MCW IRB Committee Procedures

INFORMED CONSENT FOR HUMAN SUBJECT RESEARCH

Unit: Human Research Protections Program (HRPP), Office of Research

Applies to: Institutional Review Board Committees

PURPOSE:
This procedure outlines the responsibilities of the Medical College of Wisconsin (MCW) Institutional Review Board (IRB) to ensure that legally effective and prospective informed consent from research subjects is obtained and that the required elements are incorporated into the informed consent document as required by the federal regulations, tribal law passed by the official governing body of an American Indian or Alaska Native tribe and institutional policies.

DEFINITIONS:
Assent: an affirmative agreement to participate in research. The failure to object should not, without an affirmative agreement, be construed as assent.

Coercion: the use of force or intimidation to persuade someone to do something which they are unwilling to do

Consent: refers to an explicit agreement to participate in a certain action, particularly and especially after thoughtful consideration.

Exculpatory language: language that waives or appears to waive any of the subject's legal rights or attempts to prospectively remove responsibility from the Sponsor or project team

Impartial witness: An International Conference on Harmonization Guideline for Good Clinical Practice (ICH-GCP): A person, who is independent of the research, who cannot be unfairly influenced by people involved with the research, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the consent form and any other written information supplied to the subject.

Legally Authorized Representative (LAR): "An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research."

Reasonable person: A phrase in law to denote a hypothetical person in society who exercises average care, skill and judgment in conduct and who serves as a comparative standard by which to make a determination.

Undue Influence: (as a term in jurisprudence) is an equitable doctrine that involves one person taking advantage of a position of power over another person.

PROCEDURE:

Informed Consent Process

1. Investigators must provide the information regarding the consenting process to the IRB for review:
    a. A detailed description of the intended method for obtaining initial informed consent
    b. All informed consent documents (full written documents, oral scripts, a list of talking points, videos, comprehension materials, any type of comprehension or assessment aids, and short forms)
    c. Assurance that the informed consent process in research is an ongoing exchange of information between the research team and the project participants throughout the course of a research project. Informed consent is a continuous process of communication and acknowledgement over time, not just a signed document.
2. The IRB Committee should ensure that the Investigator describes in their eBridge application that informed consent will:
    a. Begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject in understanding the reasons why one might or might not want to participate in the research. This subscription must be organized and presented in a way that facilitates comprehension.
    b. Be obtained in circumstances that minimize the possibility of coercion and undue influence;
    c. Utilize language to promote the subject's understanding of the information;
        i. The information provided in the informed consent documents must be in a language understandable to the subject (target population).
        ii. Technical and scientific terms should be adequately explained using common or lay terminology.
        iii. Generic names are preferable when describing pharmaceuticals unless the brand name is more commonly known and understood.
        iv. Regardless of which name is preferred, it should be used consistently throughout the informed consent documents.
        v. Devices and procedures should also be described consistently throughout the documents and explained in simple language.
        vi. It is generally recommended that consent documents be written at a sixth to eighth grade reading level.
    d. Provide the essential information a reasonable person would want to have in sufficient detail and organized to facilitate the prospective subject's understanding of the reasons one might consider to make an informed decision about whether to participate in research and provide an opportunity to discuss that information.
    e. Allow sufficient time for consideration of the information and decision regarding participation
    f. Not waive or appear to waive subjects' rights; and
    g. Include each of the required elements and applicable additional elements of informed consent describing the research and the nature of research participation as required by institutional policy.
    h. Include a discussion regarding the use and retention of data if they choose to withdraw from a project. *See IRB SOP Withdrawal of Informed Consent for Human Subject Research.*
    i. Include documentation of informed consent by the subject or the subject's legally authorized representative (LAR) unless requirement has been waived by the IRB.
3. If any of the subjects included in the research currently have decreased decisional ability or are likely to develop decreased decisional ability in the future, the IRB Committee must ensure that additional safeguards have been proposed in

accordance with the *IRB Member SOP: Research with Subjects Likely to Manifest or Develop Decreased Decisional Ability.*

4. The IRB Committee must review and approve all informed consent documents (full written documents, oral scripts, videos, comprehension materials, any type of comprehension or assessment aids, and short forms) during their review of submissions.

IRB Committee Responsibilities

1. The IRB Committee, the IRB Chair or designated reviewer reviews the proposed research activities to assure that the informed consent document aligns with the eBridge application, Investigator's brochure, the Protocol, grant and/or contract, and contains the necessary elements of informed consent as required by federal regulations and institutional policy.
2. When reviewing the informed consent document, the IRB members may request necessary revisions to the content, language, punctuation, and/or grammar in order for the intended target population to clearly understand the proposed research activities and make an informed decision on whether to participate in the research.
3. The IRB Committee, the IRB Chair or designated reviewer approves the informed consent process and method of documentation, indicating whether the proposed consent process is appropriate for the proposed research activities and the target population as a part of the overall IRB approval of the project.

Informed Consent Documents:

1. Investigators are responsible for incorporating the elements of informed consent and the Health Insurance Portability and Accountability Act (HIPAA) standards as required by institutional policy into each informed consent document for their research studies.
2. Investigators are required to use the MCW IRB Consent Form Templates in their development of a consent form for use in research projects.

   Required Elements: The required elements of consent to be included in each informed consent document are:

   - A concise and focused presentation of the key information that is most likely to assist a prospective subject in understanding the reasons why one might or might not want to participate in the research. This subscription must be organized and presented in a way that facilitates comprehension
   - A clear statement that the project involves "research";
   - An explanation of the purposes of the research;
   - Information organized and presented in sufficient detail to facilitate the understanding of the reasons one might or might not want to participate in research;
   - Information that a reasonable person would want to have to make an informed decision and an opportunity to discuss that information, information to include the following unless waived by the IRB:
     - The expected duration of the subject's participation;
     - A complete description of the procedures to be followed, and identification of procedures that are experimental and performed solely for the purposes of research;
     - A description of the reasonably foreseeable risks and discomforts;
     - A description of any benefits to the subject or others that may reasonably be expected from the research;
     - A disclosure of appropriate alternative procedures or courses of treatment that might be advantageous to the subject;

- When the research involves the collection of identifiable private information or identifiable biospecimens, the following statement must be included:
    - "The subject's information or biospecimens will not be used or distributed for future research studies even if identifiers are removed unless additional consent is obtained or is waived by the IRB."
- A description of the extent to which confidentiality of records identifying the subject and privacy will be maintained
- For research involving more than minimal risk, an explanation as to whether any compensation, and an explanation as to whether any medical treatments are available, if injury occurs and, if so, what they consist of, or where further information may be obtained;
- An explanation of whom to contact for answers to pertinent questions about the research (e.g., Investigator), the research subjects' rights (e.g., Research Subject Advocate), and whom to contact in the event of a research-related injury; and
- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

3. The required elements of informed consent may not be omitted unless specifically waived by the IRB. In addition, there may not be discrepancies within the informed consent documents, the eBridge application, the Protocol, the Investigator's Brochure, the grant and/or the contract regarding the purpose, foreseeable risks, and benefits of the research.

   Additional Elements: Per institutional policy, the informed consent document should, where appropriate, include the following additional elements:
   - A statement that biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;
   - A statement indicating whether clinically relevant results, including individual results, will be disclosed to subjects, and if disclosed under what conditions;
   - A statement about whether the research project will or might include whole genome sequencing;
   - For women of child bearing potential, a statement that the particular treatment or procedure may involve risks to the subject (or the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;
   - Anticipated circumstances under which the subject's participation may be terminated by the Investigator without regard to the subject's consent;
   - If there is the potential that costs of research procedures will not be paid by the sponsor or the subject's insurance, a description of any additional costs to the subject that may result from participation in the research;
   - The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
   - A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject;
   - The approximate number of subjects involved in the project;
   - The MCW IRB may require that information, in addition to that required in institutional policy, be given to research subjects when in its judgment the

information would meaningfully add to the protection of the rights and welfare of subjects.

ICH GCP additional elements: In addition to the required and if applicable additional elements consent forms for clinical investigations that follow ICH GCP guidelines must include these additional elements:

- Discussion of project treatments and probability of random assignment
- Subject responsibilities
- Anticipated prorated payment, if any, to the subject for participating in the project
- Information regarding the important potential benefits and risks of alternative procedures/courses of treatment
- Authorization to access medical records by regulatory authorities, the monitor, auditor and the IRB for verification of clinical trial procedures or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations.

These elements will be documented by the IRB members via *IRB Member Form: ICH-GCP E6 Reviewer Checklist.*

Additional Elements if the project involves test articles regulated by the FDA: In addition to the required and if applicable additional elements, consent forms for clinical investigations that involve a test article (drug, device or biologic) regulated by the FDA must include these additional elements:

- A statement noting the possibility that the FDA may inspect the records that will be provided to each subject.
- A statement that a description of the clinical trial will be available on http://www.clinicaltrials.gov as required by US law.
- In studies that evaluate the safety of the test article, include the statement:
    - "A purpose of the project includes an evaluation of the safety of the test article."
    - Statements that test articles are safe or statements that the safety has been established in other studies are not appropriate when the purpose of the project includes determination of safety.
- In studies that evaluate the effectiveness of the test article, include the statement:
    - "A purpose of the project includes an evaluation of the effectiveness of the test article."
    - The consent document should not contain claims of effectiveness.
- Phase I Studies. Phase I studies are typically designed to determine safety, but not effectiveness. Phase I consent documents will include the approved Phase I template language that can be found within the MCW Informed Consent Templates
- Phase II and Phase III Studies. Potential subjects should be told, and a statement included in the purpose of the informed consent document, that Phase II and III studies are designed to determine both safety and effectiveness.
- Phase II & III consent documents will include the approved template language that can be found within the MCW Informed Consent Templates.

Other Federal Agency Requirements

For research conducted within the Bureau of Prisons, or funded or supported by the Department of Defense, Department of Justice, or Department of Energy, the IRB C2

should confirm all the required additional elements are included in the consent form, as described in *IRB SOP: Informed Consent*.

Prohibited Elements

- No unproven claims of effectiveness or certainty of benefit, either implicit or explicit, may be included in the informed consent documents.
- The informed consent documents may not contain any exculpatory language through which the subject is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the Investigator, the sponsor, or its agents from liability for negligence.
    a. Examples of Acceptable Language:
    - There are no plans to provide financial compensation to you should this occur.
    - By consenting to participate, you authorize the use of your private health information for the research described above.

    b. Examples of Unacceptable Exculpatory Language:
    - By agreeing to this use, you should understand that you would give up all claims to personal benefit from commercial or other use of these substances.
    - I voluntarily and freely donate any and all blood, urine, and tissue samples to the U.S. Government and hereby relinquish all right, title, and interest to said items.
    - By consenting to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research.
    - I waive any possibility of compensation for injuries that I may receive as a result of participation in this research.

Waiver of Consent

1. The IRB may waive or alter the requirement for Investigators to obtain a potential subject's consent for research participation. To approve such a waiver or alteration, the IRB must find:
    - The research involves no more than minimal risk to the subjects;
    - The waiver or alteration will not adversely affect the rights and welfare of the subjects;
    - The research could not practicably be carried out without the waiver or alteration; and
    - Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
        - The above waiver conditions must be met for research that involves the use of identifiable private information or identifiable biospecimens and the research could not be practicably carried out without using such information or biospecimens in an identifiable format;
2. When considering a waiver of the consent process for Public Demonstration Projects, the IRB must find:
    - The research is conducted by or subject to the approval of state or local government officials
    - The research or demonstration project is designed to study, evaluate, or otherwise examine:
        - Public benefit or service programs
        - Procedures for obtaining benefits or services under those programs
        - Possible changes in or alternatives to those programs or procedures

    - Possible changes in methods or levels of payment for benefits or services under those programs
- The research cannot practicably be carried out without the waiver or alteration

3. Research subject to FDA regulation may occur without prior consent of the subject in these circumstances:

- When the research involves planned research in life-threatening emergent situations where obtaining prospective informed consent has been waived for some or all of the potential research subjects, as provided by 21 CFR 50.24. The research plan must be approved in advance by FDA and the IRB, and publicly disclosed to the community in which the research will be conducted. For more information refer to *IRB Member SOP: Planned Emergency Research*
- When the research involves an unplanned emergency use of an FDA regulated product for a single subject. The investigator is required to obtain informed consent of the subject or the subject's legally authorized representative as described in the *IRB Member SOP: Emergency Use of an Investigational Drug, Biologic or Device*.
- When biospecimens are utilized for an investigational in vitro diagnostic test, under specific conditions conferring IDE exemption defined by institutional policy and falling under the 2006 FDA guidance: *Guidance on Informed Consent for Invitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable.*
- When the clinical investigation involves no more than minimal risk; and the waiver will not adversely affect the rights and welfare of the subjects; and the clinical investigation could not be practicably carried out without the waiver and whenever appropriate, the subjects will be provided with additional pertinent information after participation.

4. The IRB may not waive the consent process for any research to be conducted under DoD regulations where the research subject meets the DoD definition of an experimental subject. *Research involving an experimental subject is defined as: An activity, for research purposes, where there is an intervention or interaction with a human subject for the primary purpose of obtaining the effect of the intervention of interaction.*

- A waiver of the consent process for such DoD regulated research requires permission of the Secretary of Defense
    i. If a waiver of consent is granted, the PI must identify their process to solicit and obtain consent from an experimental subject's legally authorized representative, and the PI must include a description regarding how the research will benefit the individual subject.
        1. The convened IRB will make a final determination if research is intended to be beneficial to the individual experimental subject.
- The Assistant Secretary of Defense for Research & Engineering may waive the requirement of consent when all of the following elements have been met:
    i. The research is necessarily to advance the development of a medical product for the Military Services.
    ii. The research might directly benefit the individual experimental subject.
    iii. The research is conducted in compliance with all other applicable laws and regulations

5. For research subject to Department of Education regulations, the IRB will follow the requirements of the Family Educational Rights and Privacy Act (FERPA) when considering whether it may grant exceptions to parental/student consent to release of records for research.

- In addition, the IRB will ensure the project complies with and follows the requirements set forth the Protection of Pupil Rights Amendment, for research seeking a waiver of consent involving students.

Waiver of Documentation of Consent

1. For certain types of research, the IRB may approve a waiver of documentation of consent. Whenever the IRB approves a consent process involving waiver of documentation of consent, the IRB will need to approve a written description of the project that also contains all of the elements of consent. This written description may be in the form of a script for verbal use, such as during a telephone conversation. However, the IRB may approve an alteration of consent/authorization if some elements are omitted. The IRB must always approve a waiver of documentation of consent and, where appropriate, an alteration of authorization if the investigator will not obtain a consent document signed and dated by the research subject or their LAR.
2. An IRB may waive the requirement for the investigator to obtain a signed and dated consent document for some or all subjects, if it finds:
    - That the subjects are members of a distinct cultural group or community in which signing forms is not the norm. This is limited to minimal risk research and requires an appropriate alternative method for recording that informed consent was obtained; or
    - That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or
    - That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context.
3. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.
4. When the research involves an FDA-regulated product, the IRB may waive written consent only for research that meets criteria listed in federal regulations and institutional policy.
5. The IRB considers the following points when assessing whether to approve waiver of documentation of consent:
    - Does the written description or script for presentation to the potential subject include the required elements of consent, and additional elements, if applicable?
    - Does the written description or script for presentation to the potential subject include the required elements of HIPAA authorization?
    - Does the written description or script include the requirement for the signature of the subject or their LAR?
    - If the written description or script is to be signed and dated by the subject or their LAR, and the consent process occurs by telephone, does the written description or scripts include the requirement for signature by a witness to confirm the identity of the subject?
    - Does the research involve no more than minimal risk, and would written consent be required for the procedures if they were not part of a research project?

Use of the Short Form or Translated Consent Documents

1. When a potential subject who does not speak English is **unexpectedly** encountered, institutional policy allows for use of a "short form" in a language the subject understands, to document that all required elements of informed consent were presented orally. A summary in English (the IRB-approved consent form in English) of what is to be presented to the subject, as well as the short form must be approved by the IRB, and a witness to the oral presentation is required.
2. IRB member should refer to *IRB Member SOP: Recruitment and Enrollment of Limited English or Non-English Proficient Subjects* for further guidance on the use of short form consents or a fully translated consent form.

Consent Monitoring

1. The IRB has the authority under institutional policy to observe or have a third party observe the consent process and the research. In order to ensure that the consent process is appropriate, and the approved process is being followed, the IRB may determine that special monitoring of the process must occur. Such monitoring may be particularly needed for the IRB to meet its responsibilities to ensure human subject protections for research that:
    - Involves a vulnerable population
    - Involves use of a highly risky and innovative procedure
    - Is conducted by an inexperienced investigator and/or research team
    - Is research about which the IRB has concerns that the consent process is not being conducted properly.
2. In reviewing the adequacy of proposed informed consent procedures, the IRB may determine on a project-by-project basis as a part of the initial and continuing review process, those research projects that require third party observation/monitoring of the consent procedures in accordance with *IRB Member SOP: Use and Requests to Quality Assurance/Quality Improvement*.
3. MCW QA/QI staff and IRB Members authorized to conduct the monitoring will be identified by the IRB Chair and the HRPP Director and the meeting minutes will document these plans.
4. The monitoring results will be reported to the IRB that requested the monitoring and reflected in the minutes, and the monitoring report will be included in the protocol file.
5. If the initial determination requiring third party observation/monitoring of the consent procedures was open-ended, when the IRB determines that the monitoring is no longer required, the minutes will record that determination.

REFERENCES:

21 CFR 50.24

SUPPORTING DOCUMENTS:
IRB Member SOP: Research with Subjects Likely to Manifest or Develop Decreased Decisional Ability
IRB Member SOP: Emergency Use of Investigational Drugs, Devices and/or Biologics
IRB Member SOP: Planned Emergency Research
IRB Member SOP: Use and Requests to Quality Assurance/Quality Improvement
IRB Member SOP: Recruitment and Enrollment of Limited English or Non-English Proficient Subjects
IRB SOP: Informed Consent
IRB SOP Withdrawal of Informed Consent for Human Subject Research
MCW Informed Consent Templates

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