

## **Board Meetings and Administrative Policies**

### **Introduction:**

This policy outlines the operational activities and actions of the IRB of UHCMC to comply with Federal regulations on IRB functions and operations in the review of research.

### **Policy:**

The IRB is a committee of the Medical Staff and reports to the Chief Medical Officer of UHCMC. The IRB also serves as a medical IRB for Case. The minutes of the IRB meetings are sent to the Chief Medical Officer for review and approval by the Clinical Council.

The IRB will be constituted and review research involving human subjects according to Federal regulations. Meetings of the IRB will conform to Federal regulations and guidelines for the review of research.

### **A) Meetings of the IRB**

UHC has two equally constituted institutional review boards. One meets on the first and third Tuesday of each month and the other on the second and fourth Tuesday of each month. The fifth Tuesdays alternate between the Boards. The agenda, along with meeting materials, is sent to IRB members five days in advance of the meeting.

Protocols may be submitted to the IRB at any time. Protocols that require Board review are usually scheduled for a meeting within 14 days of receipt by the IRB. Protocols are not reviewed unless the submission is complete.

#### Initial Review: Information Received and Reviewed by IRB Members

The primary and secondary reviewer will receive and conduct an in-depth review of the protocol application (investigator checklist and research plan), proposed informed consent documents, recruitment materials, the full protocol, any relevant grant applications, the investigator's brochure (when one exists), the DHHS-approved sample informed consent document (when one exists) and the complete DHHS-approved protocol (when one exists).

All other IRB members will receive and review the following: the protocol application (investigator checklist and research plan), proposed informed consent documents, and recruitment materials. These members are required to review the material in enough depth to be familiar with them and prepared to discuss them at the convened meeting.

#### Continuing Review: Information Received and Reviewed by IRB Members

The primary and secondary reviewer will receive and conduct an in-depth review of the continuing review protocol application (investigator checklist and current research plan), the current informed consent document, any newly proposed consent documents and

revised research plan, the complete protocol including any protocol modifications previously approved by the IRB and a status report on the progress of the research. The information required in the status report is outlined below (also see Protocol Continuing Review policy):

- Summary of enrollment activity at UH and other sites, including withdrawals.
- A summary since the last IRB continuing review of all adverse events; unanticipated problems involving risks to participants or others; and protocol deviations ([IRB Policy, Event Reporting - Unanticipated Problems, Adverse Events and Protocol Deviations](#))
- A summary of subject complaints.
- Problems associated with the recruitment of participants.
- A summary of the study findings, including results and publications; and an assessment as to whether the risks and benefits of the research have changed.
- Any relevant publications/data that would affect the risk/benefit ratio.
- Data and Safety Monitoring Committee/Board and Data and Safety Monitors' reports, including interim findings and recommendations.
- Trial reports from multi-center sites.
- A change in investigator conflict of interest.
- A description of approved amendments since the last review.
- A description of the plans for the coming year.

All other IRB members will receive and review the continuing review application (investigator checklist), the current informed consent document, any newly proposed consent documents and revised research plan, the complete protocol including any protocol modifications previously approved by the IRB and a status report on the progress of the research, in enough depth to be familiar with them and be prepared to discuss them at the convened meeting.

If a study has expired because the IRB has not granted continuing approval by the expiration date (regardless of whether the application materials have been received by the expiration date), a member of the IRB staff will send a correspondence to the investigator to inform them that all research activities must cease once the study expires. In addition, clarification as to whether any research activities have occurred after the expiration date is requested from the investigator. The correspondence, together with the investigator response is placed in the IRB file. The information is copied and distributed to all IRB members at the IRB meeting when the study is reviewed; or in case of expedited review it is provided to the IRB member performing the review.

#### Amendments/Modifications to Previously Approved Research: Information Received and Reviewed by IRB Members

The primary and secondary reviewer will receive and conduct an in-depth review of the amendment application (investigator checklist), all modified documents with the changes highlighted, all relevant currently IRB approved documents (approved consent, research

plan) the investigator's written explanation for the changes, and a clean copy of the revised documents. All other IRB members will receive and review the amendment application (investigator checklist), all modified documents with the changes highlighted, all relevant currently IRB approved documents (approved consent, current protocol), the investigator's written explanation for the changes, and a clean copy of the revised documents in enough depth to be familiar with them and be prepared to discuss them at the convened meeting.

Additional Information Available to IRB Members:

Before and after the meeting IRB members may come to the IRB office to obtain the complete IRB protocol file, meeting minutes, and information provided to the primary reviewers. IRB staff will make these items available to them upon request.

During the meeting, IRB members may ask the IRB staff for a copy of the protocol file, meeting minutes, and information provided to the primary reviewers. IRB staff will make these items available.

Each month a copy of the Report of Administrative Actions for the preceding month is distributed to the members of the IRB for review. The report is reviewed and voted on at the IRB meeting.

## **B) Reviewer System**

Each protocol on an IRB agenda will be assigned a primary and secondary reviewer. The IRB staff will assign a primary and secondary reviewer to each protocol. The IRB Director or Manager is responsible to ensure that at least one of these two reviewers has the required scientific and scholarly expertise required to review the protocol. If the research is a treatment protocol, the IRB staff must assign a physician or nurse as the primary reviewer. If a primary or secondary reviewer with the appropriate scientific or scholarly expertise and background is not available, the IRB Vice-President of Research or IRB Manager either refers the protocol to another IRB in the Case HRPP, or will utilize an appropriate consultant as described in the standard operating procedures in the "[Membership](#)" policy.

The primary reviewer is responsible to review all materials in depth and present the research proposal at the meeting of the IRB. The secondary reviewer is responsible to review all materials in depth, substitutes for the primary reviewer if the latter is absent at the meeting, and otherwise provides an additional level of review and discussion. After the primary and secondary reviewers have presented their comments, all Board members discuss the documents received for review and add their comments.

## **C) Quorum and Voting**

A majority of IRB members and at least one member, whose primary concerns are in nonscientific areas must be present at a convened IRB meeting. Each action to be reviewed and voted upon requires a quorum, which is defined as the presence of at least 51% of the voting members. A protocol must receive approval of a majority of the

members present at a meeting for it to be approved. The IRB Chair or a member of the IRB Office staff is responsible for monitoring the members present at convened meetings to determine that the meetings are appropriately assembled and remain appropriately convened. When quorum is lost during a meeting, the IRB must not take further actions or votes until the quorum is restored. If the quorum cannot be restored, the meeting adjourns. Abstentions count toward the quorum but not toward the required majority. The Chair abstains on each voted action, but counts towards meeting the quorum. However if the vote “for” or “against” an action is tied, the Chair will cast the deciding vote i.e., to vote “for” or “against” an action.

### **D) Criteria for IRB Approval of Research**

Initial Review Procedures:

Except for research that is exempted or waived under [45 CFR 46.101\(b\)](#) or [45 CFR 46.101\(i\)](#), all human subject research conducted under the Case HRPP will be reviewed, prospectively approved and subjected to continuing oversight and review at least annually by the IRB.

For the IRB to approve research it must determine that all of the following requirements are satisfied ([45 CFR 46.111](#) and [21 CFR 56.111](#)):

- Risks to subjects are minimized (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk; and (ii) whenever appropriate, by using procedures already being performed on subjects for diagnostic or treatment purposes.
- Risks are reasonable in relation to anticipated benefits, if any, and the importance of the knowledge that may reasonably be expected to result.
- Selection of subjects is equitable, taking into account the purposes of the research and the setting in which it is conducted.
- Informed consent will be sought from each prospective subject or the subject’s legally authorized representative in accordance with [45 CFR 46.116](#).
- Informed consent will be appropriately documented in accordance with [45 CFR 46.117](#).
- The research plan appropriately monitors the data collected to ensure safety of subjects.
- The subject’s privacy is appropriately protected and confidentiality of the subject’s data is maintained.
- Appropriate safeguards are included to protect the rights and welfare of subjects who are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, decisionally impaired, mentally disabled persons, or economically or educationally disadvantaged persons.

### **E) Actions of IRB**

The IRB will set conditions as recommended by OHRP, for the approval of research at a convened meeting. In cases where the convened IRB requests substantive clarifications or modifications regarding the protocol or informed consent documents that are directly

relevant to the determinations required by the IRB under HHS regulations at [45 CFR 46.111](#), IRB approval of the proposed research will be deferred, pending subsequent review by the convened IRB of responsive material. Only when the convened IRB stipulates specific revisions requiring simple concurrence by the investigator, will the IRB Chair, vice-Chairs or another IRB member designated by the Chair, subsequently approve the revised research protocol on behalf of the IRB under an expedited review process.

The IRB has established the following categories of actions to be taken on protocols (including new protocols, approved protocols at continuing review and amendments), reviewed at a convened IRB meeting:

### **1) Approved**

The protocol is approved as submitted with no changes. Approval is usually for one year; however, under certain circumstances (e.g., in high risk studies in which the risks and benefits of the approved research cannot be fully anticipated) the IRB may limit the approval interval to a shorter period of time or require that the research be reviewed after a specific number of subjects are studied.

### **2) Modifications Needed to Secure Approval, Pending Administrative (Expedited) Review**

The protocol is approved pending receipt and administrative review of additional information, which can include minor clarification or modification of the checklist, protocol, consent form, or supporting materials. To qualify for this category, the requested changes must be clearly delineated and not require substantial changes to the protocol or consent form. Written notification of required modifications will be sent to the investigator. The investigator must provide a point by point response to all the issues raised by the Board. If a consent form is modified, two copies of the new consent form must be returned with one copy showing all deleted and inserted text. The other copy incorporates all the changes. The responses and requested modified documents will be administratively reviewed by the Chair, Vice-Chair or another IRB member designated by the Chair, on behalf of the IRB; and if appropriate, an approval will be granted.

### **3) Deferred**

A protocol is deferred when the changes proposed or questions raised by the Board are significant enough to warrant re-review of the protocol at a subsequent Board meeting. The investigator will receive notification of the issues the IRB needs addressed or changed. If a protocol is deferred it will usually be reconsidered by the same Board that deferred it. In addition to deferring the protocol the IRB may ask for additional review by expert consultants ([IRB Policy, Membership](#)), or it may refer the protocol for an ethics consultation ([IRB Policy, Ethics Consultations](#)).

### **4) Disapproved**

If the protocol is judged to be lacking in scientific merit, if it raises ethical questions that cannot be resolved, or if it is decided that the risks outweigh the benefits to the subjects, the protocol will be considered unacceptable and disapproved. The investigator will be

notified in writing by the IRB including the reason(s) for the disapproval; however, a detailed critique of the protocol is not provided. The investigator may rewrite and submit the study as a new protocol.

## **F) Special Determinations by the IRB**

At Board meetings special determinations will be made, if appropriate, regarding pediatric risk, waiver of assent, waiver of informed consent, and waiver of written consent.

### **1) Pediatric Risk**

All studies involving children require IRB review in accordance with the provisions of [45 CFR 46 Subpart D](#). The IRB will determine the pediatric risk level of a protocol and document its determination by the appropriate Federal citation number in the minutes of the IRB meeting. The following determinations may be made according to Federal regulations:

#### **a) [45 CFR 46.404](#) Research not involving greater than minimal risk to the children.**

To approve this category of research, the IRB must make the following determinations:

- The research presents no greater than minimal risk to the children.
- Adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in DHHS regulations at [45 CFR 46.408](#).

#### **b) [45 CFR 46.405](#) Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child subjects involved in the research.**

To approve research in this category, the IRB must make the following determinations:

- The risk is justified by the anticipated benefits to the subjects.
- The relation of the anticipated benefit to the risk presented by the study is at least as favorable to the subjects as that provided by available alternative approaches.
- Adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in DHHS regulations at [45 CFR 46.408](#).

#### **c) [45 CFR 46.406](#) Research involving greater than minimal risk and no prospect of direct benefit to the individual child subjects involved in the research, but likely to yield generalizable knowledge about the subject's disorder or condition.**

In order to approve research in this category, the IRB must make the following determinations:

- The risk of the research represents a minor increase over minimal risk.
- The intervention or procedure presents experiences to the child subjects that are reasonably commensurate with those inherent in their actual, or expected medical, dental, psychological, social, or educational situations.

- The intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the disorder or condition.
- Adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in DHHS regulations at 45 CFR 46.408.

**d) [45 CFR 46.407](#) Research that the IRB believes does not meet the conditions of [45 CFR 46.404](#), [46.405](#), or [46.406](#), but finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.**

If the IRB believes that DHHS supported research does not meet the requirements of [45 CFR 46.404](#), [46.405](#), or [46.406](#), but finds that it presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, it may refer the protocol to DHHS for review.

Before submitting a protocol to OHRP, the IRB must determine that, in addition to meeting the requirements of 45 CFR 46.407(a) and other applicable sections of subpart D, the proposed research also meets all of the requirements of 45 CFR part 46, subpart A. The research may proceed only if the Secretary, DHHS, or his or her designee, after consulting with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following an opportunity for public review and comment, determines either: (1) that the research in fact satisfies the conditions of [45 CFR 46.404](#), [46.405](#), or [46.406](#), or (2) the following:

- The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.
- The research will be conducted in accordance with sound ethical principles.
- Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in DHHS regulations at [45 CFR 46.408](#).

Recent [OHRP guidance](#) for review of research classified as 407 by the IRB now states that OHRP will only review DHHS funded research. The DHHS position is:

“DHHS will consult with a panel of experts under 46.407 only when the proposed research is conducted or supported by DHHS. Note that if an institution has elected in its assurance to apply all of the subparts of 45 CFR part 46 to all of its human subjects research regardless of the source of support, and the IRB finds that the proposed research meets the conditions for review under 46.407, the IRB is not required to submit the protocol to OHRP for review if the research under consideration is not supported by DHHS. In such cases, OHRP recommends that the institution consult with appropriate officials at the relevant federal agency or department supporting the research. When such research is supported by a non-federal sponsor, OHRP recommends that the institution consider convening an independent

panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and provide an opportunity for review and comment by the local community where the research is to be conducted before deciding whether to proceed with the research.”

Protocols meeting the conditions of [45 CFR 46.407](#) also may be subject to Food and Drug Administration regulations under [21 CFR 50.54](#) if the protocols involve a clinical investigation of an FDA-regulated product. Other protocols may be subject to FDA regulation at [21 CFR 50.54](#) but not subject to DHHS regulations at [45 CFR 46.407](#). The reader is advised to consult with The FDA should be consulted in the event that the review process falls within FDA's regulatory purview.

## 2) Waiver of Assent

The assent plan and documentation of assent for minors must be recorded in the meeting minutes. The IRB will determine if the assent may be waived for all or some of the population, based on the justification provided by the investigator, and according to Federal regulations ([45 CFR 46.408](#)). This determination will be documented using the Federal citation number in the minutes of the Board meeting.

## 3) Alteration or Waiver of Consent

a) **Alteration/Waiver of Consent Approved under [45 CFR 46.116\(c\)](#)**  
The research could not practicably be carried out without waiver or alteration.

b) **Alteration/Waiver of Consent Approved under [45 CFR 46 116\(d\)](#)**  
Involves no more than minimal risk, does not adversely affect rights and welfare of subjects, research could not be carried out without waiver or alteration, and subjects may be provided with information regarding the study.

## 4) Waiver of Signed Consent

a) **Waiver of Signed Informed Consent Approved under [45 CFR 46.117\(c\)\(1\)](#)**  
The only record linking the subject and the research would be the consent document and the principal risk would be a breach of confidentiality.

b) **Waiver of Signed Informed Consent Approved under [45 CFR 46.117\(c\)\(2\)](#)**  
Research presents no more than minimal risk and involves no procedures for which written consent is normally required outside of the research context.

## 5) Waiver of Consent in Emergency Settings

The IRB will consider protocols that require waiver of informed consent for emergency research. There is a limited class of research that may be carried out in human subjects who are in a life-threatening situation and in need of emergency therapy for whom, because of the subject's medical condition and the unavailability of legally authorized representatives of the subjects, no legally effective informed consent can be obtained. In these situations a waiver of consent may be granted. The IRB has developed a detailed policy in these situations (IRB Policy, Decisionally Impaired Research Subjects). Protocols that request waiver of informed consent for research in emergency settings will

always receive convened Board review. These research activities must be conducted in accordance with FDA regulation 21 CFR 50 and will be carried out under an FDA investigational new drug application (IND) or an FDA investigational device exemption (IDE). The research plan and all associated research protocol materials must clearly identify that will include subjects who are unable to consent and provide ample justification (in compliance with 21 CFR 50) as to why these subjects should be enrolled in the research.

Because of the special regulatory limitations relating to research involving pregnant women, fetuses and human in-vitro fertilization ([45 CFR 46, Subpart B](#)), and research involving prisoners ([45 CFR 46, Subpart C](#)), this waiver is inapplicable to these categories of research. The policies are stated in FDA regulation [21 CFR 50.24](#) and the joint publication by DHHS and the FDA of “Waiver of Informed Consent Requirements in certain Emergency Research, Federal Register, 61:51531-3, 1996.” See also FDA Draft Guidance for Institutional Review Boards, Clinical Investigators and Sponsors: Exception from Informed Consent Requirements for Emergency Research Federal Register, 71:51198-9, 2006.

The waiver can only be applied to all subjects in a protocol and never to only some study participants and always requires Law Department approval. To qualify for this waiver:

- If the research is FDA-regulated, it must meet the requirements of [21 CFR 50.24](#), Exception from informed consent requirements for emergency research.
- If the research is not FDA-regulated, it must meet the requirements of the October 31, 1996 45 CFR 46 Waiver Of Informed Consent Requirements In Certain Emergency Research (see IRB policies *Emergency Use of Investigational Drug, Biologics*).
- In either case, if required by applicable regulations, the research plan will be submitted to the FDA or DHHS following IRB approval but in advance of its implementation.

#### **Requirements for Emergency Research Subject to FDA regulation.**

The IRB may review and approve a clinical investigation without requiring that informed consent of all research subjects be obtained if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following:

1. The human 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.
2. Obtaining informed consent is not feasible because: The subjects will not be able to give their informed consent as a result of their medical condition; The intervention

under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

3. Participation in the research holds out the prospect of direct benefit to the subjects because: Subjects are facing a life-threatening situation that necessitates intervention; 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 Risks associated with the investigation 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.
4. The clinical investigation could not practicably be carried out without the waiver.
5. 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 legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator shall summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.
6. The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with Federal Regulations. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible.
7. Additional protections of the rights and welfare of the subjects will be provided, including, at least: 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; Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits; Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results; Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and If obtaining informed consent is not feasible and a legally authorized representative 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 legally authorized representative, and asking whether he or she 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.
8. Procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative 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, and 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.
  9. If a legally authorized representative 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.
  10. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.
  11. All clinical investigation records, including IRB determinations and regulatory files, shall be retained by the IRB for at least 3 years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by the regulatory authorities, as applicable.
  12. Protocols involving 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 such protocols as protocols that may include subjects who are unable to consent. The submission of those protocols to the FDA in 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 investigations under this section may not be submitted as amendments to the existing IND/IDE.
  13. If an IRB determines that it cannot approve a request for exception from informed consent requirements in emergency research because the clinical investigation does not meet the criteria in the applicable Federal regulations or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation, which must disclose the information as required by applicable regulations.

**Requirements for Emergency Research Not Subject to FDA regulation.**

The IRB may review and approve a clinical investigation without requiring that informed consent of all research subjects be obtained if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following:

1. The research is not subject to FDA regulations; and

2. Item # 1 through item #8 as stated in the Requirements for Emergency Research Subject to FDA regulation as satisfied.

#### **6) Review of Sponsor-Investigator**

As detailed in the IRB Policy, Investigator Responsibility, investigator-sponsors are required to be knowledgeable of the additional regulatory requirements of sponsors and knew how to comply with them. In order to ensure the investigator-sponsor is knowledgeable about the additional regulatory requirements of sponsors and knows how to follow them, the IRB coordinator will verify that all Investigators and key study personnel have completed the required training upon receipt of a new IRB application. The IRB may request from the Principal Investigator (PI) additional documentation to assure the Investigators and key study personnel have adequate knowledge, processes, personnel, and facilities to conduct human subject research of investigational drugs, agents, biologics and devices. The IRB coordinator will not process IRB applications until all Investigators and key study personnel have completed the required training. The IRB coordinator will contact the PI or study contact when required training of all Investigators and key study personnel is incomplete and inform the PI that the study cannot be processed by the IRB until required training is complete. The IRB coordinator will document the name of the person called, the date called, the discussion and the response in the IRB database.

In addition to the initial assessment by the IRB coordinator, the Research Compliance Specialists from the Office of Research Compliance will monitor investigators holding an IND/IDE to determine compliance with FDA sponsor requirements. Investigational medical devices that involve electrical power and are not FDA approved or licensed for human use must be reviewed by the UH Electrical Safety Committee to determine that they are safe for use in or with human subjects.

#### **G) Determinations on Non-Compliance Issue or Allegation**

The IRB will review issues or allegations of non-compliance according to IRB policy ([IRB Policy, Non-Compliance with Human Subjects' Regulations](#)). The following determination will be made and documented in the minutes according to Federal regulations:

- Serious Non-Compliance
- Non-Serious Non-Compliance

#### **H) Minutes of a Convened Board Meeting**

It is the policy of IRB that the minutes of a convened Board meeting will contain the relevant information as stipulated by Federal regulations ([45 CFR 46.115\(a\)\(2\)](#) and [21 CFR 56.115\(a\)\(2\)](#)).

#### **1) Procedures for Documentation of IRB meeting Minutes**

An IRB non-voting staff member will attend each committee meeting and will draft detailed notes to document the discussions and determinations of the Board for each

agenda item. The Minutes of each IRB meeting will document the separate deliberations, actions, and votes for each protocol undergoing initial or continuing review by the convened IRB, and the vote on all IRB actions including the number of members voting for, against, and abstaining. The minutes must be sufficient in detail to demonstrate:

Attendance at the meeting for each IRB action, to include:

- If an alternate is present and who they are representing.
- The initial and continued presence of a majority of members (quorum), including at least one non-scientist.
- If a consultant is present

For each protocol discussed, the minutes must document:

- If a Committee Member is excused from the meeting due to a conflict of interest during the discussion and vote on the study. The name of the committee member is also recorded.
- Actions taken by the IRB (e.g. approved; modifications required to secure approval; deferred; and disapproved)
- The discussion of any controversial issues and their resolutions, and documentation of a consultant's findings.
- The basis for required changes in research;
- The basis for disapproving research.
- The level of risk involved in the research (e.g., minimal or greater than minimal risk).
- The approval period for initial and continuing review.
- Justification for any change in study design or risk level for amendments, including those submitted with the continuing review.
- The vote on the actions including the number of voting "for; against; and abstaining." In order to document the continued existence of a quorum, votes should be recorded in the minutes using the following format: Total = xx, For: xx, Against: xx, and Abstained: xx. (Board members who abstain are identified by name in the minutes.) Determinations required by the regulations (e.g., waiver or alteration of informed consent; research involving pregnant women, human fetuses, or neonates; research involving prisoners; research involving children); and protocol specific findings justifying those determinations.
- The IRBs rationale for significant risk/non-significant risk device determinations.
- Justification of deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample informed consent document.

When the suspension of an approved protocol is considered, documentation of the discussion to allow for continued treatment of enrolled subjects must be included.

## **2) Chairman's Report**

The minutes document items announced and discussed during the Chairman's report. These include the addition or resignation of Board members; articles related to IRB

issues for education purposes; continuing education meetings; and the Board review and approval of IRB policies and submission forms.

### **3) Report of Administrative Actions**

The Report of Administrative Actions is a monthly report of the actions taken by the IRB using the expedited review procedures; and includes a listing of the approved protocols (new studies; continuing reviews; and addenda to approved protocols). Each month, the report is reviewed by both Boards at a convened meeting. The IRB will make the determination whether to accept the administrative actions listed on the report. If the IRB votes not to accept any of the actions, e.g., the approval of a protocol; then the items must be brought to a subsequent Full Board meeting for additional review and discussion.

The review and vote of acceptance is documented in the minutes as: Total = xx, For: xx, Against: xx, and Abstained: xx.

### **4) Distribution and Approval of the Minutes**

Draft minutes will be prepared by a member of the IRB staff and forwarded to the meeting Chair for review. At the request of the meeting Chair, additional Board members who were present at the convened meeting may be asked to review sections of the minutes before they are finalized. After review by the meeting Chair, the IRB Coordinator will make the necessary revisions and sign the document. The Board members will receive copies of the minutes with a subsequent meeting packet. The minutes will be reviewed at a convened meeting of the Board that generated the minutes. Any requested revisions will be discussed and incorporated in the minutes. The approval of the finalized minutes will be documented in the minutes of the meeting, along with documentation of the vote (i.e., the number of votes “for,” “against,” and “abstaining”) if it is not unanimous.

A signed copy of the approved finalized minutes will be retained in the IRB meeting minutes file. The minutes will be forwarded to the Vice-president of Research and Technology, who will forward the document to the Chief Medical Officer and the UH Clinical Council.

### **I) Notification of Action and Review of Responses**

When the IRB approves a protocol or an Exemption application, written notification in the form of an approval letter is sent to the Principal Investigator/Responsible Investigator from the IRB Administrative Office. When the IRB requires major or minor modifications to secure approval, written notification of the IRB’s action, together with the reason(s) for its decision are provided to the Principal Investigator/Responsible Investigator. The results of IRB actions are conveyed in writing usually within one week of the meeting at which the protocol was considered. Furthermore, when a primary reviewer (either through Full Board or expedited review) determines that additional modifications or clarifications are required, these are also forwarded in writing to the Responsible/Principal Investigator. All communications are sent by the IRB Administrative staff.

The investigator must respond to all IRB requests and enquiries in writing or in person. When an investigator responds to the IRB actions, these correspondences are reviewed by the IRB members to determine whether the information provided satisfies the Board's requests and the criteria for IRB approval. The information can be reviewed administratively by expedited review (when the investigator has agreed to the changes requested by the IRB or the protocol is eligible for review using the expedited procedure). Otherwise, the modifications are reviewed by the convened IRB.

When the IRB disapproves a protocol, the Principal Investigator/Responsible Investigator is provided with written notification for the reason(s) for the disapproval; however, a detailed critique of the protocol is not provided. The investigator is instructed to contact the IRB office with any questions. An investigator may rewrite and submit the study as a new protocol if they wish, but must take in to account the Board's concerns and reason(s) for the disapproval of the protocol.

A copy of all findings and actions of the IRB, either during Full Board or Administrative review, are provided in writing to the Vice-President of Research and Technology. They are subsequently sent and presented to the Chief Medical Officer and the UH Clinical Council. They are reviewed and administratively noted. The Institutional Official on the UH Federalwide Assurance, is also the President and Chief Executive Officer for UH, and a member of the UH Clinical Council.

### **J) Investigators at IRB Meetings**

IRB meetings are not open to investigators. The IRB, in rare cases, may invite an investigator to attend during part of the discussion of his or her protocol to respond to questions from members of the IRB or provide additional information. The investigator would not be present during the final discussion about the protocol or the protocol vote.

### **K) Visitors at IRB Meetings**

A visitor is anyone who is not a voting or non-voting member of the IRB, or an employee of the Office of Institutional Review. Visitors may attend an IRB meeting with the approval of the Chair of the meeting. Visitors may not be present during discussions and voting on compliance issues. Visitors who attend meetings of the IRB must sign an IRB Form, Board Meeting Visitor Confidentiality Agreement. Copies of signed Confidentiality Agreements will be kept on file in the Office of Institutional Review.

### **L) Study Closure for Lack of Response**

If a protocol has been given contingent approval with a request for minor changes; or has been deferred, a written letter outlining the required changes or reasons given for the action will be sent to the investigator. The investigator has 90 days from the time of the IRB meeting at which the protocol was considered to respond in writing to the changes requested by of the IRB. If the investigator does not respond in writing within 60 days from the time of the IRB meeting, a reminder letter will be sent. If the investigator does not respond in writing in 90 days, the protocol will be closed by the IRB. A written

notice of study closure for lack of response will be sent to the investigator and placed in the protocol file. If the investigator wishes to seek approval for the study, a new protocol must be submitted and approved. If there are unusual circumstances that prevent a timely response to requested changes, the principal investigator can request an extension of time to respond.

### **M) Length of Time of Approvals**

The DHHS and FDA regulations require reevaluation of approved research at intervals that are appropriate to the degree of risk, but not less than once a year [45 CFR 46.109\(e\)](#) and [21 CFR 56.109\(f\)](#). At UH, the maximum approval period for new protocols and the re-approval of studies at continuing review, is one year minus one day. It is important to note, that IRB approval is a temporary authority and may be withdrawn at any time if warranted by the conduct of the research activities.

When determining the approval period of protocols at initial and continuing review, the Board determines whether the estimate of the investigator's assessment of the anticipated results, risks and procedures are reasonable; whether the risk/benefit ratio is appropriate and accurate; and whether there is an adequate plan for monitoring the data collected to ensure subjects safety.

The IRB recognizes that protecting the rights and welfare of subjects sometimes requires that research be reviewed more often than annually. For example, when a highly vulnerable subject population is being researched, the risks may not be completely known at initial review. The IRB shall monitor the research project closely, and require more frequent than annual review. The IRB shall consider the following factors in determining the criteria for which studies require more frequent review and what the timeframes generally will be:

- Probability and magnitude of anticipated risks to subjects.
- Likely psychological condition of the proposed subjects.
- Overall qualifications of the Responsible Investigator and other members of the research team.
- Specific experience of the Responsible Investigator and other members of the research team in conducting similar research.
- Nature and frequency of adverse events observed in similar research at this and other facilities.
- Vulnerability of the population being studied.
- Other factors that the IRB deems relevant.

In specifying an approval period of less than one year, the IRB may define the period with either a time interval or a maximum number of subjects (i.e., after 3 months or after three subjects enrolled). The Office for Human Research Protections recommends that the minutes clearly reflect these determinations regarding risk and approval period.

The approval date is determined by the date which the research was reviewed and approved by the full Board. If the full Board requests modifications to secure approval which can be administratively approved, the approval date is calculated from the date that the protocol was reviewed at full Board approval, and not the date the changes were administratively approved. The expiration date is one day less than the period of approval, e.g., if the approval period is for one year starting April 14, 2006 then the study will expire at midnight on April 13, 2006.

For protocols approved by expedited review, the expiration date is also one day less than the period of approval that is awarded by the IRB Chair, Vice-Chair, or designated senior IRB member. When amendments are approved, the expiration date of the protocol does not change. The approved consent form will have the IRB approval stamp stating the expiration date of the protocol.

### **N) Authorized Signatures**

The Chair or Vice-Chair of the IRB signs approvals for protocols. In the absence of the Chair and Vice-Chairs, the Chief Medical Officer of UH or designated senior IRB member may sign an IRB approval.

### **O) Research Conducted at Multiple Sites**

Cooperative research projects are projects which involve more than one institution ([45 CFR 46.114](#) and [21 CFR 56.114](#)). The UHCMC IRB approves projects that have performance sites at locations other than UHCMC that do not have an IRB. For these projects the UHCMC IRB accepts primary responsibility for safeguarding the rights and welfare of human subjects and for complying with IRB regulations. This same level of responsibility applies when the UHCMC IRB serves as the IRB of Record for another institution. The IRB also has inter-institutional agreements with other Case affiliated institutions that have OHRP registered IRB's. (IRB Policy, Purpose and Scope) These agreements allow the UHCMC IRB to consider expedited review for protocols previously approved by IRB with cooperative agreements ([IRB Policy, Expedited Review](#)). In this case the responsibility for safeguarding the rights and welfare of human subjects is shared by both IRBs and significant issues with such protocols are shared with the other IRB. The UHCMC IRB also has a formal agreement with the National Cancer Institute for the NCI IRB to serve as the IRB of Record for Phase 3 cancer trials that it initiates and where UHCMC is a performance site. The UHCMC IRB can approve these protocols, and their continuing reviews, using expedited review procedures. The UHCMC IRB has primary responsibility for safeguarding the rights and welfare of human subjects enrolled at UHCMC with the NCI IRB having primary responsibility for supervising overall study safeguards.

### **P) Recruiting and Evaluation of IRB Staff**

IRB staff are selected and evaluated in accordance with the UHHS Policies [HR-75](#) and [HR-73](#). All IRB positions are posted internally and on the UHHS Career Center website and may be listed in UHHS media advertisements. Applicants are selected for employment on the basis of their qualifications for a given position as defined in the Job

Description. Human Resources reviews all candidates and refers the most qualified candidate(s) to the appropriate manager for further review and possible personal interviews. The department manager, in conjunction with Human Resources, will make the selection of the final applicant and the official job offer will be made by Human Resources. In all instances, the applicants with the most applicable experience, skills, and demonstrated ability will be selected for the position.

All IRB staff will be reviewed on an annual basis. During the performance appraisal and competency review process the manager and employee will review the duties, standards, expectations of the position and job performance rating. Appropriate feedback will be given to the employee.