MCW Office of Research
Standard Operating Procedure

INSTITUTIONAL REVIEW BOARD ACTIONS

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

Applies to: Faculty and Staff involved in human research

PURPOSE:
Medical College of Wisconsin (MCW) Institutional Review Board (IRB) has the authority to render determinations on human subject research according to the Federal Regulations. Further the MCW IRB has the authority to place restrictions, suspend or terminate approval of a research project that is not being conducted in accordance with IRB approval, institutional procedures or applicable law, or that has been associated with unexpected harm to subjects

DEFINITIONS:
Approved – Approval may be granted if the research activity meets the criteria for approval as defined in 45 CFR 46.111 or 21 CFR 56.111 and no changes to the research application are recommended.

Modifications Required – A "modifications required" status is stipulated only when the requested modifications are clear and specific in nature and do not require clarification by the Investigator. Clarifications that are minor and will not change the risk to the subject regardless of the response can also be given a "modifications required" status. Modifications will be reviewed by the IRB Chair or designated IRB member. Those that are not addressed by the Investigator and/or research team may be referred to the Full Committee, as determined by the IRB Chair or designated reviewer. The recommended modifications must be made to the eBridge PRO SmartForm, protocol, informed consent documents, and/or other required documents before final IRB approval can be granted.

The date of approval is the date the conditions were determined to be met.

The IRB Committee provides a letter to the Investigator stipulating the specific modifications required for approval.

1. Initial submissions receiving a "modifications required" status may be administratively withdrawn if an adequate response to the Committee recommendations has not been received by the IRB within 60 days of the date of the "modifications required" letter.
2. Continuing review submissions receiving a "modifications required" status will expire on the date of project expiration if required modifications have not been received and approved by the IRB prior to the project expiration date.
3. Amendments receiving a "modifications required" status may not be implemented until a response by the Investigator has been received and final approval has been granted in writing by the IRB.

Tabled – A "tabled" status is stipulated when the project does not meet the criteria for approval as defined in 45 CFR 46.111 or 21 CFR 56.111, or if the IRB Committee

requests substantive modifications to the IRB submission that are relevant to the meeting the criteria for approval as required by the federal regulations.

A project that lacks sufficient information to conduct an adequate review and confirm the criteria of approval has been met at the Full Committee review level is “tabled” pending receipt of the requested information. The revised project must be reviewed by the convened IRB and is placed on the next available agenda pending receipt of the additional information. The Investigator’s response is reviewed by the Full Committee.

1. The IRB Committee may invite the Investigator to a convened IRB Committee meeting to allow the Investigator to personally address the concerns of the Committee and to allow the Committee to ask questions and seek clarification from the Investigator.
2. Initial submissions receiving a “tabled” status may be administratively withdrawn if a response to the Committee modifications has not been received by the IRB within 60 days of the date of the tabled letter.
3. Continuing review submissions receiving a “tabled” status expire on the date of project expiration if an adequate response has not been received by the IRB prior to the project expiration date.
4. Amendments receiving a “tabled” status may not be implemented until a satisfactory response by the Investigator has been received and final approval has been granted in writing by the IRB.

Expiration Date – the last date of the IRB approval period. For example, if a project is approved from 10/02/2017 to 10/01/2018, the project activities may continue until midnight on 10/01/2018 when IRB approval expires.

Deferred – A project may be “deferred” when the Committee lacks sufficient time, at a full Committee meeting, to review a submission. The submission is placed on the next IRB Full Committee meeting agenda. A project may also be “deferred” if the primary reviewer and/or consultant or subject matter expert is unable to provide or complete their review of the submission and provide documentation of this review prior to the convened IRB Full Committee meeting.

Disapproved - A “disapproved” status is stipulated when the project does not meet the criteria for approval as defined in 45 CFR 46.111 or 21 CFR 56.111, and if the IRB Committee recognizes the project puts subjects at substantial risk, or presents an significantly unfavorable risk-benefit ratio and cannot recommend substantial revisions to the IRB submission, Sponsor’s Protocol, informed consent document(s), and/or other pertinent documents outside of not conducting the project as presented.

Suspension – A “suspended” status is a temporary halt in IRB approval of some or all research activities until identified concerns can be evaluated and resolved. Suspension may be initiated whenever:

1. The IRB determines that research is not being conducted in accordance with IRB requirements and approval based on outcome from an inquiry or investigation, or
2. When significant new risks are identified and need to be evaluated, or
3. Unexpected serious harm to subjects has occurred.

Termination – A “terminated” status is a permanent halt in IRB approval for all research activities. Termination is initiated when it is determined, through investigation, that research is not being conducted in accordance with IRB requirements in which the reported risks significantly outweigh the benefits, or unexpected serious harm to subjects has occurred.

The IRB may terminate a project without **"Suspending"** project activities previously.

PROCEDURE:

Approved

If approval is granted, Investigators may begin research activities when they receive the written letter of approval from the IRB via eBridge.

Modifications Required

1. Investigators must respond to the Committee recommendations outlining the modifications incorporated and the rationale for any modifications not incorporated.
    a. Modifications not addressed or incorporated may be referred to Full Committee for review.
2. Investigators should include in their response a copy of any revised documents in their entirety. The changes to the documents are tracked.
3. Amendments which have modifications required may not be implemented until a satisfactory response by the Investigator has been received and final approval has been granted in writing by the IRB via eBridge.
4. Research activities may not start until all conditions have been met and the IRB Chair or designee has reviewed the modifications and issued the final approval letter via eBridge.

Tabled

1. Investigators must respond to the Committee recommendations outlining the changes incorporated and the rationale for any changes not incorporated.
2. Investigators should include in their response a copy of any revised documents in their entirety. The changes to the documents are tracked.
3. Amendments which are tabled may not be implemented until a satisfactory response by the Investigator has been received and final approval has been granted in writing by the IRB via eBridge.
4. Tabled studies must go back to the Full Committee for review once a response is received.
5. Research activities may not begin until all conditions have been met and the IRB Chair or designee has issued a final approval letter via eBridge.

Disapproved

1. Investigators may not implement a change or begin a research project which has been disapproved by the Full Committee.
2. Investigators have the right to appeal and respond to the Committee decision. The appeal should outline any changes incorporated and the rationale for any changes not incorporated. The Investigator includes in the response a copy of any revised documents in their entirety. The changes to the documents are tracked.
3. Disapproved projects must go back to the Full Committee for review if an appeal is received.
4. Amendments which are disapproved cannot be implemented unless an appeal by the Investigator have been received; changes made and final approval has been granted in writing by the IRB via eBridge.

Suspension

1. A single project or multiple projects for a single Investigator may be suspended. This action will ordinarily be initiated by the IRB Chair or Committee, but may also be initiated by the HRPP Director or the Associate Provost for Research. When IRB approval is suspended, the following will be considered:
    a. What actions, if any, may be needed to protect the rights and welfare of currently enrolled subjects
    b. Whether procedures for withdrawal of enrolled subjects take into account their rights and welfare (e.g. making arrangements for medical care outside of a

research project, transfer to another researcher, and continuation in the research project under independent monitoring)
   c. Whether current subjects need to be informed of the suspension
   d. Any adverse events, UPIRSOs, or outcomes that have been reported to the IRB.
2. Suspensions not initiated by the IRB Committee must be reported to and reviewed by the convened IRB as a reportable event in accordance with *IRB SOP: Requirements for Reporting to the IRB.*
3. ***Suspension*** of a project means the following activities will cease immediately:
   - Enrollment of new subjects
   - Screening and recruiting of new subjects
   - Presenting or publishing any data or results

The following activities may continue only at the direction of the IRB:
   - Submission of amendments
   - Follow-up on enrolled subjects (evaluate continuation of all enrolled subjects on a case by case basis)
   - Treatment of enrolled subjects

The following activities may continue:
   - Submission Continuing Progress Reports
   - Submission of Reportable Events requiring prompt reporting

4. If the IRB Chair or IRB Committee suspends approval of a project due to the Investigator's failure to comply with the requirements of the approved protocol or institutional policies and procedure, the HRPP Director shall notify the Associate Provost for Research, who shall provide written notice to the Dean, applicable Institutional Officials, Institutions where the project is being conducted and where MCW is serving as the IRB of Record, OHRP and/or the FDA and/or the head of the supporting Federal Agency.

Termination

1. Termination will ordinarily be initiated by an IRB Chair or an IRB Committee, but may also be initiated by the HRPP Director or the Associate Provost for Research. A single project or multiple projects for a single Investigator may be terminated to eliminate immediate risks to the subjects, or the institution.
2. When study approval is terminated, the following will be considered:
   a. What actions, if any, may be needed to protect the rights and welfare of currently enrolled subjects
   b. Whether procedures for withdrawal of enrolled subjects take into account their rights and welfare (e.g. making arrangements for medical care outside of a research project, transfer to another researcher, and continuation in the research project under independent monitoring)
   c. Whether current subjects need to be informed of the termination
   d. Any adverse events, UPIRSOs, or outcomes that have been reported to the IRB
3. Terminations not initiated by the IRB Committee must be reported to and reviewed by the convened IRB as a reportable event in accordance with *IRB SOP: Requirements for Reporting to the IRB.*
4. ***Termination of Approval*** of a project means the following activities will cease immediately:
   - Enrolling new subjects into the project(s)
   - Screening and recruiting of new subjects
   - Presenting or publishing any data or results
   - Submission of Amendments
   - Submission of Continuing Progress Reports

The following activities of the project may continue at the direction of the IRB:
   - Follow-up on enrolled subjects (evaluate continuation of all enrolled subjects on a case by case basis)

- Treatment regimen for currently enrolled subjects to end participation on project safety
- Development of a plan to notify subjects of termination of the project, and describe how the Investigator will safely withdraw subjects from the project, and transfer into clinical care

The following activities may continue:

- Submission of Reportable Events requiring prompt reporting that occurred prior to termination.

5. If an IRB Committee terminates approval of a project due to the Investigator's failure to comply with the requirements of the approved protocol or institutional policies and procedure, or due to identification of immediate harm or risk to subjects, the HRPP Director shall notify the Associate Provost for Research, who shall provide written notice to the Dean, applicable Institutional Officials, Institutions where the project is being conducted and where MCW is serving as the IRB of Record, OHRP and/or the FDA and/or the head of the supporting Federal Agency.
6. The Investigator must submit a final report for the project to the IRB within 90 days from the date of the IRB termination of approval.

Expedited Review of Submissions

The same procedures as described will apply to studies that meet criteria for Expedited review. The actions will either be performed by a single designated expedited reviewer or may be performed by a convened Full Committee; if a submission is deemed to warrant review by a convened Full Committee as determined by the IRB Chair of either the Expedited Committee or any one of the Full Committees.

Appeal Process

1. Investigators have the right to appeal an IRB determination and/or decision.
2. The appeal be written and addressed to the IRB Chair and the HRPP Director.
3. The appeal must contain the following information:
    - Reason for the appeal including new information which was not initially provided or considered by the IRB.
    - Scope of the appeal including the activities, length of time, and limitations
4. The appeal will be evaluated by the IRB Chair and the HRPP Director and/or Institutional Officials as deemed necessary by the MCW IRB Office.
5. The IRB Chair will provide the Investigator with a response to the appeal to the appeal that includes;
    - The decision
    - The rational for the decision
    - Any additional action required

REFERENCES:

45 CFR 46.109
45 CFR 46.111
45 CFR 46.112
45 CFR 46.113
21 CFR 56.109
21 CFR 56.111
21 CFR 56.112
21 CFR 56.113

SUPPORTING DOCUMENTS:
N/A

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Approved By
HRPP Authorized Official: Ryan Spellecy, PhD, Director, HRPP
Human Research Protections Program (HRPP)
Office of Research
Medical College of Wisconsin