Description

1.0	New Document in Document Control system transferred from Policy & Handbook Library - #4333.0 (no changes made)
2.0	Added hyperlinks to applicable policies/procedures and IRB Form referenced in this document.
3.0	Sect. 2.2 & 2.4 definition revised to have wording consistent throughout all policies/procedure/resource guides. Sect. 3.4 Update title of deferring policy. Fix broken hyperlinks. Sect 4 deleted link to a form and policy reference.

6. DOCUMENT PROPERTIES

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