



MCW Office of Research Standard Operating Procedure

PLANNED EMERGENCY RESEARCH

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

Applies to: Faculty and Staff involved in human research

PURPOSE:

Planned Emergency Research is a planned clinical investigation and involves subject(s) who are in a life-threatening situation for which available treatments or in vitro diagnostic tests are unproven or unsatisfactory. For planned emergency research the MCW IRB must also evaluate materials to determine if the investigation satisfies the criteria outlined and determine whether it is appropriate to proceed under federal regulations and institutional policies.

DEFINITIONS:

Community Consultation: Community consultation means providing the opportunity for discussions with, and soliciting opinions from, the communities in which the project will take place and from which the subjects will be drawn.

Emergency Research: is a planned clinical investigation that requires prior written FDA authorization to proceed and involves subject(s) who are in a life-threatening situation for which available treatments or in vitro diagnostic tests are unproven or unsatisfactory.

Life-threatening: Diseases or conditions where the likelihood of death is high unless the course of the disease or condition is interrupted. The FDA regulations which allow an exception from informed consent for emergency research (21 CFR 50.24) apply only to life-threatening emergency situations.

Public disclosure: Public disclosure means dissemination of information about the emergency research sufficient to allow a reasonable assumption that the communities are aware of the plans for the investigation, its risks and expected benefits, and the fact that the project will be conducted. Public disclosure also includes dissemination of information after the investigation is completed so that the communities and scientific researchers are aware of the project's results.

Therapeutic window:

1. The therapeutic window is the time period, based on available scientific evidence, during which administration of the test article might reasonably produce a demonstrable clinical effect.
2. For investigations of in vitro diagnostic devices (IVDs) that meet the criteria for emergency research, the therapeutic window is the time period, based on available scientific evidence, during which diagnosis must occur to allow administration of appropriate therapy.

PROCEDURE:

Projects subject to FDA Regulations

1. Federal Regulations (21 CFR 50.24) allow investigators to conduct clinical investigations subject to FDA regulations where obtaining consent from the subject would not be possible prior to the event, providing required conditions are met.
2. Investigators who wish to conduct this type of clinical investigation must submit an eBridge PRO SmartForm for review and approval. The application must describe and satisfy the following identified regulatory requirements set forth by the FDA for this type of clinical investigation.
 - a. The target population for the research is in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
 - b. Obtaining informed consent is not feasible because:
 - i. The subjects will not be able to give their informed consent as a result of their medical condition;
 - ii. The intervention under investigation must be administered before consent from the subjects' legally authorized representatives (LAR) is feasible; and
 - iii. There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.
 - c. Participation in the research holds out the prospect of direct benefit to the subjects because:
 - i. The subjects are facing a life-threatening situation that necessitates intervention;
 - ii. Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and
 - iii. The risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, and what is known about the risks and benefits of the proposed intervention or activity.
 - d. The clinical investigation could not practicably be carried out without the waiver.
 - e. The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the Investigator has committed to attempting to contact a LAR for each subject within that window of time and, if feasible, to asking the LAR contacted for consent within that window rather than proceeding without consent. The Investigator must agree to summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.
 - f. The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with Federal regulations and IRB policies and procedures. The informed consent procedures and the informed consent document are to be used with subjects or their LAR in situations where use of such procedures and documents is feasible.
 - g. Additional protections of the rights and welfare of the subjects will be provided, including, at least:
 - i. Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;

- ii. Prior to the initiation of the clinical investigation, public disclosure to these communities of plans for the investigation and its risks and expected benefits;
- iii. At the completion of the clinical investigation there are plans for Public disclosure of sufficient information to apprise the community and researchers of the project. The information must include the demographic characteristics of the research population and results of the clinical investigation.
 - 4. Establishment of an independent data and safety monitoring committee to exercise oversight of the clinical investigation; and
 - 5. If obtaining informed consent is not feasible and a LAR is not reasonably available, the Investigator must commit to attempting to contact within the therapeutic window, the subject's family member who is not a LAR, and asking whether the family member objects to the subject's participation in the clinical investigation. The Investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.
- h. Procedures must be in place to inform, at the earliest feasible opportunity, each subject, or, if the subject remains incapacitated, a LAR of the subject, or, if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document, specifically that the he/she may discontinue the subject's participation at any time without penalty or loss of benefits of which the subject is otherwise entitled.
- i. If a LAR or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible.
- j. If a subject is entered into a clinical investigation with waived consent and the subject dies before a LAR or family member can be contacted, information about the clinical investigation is to be provided to the subject's LAR or family member, if feasible.
- k. All clinical investigation records, including regulatory files, must be maintained for at least 10 years after the completion of the clinical investigation in accordance with *IRB SOP: Project Closure*. The investigator records will be accessible for inspection and copying by the regulatory authorities, as applicable.
- l. Clinical investigations that are granted an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies that the clinical investigation may include subjects who are unable to consent. The submission of these clinical investigations to the FDA for a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for this IND/IDE may not be submitted as an amendment to the existing IND/IDE.
- m. If the IRB determines it cannot approve a request for exception from informed consent requirements in emergency research because the clinical investigation does not meet the criteria according to Federal regulations, IRB policies and procedures, or other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator who will forward to the sponsor of the clinical investigation.

Projects not subject to FDA Regulations

1. Federal Regulations (45 CFR 46.101 (i)) allow investigators to conduct research which are not subject to FDA regulations in instances where obtaining consent from the subject would not be possible prior to the event as noted in 61 FR 51531.
2. Investigators who wish to conduct this type of research must submit an eBridge PRO SmartForm for review and approval. The application must describe and satisfy the following identified regulatory requirements set forth by OHRP for this type of investigation.
 - a. The research subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
 - b. Obtaining consent is not feasible because:
 - i. The subjects are not able to give their consent as a result of their medical condition.
 - ii. The intervention involved in the research is administered before consent from the subjects' LAR is feasible.
 - iii. There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research.
 - c. Participation in the research held out the prospect of direct benefit to the subjects because:
 - i. Subjects are facing a life-threatening situation that necessitated intervention.
 - ii. Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence supported the potential for the intervention to provide a direct benefit to the individual subjects.
 - iii. The risks associated with the research are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.
 - d. The research could not practicably be carried out without the waiver.
 - e. The proposed research project defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a LAR for each subject within that window of time and, if feasible, asking the LAR contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact representatives and make this information available to the IRB at the time of continuing review.
 - f. The IRB has reviewed and approved consent procedures and a consent document in accord with 45 CFR 46.116 and 46.117.
 - g. These procedures and the consent document are to be used with subjects or their LARs in situations where use of such procedures and documented is feasible.
 - h. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the research.

- i. Additional protections of the rights and welfare of the subjects are provided, including, at least:
 - i. Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the research is conducted and from which the subjects are drawn.
 - ii. Public disclosure to the communities in which the research is conducted and from which the subjects are drawn, prior to initiation of the research, of plans for the research and its risks and expected benefits.
 - iii. Public disclosure of sufficient information following completion of the research to apprise the community and researchers of the project, including the demographic characteristics of the research population, and its results.
 - iv. Establishment of an independent data monitoring committee to exercise oversight of the research.
 - v. If obtaining consent is not feasible and a LAR is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a LAR, and asking whether the family member objects to the subject's participation in the research.
- j. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.
- k. Procedures are in place to inform, at the earliest feasible opportunity, each subject, or, if the subject remained incapacitated, a LAR of the subject, or, if such a representative is not reasonably available, a family member, of the subject's inclusion in the research, the details of the research, and other information contained in the consent document.
- l. There is a procedure to inform the subject, or, if the subject remained incapacitated, a LAR of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
- m. If a LAR or family member is told about the research and the subject's condition improves, the subject is also informed as soon as feasible.
- n. If a subject is entered into research with waived consent and the subject dies before a LAR or family member can be contacted, information about the research is provided to the subject's LAR or family member, if feasible.
- o. For the purposes of these regulations "family member" means any one of the following legally competent persons: spouses; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.

Other Federal Agency Requirements:

For projects which receive funding or support from the Department of Defense (DoD) or a component of the DoD, the following type of research must be considered an exception from consent in emergency medicine research and is prohibited unless a waiver is obtained from the Secretary of Defense.

IRB Review

MCW IRB reviews and approves these projects in stages.

1. The IRB will review the initial submission and the details of the community consultation plan. For research which is not subject to FDA regulations, the IRB will find, document, and report to DHHS the following:
 - a. The IRB found and documented that the research project is not subject to regulations codified by the FDA 21 CFR 50 and meets the criteria under 45 CFR 46.101 (i) allowing research which is not subject to FDA regulations in instances where obtaining consent from the subject would not be possible prior to the event as noted in 61 FR 51531.
2. The IRB Committee will determine if the project meets the criteria for approval, and the additional requirements as defined in the federal regulations and issue an approval for the project to allow the Investigator to conduct the community consultation.
3. Using the amendment pathway, the Investigator should submit to the IRB results of the community consultation along with the feedback received. The Investigator should indicate if additional changes have been made to the original protocol in light of community feedback. The amendment should also include plans to conduct public notification.
4. The IRB Committee will review the results of the community consultation and any changes made to the original protocol. Information that will be publicly disclosed will be reviewed to assure that the information will reach the broader communities involved and will adequately inform affected communities of plans to conduct this research. The IRB will issue an approval to conduct public notification.
5. Using the amendment pathway, the Investigator should submit the results of public notification to the IRB. The IRB Committee will review the report and determine if final approval can be granted or if additional changes are required. An IRB decision letter granting approval to begin the investigation and enroll human subjects will be issued to the Investigator.
6. If the IRB determines that the project cannot be approved because it does not meet the criteria for exception from informed consent regulations or because of relevant ethical concerns, the IRB will promptly (within 30 days) provide this information to the Investigator and Sponsor.

REFERENCES:

21 CFR 50

21 CFR 50.24

45 CFR 46.101 (i)

45 CFR 46.116

45 CFR 46.117

61 FR 51531

OHRP Guidance: Informed Consent Requirements in Emergency Research

FDA Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors:
Exception from Informed Consent Requirements for Emergency Research

SUPPORTING DOCUMENTS:N/A

Effective Date: 07/01/2023
Version number: 6.0
Previous Version/date: 5.0, 06/15/2018
Responsible Office: HRPP Office
Approval Date: 05/29/2023

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