Standard Operating Procedure: Utilizing a Single or External IRB Mechanism

PURPOSE

The purpose of this document is to provide guidance to investigators about how to utilize a single or external IRB.

PROCEDURE

Federal regulations [45CFR46.103(a)] require that each institution “engaged” in research must have an assurance of compliance with the Office of Human Research Protections (OHRP), unless the research is exempt. Moreover, a registered Institutional Review Board (IRB) must review all such research. MD Anderson has both an assurance and registered IRBs for research conducted by MD Anderson faculty, staff, and students.

Both OHRP and the FDA permit an IRB the option to rely on the review of another IRB. When this is the intention, the two institutions enter into an agreement referred to variously as either a Cooperative Agreement or an IRB Reliance Agreement (see Types of IRB Agreements). These agreements are executed between a Reviewing IRB and one or more Relying Institutions. The agreements can be for a single research study or for multiple studies (e.g., a Master Reliance Agreement).

MD Anderson investigators collaborating in research at an external site where no MD Anderson participants, data or biospecimens will be involved must still submit the research to the MD Anderson IRB for approval and provide documentation that IRB approval has been obtained at the external site(s). The MD Anderson IRB will review the investigator’s role in the research project to determine whether MD Anderson is engaged in research, and to assure that all IRB requirements have been met. The IRB will consult with ancillary reviewers, Legal Services, and/or Institutional Compliance, as needed.

The MD Anderson IRB does not provide regulatory oversight for an external site participating in human subjects research that does not involve an MD Anderson faculty, staff or student. Investigators considering requesting reliance on another IRB should contact the MD Anderson IRB early in the research proposal process. Decisions about whether to permit reliance on another IRB shall be determined by the Institutional Official (IO), after review and recommendation by the IRB and the OHSP Director/Associate Director. MD Anderson may rely on another appropriately constituted IRB for the review of cooperative research projects under the conditions set forth below.

In deciding whether or not to rely on another IRB, the IO will consider the following criteria:

- Whether the use of a Central IRB mechanism has been mandated by the study sponsor.
- The number of proposed studies involved in the collaboration.
- The anticipated level of risk associated with proposed studies.
• Whether the reviewing IRB’s policies and procedures meet MD Anderson standards. If the other IRB is AAHRPP accredited, then it will be presumed that the MD Anderson IRB standards are being met; however, accredited status does not in itself necessarily suffice as a basis for the IO’s decision.
• The outcome of any internal or federal audits conducted on the IRB in the previous 5 years prior to IRB review.
• The type and outcome of any federal reporting to regulatory agencies for non-compliance for studies which the IRB has oversight, or for the IRB specifically.
• The internal quality assurance and monitoring measures the IRB or institution has in place to monitor compliance with federal regulations, institutional policies and procedures.
• The location where the interventional human research activities will take place.
• The capacity of the other institution and its IRB to sufficiently be informed about the MD Anderson local research context and applicable laws and regulations.
• Approval of MD Anderson for any cases where the requesting IRB will be serving as the HIPAA Privacy Board.

In order to initiate discussions with the institution requesting the reliance agreement, the MD Anderson investigator must provide the MD Anderson IRB with: 1) contact information for the collaborating institution’s IRB, 2) a draft version of the agreement (if available from the external site) and standard operating procedures, and 3) a copy of the Local Considerations Form. The OHSP Director or his/her designee will ensure that the finalized agreement is appropriately signed by the IOs for the involved institutions. Copies of all agreements will be maintained in OHSP.

In order to maintain an accurate record of studies being done at the institution, as well as to manage required ancillary reviews, investigators are required to submit a PDOL application. The protocol will be required to go through the MD Anderson scientific review process unless the investigator can provide written documentation that an extensive scientific review has been conducted at an external site. The MD Anderson IRB will be notified of the submission once the scientific review process and ancillary review process has been completed.

The investigator will need to submit the following to the MD Anderson IRB: 1) documentation that continuing review has been completed by the external IRB; 2) changes to the research plan including study team changes; 3) any reportable events including unanticipated problems or incidences of non-compliance; 4) submission of a PDOL PI Generic Memo that includes a request for the MD Anderson IRB to rely on the single IRB and the rationale for the request OR a request for the MD Anderson IRB to be the single IRB and the rationale for the request.

Investigators should reference the attached Responsibilities Matrix for Utilizing a Single or External IRB Mechanism and an IRB Authorization Agreement for additional requirements.

When MD Anderson Serves as the IRB for Another Organization

Investigator Procedures

The MD Anderson investigator will be responsible for assuring that the external organization’s role in the protocol is clearly delineated (see Responsibilities Matrix for Utilizing a Single or External IRB Mechanism and an IRB Authorization Agreement). As part of the IRB submission, the investigator should include the following:
• Protocol describing components of the research that the external site will be involved in.
• Name of the primary investigator at the external organization that will oversee the research.
• Local Considerations Form that has been completed by the external site’s IRB or primary investigator/research team.
  o Study Team Information
  o Community Considerations
  o Study-Specific Local Requirements
  o Consent Forms
  o Additional Local Considerations
  o Conflict of Interest Concerns
  o Signatures/Approvals
• Written statement from the external site requesting to cede oversight to the MD Anderson IRB. This statement is required to be approved or signed by the external site’s IRB Official (usually the IRB Director or Vice President for Research).
• PI Survey for the external site that has been completed by the external primary investigator/research team. The PI Survey includes information that the external collaborator must provide including:
  o Study Team Information
  o Study team training and education
  o Study Team Information including Conflict of Interest information
  o Site Specific Plans for Recruitment, Consenting, and Data and Safety Monitoring
  o Signatures/Approvals

IRB Procedures

The MD Anderson IRB review will include a process for reviewing external sites and providing a determination of their review to the MD Anderson investigator and the IRB of the external site.

The MD Anderson IRB will:
• Review requests to add research sites (see Policy on IRB Revision Procedures to Previously Approved Research Protocols)
• Review conflict of interest management plans from external site, if applicable. The IRB may place additional monitoring requirements on the research to protect the safety of participants. The IRB may also confer with the external site’s conflict of interest committee or the MD Anderson Conflict of Interest Committee, as needed.
• Assure documentation of IRB review at the external site is on file;
• Obtain a consultation from an individual familiar with the cultural background, local context, and community attitudes of the location in which the research is being conducted in order to meet its local context review requirements, if necessary;
• Review the contract, grant or other agreement as necessary;
• Evaluate the need for other types of agreements with external site(s);
• Require training, as necessary, of external site staff participating in research;
• Consult Institutional Official for review and approval of arrangements with the external site(s), as necessary.
• Follow its reporting requirements for review of unanticipated problems, participant complaints, protocol deviations, and other events.
• Follow its process for communicating suspension or termination of IRB approval including notification the external site’s primary investigator and IRB.
Relying IRB
- Report timely Unanticipated Problems, Serious Non-Compliance
- Provide Institutional Profile and Local Considerations Form
- Provide HIPAA information
- Provide COI information

Reporting Research-Related Reportable Events and Communication Procedures

Investigators are expected to adhere to the MD Anderson IRB reporting requirements for unanticipated problems, participant complaints, protocol deviations, and other events (see IRB Policy on Reporting Deviations, Protocol Violations and Unanticipated Problems and the MD Anderson Human Subjects Research Protection Program Policies and Procedures Manual (HRPP Manual) - Chapter 7). External site investigators are required to submit research-related events to the MD Anderson investigator in accordance with the MD Anderson policy. The MD Anderson investigator is responsible for submitting reportable events to the MD Anderson IRB in accordance with the MD Anderson IRB reporting timeframes.

The MD Anderson IRB will follow the MD Anderson IRB policy when reviewing reportable events and making determinations. IRB determinations regarding reportable events will be submitted to the MD Anderson investigator and the external site’s IRB.

The MD Anderson IRB will confer with the external site’s IRB if an event requires reporting to federal regulatory agencies, however, the IRB will report to the agency within the timeframe outlined in the MD Anderson IRB policy.

The external site’s IRB may request minutes of IRB determinations and outcome letters by submitting a request to the MD Anderson IRB. IRB policies will be provided to the external site’s IRB during the initial IRB review of the site. The MD Anderson IRB will provide a copy of any changes to IRB policies to the external site’s IRB, as applicable. MD Anderson investigators are expected to communicate directly with the external site’s investigator and research team and to provide copies of the protocol and related documents, standard operating procedures and relevant policies throughout the protocol lifecycle.

The Local Considerations Form that is provided to the external site’s investigator and IRB at the time a site is added to the protocol will include the contact information for the MD Anderson IRB and the Institutional Official. External sites are encouraged to communicate with the MD Anderson IRB to express concerns or convey suggestions regarding the IRB process.

When MD Anderson Relies Upon Another Organization’s IRB

The MD Anderson investigator must assure that the protocol is submitted to both the MD Anderson IRB and the external site’s IRB for approval prior to activation. When a collaborator is involved, the collaborator at the external site may take responsibility for submitting the application to their IRB since they will be most familiar with their IRB’s submission process.

In some cases, the MD Anderson IRB staff may be required to initiate the external IRB review process. In these instances, the MD Anderson IRB staff will submit the initial protocol to the external IRB, however the MD Anderson investigator will remain responsible for assuring that the external collaborator receives a copy of the protocol and related documents, and for submitting subsequent submissions including modifications to the external IRB.
Investigator Responsibilities

In either scenario, the investigator should submit the following documents to both the MD Anderson IRB and the Reviewing IRB:

- Protocol and other documentation (including institutional biosafety committee, scientific review documentation, etc.)
- Informed consent document and any patient-facing materials including recruitment material
- Local Considerations Form completed by OHSP (unless the Reviewing IRB has provided a specific form to capture this information). The MD Anderson investigator will be required to assist in the completion of this form.
- Information regarding conflicts of interest related to the research including a copy of any conflict of interest management plans.
- Reviewing IRB specific intake form
- Comply with determinations of the Reviewing IRB
- Comply with institutional requirements
- Report unanticipated problems and incidences of non-compliance to both the MD Anderson IRB and the Reviewing IRB as per the IRB policies.
- Not initiate study until IRB has provided approval

See the External IRB Submissions SOP and External IRB Submissions for Studies with an Institutional Conflict of Interest SOP for institutional requirements not specific to IRB review such as the inclusion of protocol documents within the MD Anderson electronic system for accessibility by other MD Anderson central offices such as Clinical Research Finance, Investigational Pharmacy, etc. This allows for the implementation/activation of a protocol once IRB approved by the external IRB.

OHSP Responsibilities (in coordination with the MD Anderson IRB)

For protocols where MD Anderson will not serve as the Reviewing IRB, OHSP staff will conduct an abbreviated review of the protocol to confirm that MD Anderson IRB and institutional requirements are met. The OHSP staff will serve as the facilitator for the institutional ancillary review process. The OHSP staff review will include:

- Assure that all protocol documentation submitted to the external IRB are included in the MD Anderson electronic system
- Assure that the MD Anderson local context information is included in the informed consent document
- Assures that the Institutional Conflict of Interest Management plan is submitted to the Reviewing IRB in the event of an Institutional Conflict of Interest
- Assures ancillary reviews are complete prior to submission to the Reviewing IRB
- Assure documentation of IRB review at the external site is on file; Evaluate the need for other types of agreements with external site(s);
- Confirm Institutional Official approval of the IRB Reliance Agreement

Reviewing IRB Responsibilities

The Reviewing IRB will serve as the IRB for the protocol. MD Anderson will assure that the Reviewing IRB performs the following functions:
• Review and approve the protocol and related documents including the informed consent document, patient-facing material and recruitment material prior to implementation
• Review protocol modifications
• Review requests to add research sites
• Review conflict of interest management plans for MD Anderson investigators, if applicable.
• Obtain a consultation from an individual familiar with the cultural background, local context, and community attitudes of the location in which the research is being conducted in order to meet its local context review requirements, if necessary
• Review the contract, grant or other agreement as necessary
• Require additional training, as necessary
• Consult the MD Anderson IRB or MD Anderson Institutional Official, as necessary.
• Follow its reporting requirements for review of unanticipated problems, participant concerns and incidences of non-compliance

Reporting Research-Related Reportable Events and Communication Procedures

Investigators are required to adhere to the Reviewing IRB’s policy for submitting reportable events. A copy of the reportable event should be submitted to the MD Anderson IRB at the same time the event is submitted to the Reviewing IRB. The Reviewing IRB will make a determination on the event. The Reviewing IRB’s determination must be submitted to the MD Anderson IRB as soon as it is received. The MD Anderson IRB will confer with the Reviewing IRB regarding any events that require reporting to federal regulatory agencies, or if there are questions regarding the IRB determinations.

The MD Anderson IRB will request minutes from the Reviewing IRB, as needed.

The Local Considerations Form that is provided to the Reviewing IRB will include the contact information for the MD Anderson IRB and the Institutional Official. External sites are encouraged to communicate with the MD Anderson IRB to express concerns or convey suggestions regarding the IRB process.

MD Anderson has established an Advisory Committee for Review of Events Occurring Under External IRB Oversight that reviews submissions to the CIRB of local serious or continuing noncompliance and UPs. The Institutional Official has given this committee the authority to review these reports for externally IRB reviewed studies. As such, the committee may recommend reporting to appropriate regulatory agencies in the event that serious or continuing noncompliance has occurred, or may recommend that the Institutional Official take other actions in order to protect the safety of MD Anderson participants.

Shared Oversight of Research

In a multicenter research study, the individual or group of individuals charged with study oversight, coordination and overall conduct need to be identified. Those responsible could be simply the study Principal Investigator or there could be a more formal study Data Coordinating Center. In addition, oversight may be the responsibility of a single entity or divided between multiple organizations. For industry sponsored studies the study sponsor or their designated CRO(s) (contract research organization) are required by the FDA to provide trial oversight.

When one or more IRBs are responsible for providing regulatory oversight of the protocol, responsibilities of each IRB must be clearly delineated in an IRB Authorization Agreement.
Depending on the nature and complexity of the protocol, the IRB Authorization Agreement will address the following areas:

- Providing education to researchers and research staff.
- Conducting scientific review.
- Ensuring concordance between any applicable grant and the IRB or EC application.
- Reviewing potential non-compliance, including complaints, protocol deviations, and results of audits:
  - Identifying which organization is responsible for deciding whether each allegation of noncompliance has a basis in fact.
  - Identifying which organization’s process is used to decide whether each incident of noncompliance is serious or continuing.
  - Obtaining management plans for researcher and research staff conflicts of interest. If the relying organization maintains responsibility for this issue, the management plan must be provided to the IRB in a timely manner prior to the decision by the IRB.
- Managing organizational conflict of interest related to the research.
- Ensuring that, should termination of a reliance agreement occur, one of the parties clearly is responsible for continued oversight of active studies until closure or a mutually agreed upon transfer of the studies.

The agreement is drafted by the OHSP Director in consultation with Legal Services and Institutional Compliance. The agreement is signed by the Institutional Official and is considered executed once all parties have signed and dated the agreement, and the signed agreement is on file in OHSP. Once the agreement has been executed, the research may commence.

**NIH Certificates of Confidentiality (CoC)**

In accordance with NIHGPS Chapter 15.2.1, federal award recipients are also responsible for ensuring that any subrecipient that receives funds to carry out part of the NIH award involving a copy of identifiable, sensitive information protected by a Certificate issued by this Policy understand they are also subject to subsection 301(d) of the Public Health Service Act. Investigators are responsible for adhering to the NIH CoC Policy when conducting research that is funded by NIH. Investigators should work with their collaborators at external sites to assure that the NIH CoC requirements are met.

For studies where the MD Anderson IRB serves as the Reviewing IRB, the IRB will determine whether a CoC needs to be completed, and will require that participating sites submit a CoC, as appropriate based on their role in the research. For studies where the MD Anderson IRB has ceded oversight, an administrative review of the study will be conducted to assure that the CoC requirements are met. The MD Anderson IRB will communicate with the Reviewing IRB, as needed.

Recipients of Certificates are required to ensure that any investigator or institution not funded by NIH who receives a copy of identifiable, sensitive information protected by a Certificate issued by the NIH Policy for Issuing Certificates of Confidentiality, understand they are also subject to the requirements of subsection 301(d) of the Public Health Service Act. In accordance with NIHGPS Chapter 15.2.1, recipients are also responsible for ensuring that any subrecipient that receives funds to carry out part of the NIH award involving a copy of identifiable, sensitive information protected by a Certificate issued by the NIH Policy for Issuing Certificates of Confidentiality understands they are also subject to subsection 301(d) of the Public Health Service Act.
For additional guidance, please feel free to contact the MD Anderson IRB Office by phone at 713-745-6477 or email IRB Help.

The full NIH CoC policy may be accessed here https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-109.html. The NIH website also has a helpful page on Frequently Asked Questions about CoCs or you may review information in the NIH Certificate of Confidentiality Kiosk.

NIH Genomic Data Sharing Policy

Investigators seeking NIH funding should contact appropriate Project Officer as early as possible to discuss data sharing expectations and timelines that would apply to their proposed studies. NIH expects investigators and their institutions to provide basic plans for following this Policy in the “Genomic Data Sharing Plan” located in the Resource Sharing Plan section of funding applications and proposals. Any resources that may be needed to support a proposed genomic data sharing plan (e.g., preparation of data for submission) should be included in the project's budget. A more detailed genomic data sharing plan should be provided to the funding IC prior to award. The Institutional Certification (for sharing human data), should also be provided to the funding IC prior to award, along with any other Just-in-Time information. NIH expects intramural investigators to address compliance with genomic data sharing plans with their IC scientific leadership prior to initiating applicable research and are encouraged to contact their IC leadership or the Office of Intramural Research for guidance. The funding NIH IC will typically review compliance with genomic data sharing plans at the time of annual progress reports or other appropriate scientific project reviews, or at other times, depending on the reporting requirements specified by the IC for specific programs or projects.

The MD Anderson IRB will provide the Institutional Certification as required by the NIH Genomic Data Sharing Policy. In the instances where the single IRB (sIRB) for the grant is not the MD Anderson IRB but the biospecimens used to generate the data to be deposited into the NIH repository were collected as part of an IRB protocol and consent document where the MD Anderson IRB was the IRB of record, the MD Anderson IRB will provide the Institutional Certification.

The Office of Research Administration/Office of Sponsored Programs will ensure that the proposed genomic data sharing plan is available and will be provided to the NIH if MD Anderson is lead on the grant. If the MD Anderson IRB is providing the Institutional Certification, the MD Anderson IRB will review the genomic data sharing plan and the consent document as well as the Institutional Certification form to ensure that they all align.

REFERENCES

• Utilizing an IRB Agreement or Authorization and Definitions
• PI Survey, Institutional Profile and Local Considerations Form
• Communications Plan for Single IRBs
• Responsibilities Matrix for Utilizing a Single or External IRB Mechanism and an IRB Authorization Agreement
• CIRB_New Submission_Workflow
• CIRB_Amendments_Workflow
• Overall Principal Investigator/Lead Study Team Guidance and Checklist
## REVISIONS

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