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Chapter 1 - The Human Research Protection Program (HRPP)

The University of Texas MD Anderson Cancer Center (MD Anderson) has and follows written policies and procedures setting forth the ethical standards and practices of the Human Research Protection Program. Relevant policies and procedures are made available to Sponsors, Researchers, Research Staff, research participants, and the Institutional Review Board, as appropriate. (AAHRPP Element I.1.D)

Chapter 1. The Human Research Protection Program (HRPP)

The MD Anderson Human Research Protection Program (HRPP) Manual provides information about the organization, scope, authority and responsibilities associated with the MD Anderson HRPP for the research community at MD Anderson and its affiliates, and explains how the HRPP has been incorporated into one core document.

MD Anderson has and follows written policies and procedures for determining when activities are overseen by the Human Research Protection Program. (AAHRPP Element I.1.A)

1.1 Organizations Covered by the HRPP

MD Anderson and any organizations listed in MD Anderson’s Federalwide Assurance (FWA) are for purposes of the HRPP covered by this HRPP Manual. Each organization listed in MD Anderson’s FWA has an agreement with MD Anderson under which MD Anderson’s IRB provides oversight of human subjects research at such organization.

1.2 Goal and Objectives of the HRPP

The goal of the HRPP is to protect human research participants by ensuring that in all MD Anderson research:

- The rights and welfare of human research participants are adequately protected.
- Such research is guided by the ethical principles of respect for persons, beneficence, and justice as set forth in the Belmont Report, and is conducted with the highest level of expertise and integrity.
- Such research complies with applicable laws.

Objectives of the HRPP

The HRPP includes mechanisms to:

- Establish a formal process to monitor, evaluate, and continually improve the protection of human research participants and dedicate resources sufficient to do so.
- Exercise oversight of research protection.
- Educate investigators and research staff about their ethical responsibility to protect research participants.
- When appropriate, intervene in research and respond directly to concerns of research participants.

Written Plan for the HRPP
The written plan for the HRPP is comprised of policies, guidance, and supporting documents governing human subjects research and the protection of participants. The HRPP is approved by the Vice President, Clinical Research Administration who serves as MD Anderson’s Institutional Official for human research protection. Documentation comprising the HRPP is available on the Office of Clinical Research Administration Website as well as its component Departments (see MD Anderson HRPP Components).

**MD Anderson delegates responsibility for the Human Research Protection Program to an official with sufficient standing, authority, and independence to ensure implementation and maintenance of the program. (AAHRPP Element I.1.B)**

**MD Anderson has and follows written policies and procedures for determining when activities are overseen by the Human Research Protection Program. (AAHRPP Element I.1.A)**

### 1.3 Delegation of Responsibility for MD Anderson HRPP Implementation

For the organizations covered by the HRPP, the President of MD Anderson delegates the primary responsibility to the Vice President, Clinical Research Administration to establish, maintain, and oversee the HRPP (see Delegation of Authority for the Human Research Protection Program).

MD Anderson considers the HRPP Manual to be a dynamic document, because the scientific developments, ethical issues, and regulatory circumstances that shape it are continuously evolving and improving. The Office of Human Subjects Protection (OHSP) maintains policies and written procedures reflecting the current practices of the IRB in conducting reviews and approvals of human research. As part of the OHSP Continuous Quality Improvement (CQI) program, the Director in the OHSP, in consultation with senior HRPP staff and the IRB Chair(s) regularly reviews (i.e., at least annually) and refines the HRPP Manual and written procedures and makes recommendations for modifications, or develops new policies and procedures as appropriate. The Vice President, Clinical Research Administration may approve a modification of any portion of the HRPP Manual. The OHSP Director may approve modifications to the HRPP Manual that relate to the day-to-day review and operational functions of the IRB; other modifications of the HRPP Manual must be approved by the Executive IRB (IRB3) Chair, convened IRB3 and/or the Vice President, Clinical Research Administration.

OHSP is responsible for making all modifications to the HRPP Manual available to MD Anderson researchers and incorporating the modifications into the relevant educational programs (discussed in Chapter 4).

**MD Anderson has and follows written policies and procedures for determining when activities are overseen by the Human Research Protection Program. (AAHRPP Element I.1.A)**

### 1.4 Research Covered by the HRPP

**Types of Human Subjects Research at MD Anderson**
MD Anderson conducts or oversees clinical protocols, and biomedical, social science and behavioral research. MD Anderson has not chosen to limit the scope of its Federalwide Assurance (FWA) to federally funded research by “unchecking the box” on its FWA.

All human subjects research in which MD Anderson is engaged is covered by the HRPP. An activity is covered by the HRPP when:

It is considered “human subjects research” - as defined in any one of the following:
- FDA regulations;
- DHHS regulations or other Common Rule regulations;
- or
- Any other applicable state or local regulations
- MD Anderson (or its employees or agents) is engaged in human subjects research – as defined by being involved in one or more of the following activities (in accordance with the OHRP guidance Engagement of Institutions in Human Subjects Research):
  - Receiving an award through a grant, contract, or cooperative agreement directly from HHS or other federal agency for non-exempt human subjects research;
  - Intervening for research purposes with any human subject of the research by performing invasive or noninvasive procedures;
  - Intervening for research purposes with any human subject of the research by manipulating the environment;
  - Interacting for research purposes with any human subject of the research;
  - Obtaining the informed consent of human subjects for the research;
  - Obtaining for research purposes identifiable private information; or identifiable biological specimens from any source for the research

Agents include all individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility, including students, faculty, staff, employees, trainees, visiting scholars or faculty.


Approvals Required Before Human Subjects Research Commences

IRB approval is required before MD Anderson may commence human subjects research activities.

Protocol Activation Process

The protocol activation process at MD Anderson is an independent process, separate from the scientific and IRB review processes, within the Office of Protocol Review & Reporting. The process consists of sign offs from various central offices, research services, various central support offices, and financial departments to ensure that all institutional, financial and
operational signoffs are captured prior to participants enrolling on to research protocols. The protocol activation process is initiated by the submission of an activation request by the Principal Investigator/Protocol Team via the electronic system. The activation checklist captures all of the necessary sign-offs in an electronic template that is embedded in the Clinical Oncology Research (CORe) database. Once all checklist sign-offs have been completed and documented in CORe, protocol eligibility criteria are entered into CORe, and the informed consent document is released for consenting research participants. If the activations coordinator is unable to verify the readiness to proceed from research services, central offices or other required signoffs, the Principal Investigator/protocol team is immediately notified and provided with the appropriate contact information to resolve the pending issue(s).

Some protocol-specific situations require additional review and approval by various component departments, as described in Chapter 2.

See Standard Operating Procedures for Activating Research Protocols (Standard Protocol Form, Protocol Application Form, and CINDs) and Protocol Activation Checklist for more information.

MD Anderson international (transnational) research activities are consistent with the ethical principles set forth in its Human Research Protection Program and meet equivalent levels of participant protection as research conducted in the MD Anderson principal location while complying with local laws and taking into account cultural context. (AAHRPP Standard I-3)

The IRB has and follows written policies and procedures for determining the risks to prospective participants who are vulnerable to coercion or undue influence and ensuring that additional protections are provided as required by applicable laws, regulations, codes, and guidance. (AAHRPP Element II.4.A as of 2011)

Approvals Required for Not Human Subjects Research (Quality Improvement)

The Quality Improvement Assessment Board (QIAB) is established by Institutional Policy, Quality Assessment Improvement Board Policy (ADM1080) and reviews all MDACC Quality Improvement (QI) projects to: assure patient safety; optimize the potential benefits being sought; and discern which projects may be more appropriately designed or categorized as research studies requiring Institutional Review Board (IRB) oversight.

1.4.1 International Research

Researchers should ensure that participants outside the US have the equivalent protections that participants would be afforded in the US. OHRP provides a compilation of regulations and guidelines that govern human subjects research in other countries, as well as standards from a number of international and regional organizations (see OHRP International Compilation of Human Subject Protections).
In addition, the Multicenter Study Support (MCSS) group provides oversight for multi-institutional and multi-trials to ensure data integrity and regulatory compliance coordinated by MD Anderson Cancer Center.

The MCSS provides support services in the following areas:
- Support multi-center study/trial preparation, development and maintenance
- Serve as a resource for development of multi-center Standard Operating Procedures (SOPs) and guidelines
- Monitor protocol compliance and study conduct
- Provide quality assurance support utilizing risk-base-monitoring
- Develop project specific Data Quality Management Plan (DQMP)
- Conduct start up and site initiation visits for multi-center studies
- Provide guidance in regulatory management for multi-center studies
- Provide education/training to assist staff in multi-center trial management
- Recommend/request on-site auditing visits if needed
- Report to the Institution Review Board (IRB), and/or the Data Safety Monitoring Board (DSMB) compliance, adherence, regulatory matters and findings or outcomes from study monitoring
- Collaborate with the Office of Institutional Compliance regarding multi-center study regulations.

See Multicenter Study Support Standard Operating Procedures
- Multicenter Subject Confidentiality
- Multicenter Subject Registrations
- Multicenter Subject Serious Adverse Event Reporting
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- Verifying Protocol Eligibility
- Protocol Response Verification
- Deviation-Violation-Unanticipated Problems Reporting
- Protocol Compliance Assessment
- Query Submission and Tracking
- Electronic Research Applications
- Note to File Guidance

**Researcher Responsibilities**

When protocols are conducted in other countries (i.e. outside the US) researchers should be knowledgeable about the local laws and customs which apply to the research, and the cultural context in which they will be working. They should ensure that participants in international research are afforded equivalent protections to those participating in the US, and must describe their qualifications and preparation for the research that enable them to estimate and minimize risks to subjects. Researchers are asked to consider these issues on the International Research Supplemental Questions for Application to IRB.
IRB Responsibilities

MD Anderson IRB review of international research adheres to the same policies applied to domestic (US) research, when appropriate. Additional legal or cultural expertise may be obtained by the IRB during its review, and the IRB will make those determinations required by the laws of the countries in which the research is conducted. The IRB will also request documentation of local IRB or local research/ethics committee review, when appropriate.

*The IRB has and follows written policies and procedures for determining the risks to prospective participants who are vulnerable to coercion or undue influence and ensuring that additional protections are provided as required by applicable laws, regulations, codes, and guidance. (AAHRPP Element II.4.A as of 2011)*

*The IRB has and follows written policies and procedures to evaluate the consent process and to require that the Researcher appropriately document the consent process. (AAHRPP Element II.3.F)*

Considerations for Informed Consent

In some circumstances it may be inappropriate to document consent by using the standard written and signed consent document, and there might be different rules on determining e.g., who may serve as a legally authorized representative (LAR). Refer to Chapter 12 for information on waivers and alteration of consent, etc.

Additional Requirements

For federally funded research, the regulations of such federal agency apply and the required federal protections must be provided; it is not sufficient to provide “equivalent” protections. See Other Federal Agencies - Additional Requirements for other requirements depending on the source of support/funding (e.g., Department of Defense).

*MD Anderson delegates responsibility for the Human Research Protection Program to an official with sufficient standing, authority, and independence to ensure implementation and maintenance of the program. (AAHRPP Element I.1.B)*

*MD Anderson has and follows written policies and procedures setting forth the ethical standards and practices of the Human Research Protection Program. Relevant policies and procedures are made available to sponsors, researchers, research staff, research participants, and the Institutional Review Board, as appropriate. (AAHRPP Element I.1.D)*

*MD Anderson has and follows written policies and procedures that allow the Institutional Review Board or Ethics Committee to function independently of other organizational entities in protecting research participants. (AAHRPP Element I.1.C)*
1.5 Primary Officials, Administrative HRPP Components and Individuals of the HRPP

Officials Responsible for the HRPP

The primary responsibility for the HRPP lies with MD Anderson. The Board of Regents of The University of Texas System, the governing body for The University of Texas System appoints the President. The President of MD Anderson has delegated the responsibility for the HRPP to the Vice President, Clinical Research Administration. Aman Buzdar, M.D. serves as Vice President, Clinical Research Administration. Dr. Buzdar’s responsibilities and organizational chart.

As MD Anderson’s Institutional Official (IO), the Vice President, Clinical Research Administration signs the Federalwide Assurance of Compliance (FWA) on behalf of the institution and is ultimately responsible for:

- Creating, establishing and maintaining the policies and procedures for the HRPP and related research policies and procedures on behalf of MD Anderson
- Overseeing the protection of human participants, regulatory compliance, and the implementation of the HRPP for MD Anderson
- Ensuring that open channels of communication are maintained between the components of the HRPP
- Overseeing research investigators and staff
- Ensuring the independence of the IRB, including the authority to act without undue influence
- Requiring periodic reviews of the HRPP
- Ensuring that the HRPP is functional, adequately staffed and funded, involving:
  - Annual review of the resources allocated to the HRPP
  - Participation in the annual budget preparation for the HRPP and incorporation of the HRPP budget into the budget of MD Anderson

The day-to-day operational and oversight responsibility for the HRPP is delegated to the following components of the Office of Clinical Research Administration.

- Office of Human Subjects Protection (OHSP) – OHSP organizational chart
  - OHSP supports the Institutional Review Board (IRB), and provides regulatory oversight and monitoring of all protocols and reviews subsequent regulatory submissions, post-IRB approval, and grants for compliance purposes as mandated per federal requirements. OHSP also provides editorial services for informed consent documents (ICDs) and other patient-facing material, including consent authoring, conflict of interest review, sponsor negotiations, and common adverse event language database maintenance, as well as maintenance of the electronic consenting system iConsent. The Data Safety Monitoring Board (DSMB) and electronic DMSB are responsible for the review of protocol safety data. OHSP provides continuous quality improvement (CQI) and is responsible for the initial submission of and maintenance of AAHRPP accreditation. CQI consists of continuous assessment of the human subjects research program components to ensure compliance with institutional, federal and state policies and procedures. OHSP continuously implements mechanisms to assure that researchers and staff involved
in human subjects research receive educational and training sessions. Effectiveness of the program is measured through the conduct of audits, surveys, or other compliance tools.

- **Office of Protocol Review & Reporting (OPRR)** – [OPRR organizational chart](#)
  o The Office of Protocol Review and Reporting (OPRR) provides support for the scientific review and regulatory oversight of all research protocols conducted at MD Anderson, including coordination of scientific reviews through the SRCs and PBHSRC, in close collaboration with the PRMS and the Biostatistics Resource Group.

- **Office of Protocol Support & Management (OPSM)** – [OPSM organizational chart](#)
  o OPSM has dedicated support for NCI-sponsored clinical protocols, including those that are part of the NCTN and the Early Therapeutics Clinical Trial Network (ETCTN). This group acts as a liaison between MD Anderson and the NCI to facilitate communication, collaboration, and quality in the conduct of NCI-supported research. Services for NCTN/ETCTN protocols include protocol development, protocol management, data support, investigator registration, research staff credentialing, quality assurance, and administrative support.

- **Investigational New Drug Development Office (IND)** – [IND organizational chart](#)
  o The IND office provides regulatory and monitoring oversight for investigator-initiated IND protocols are provided by the IND Office on behalf of the Vice President, Clinical Research, the official IND sponsor. Services include assisting the PI in the preclinical concept stage, arranging a pre-IND meeting with the FDA, formatting the initial IND submission, and facilitating all communications with the FDA and the Recombinant DNA Advisory Committee (RAC) throughout the life of the trial. Clinical Research Monitors review these IND trials for compliance every 8-12 weeks based on protocol-specific, risk-based monitoring plans. Medical Affairs/Safety is a new group initiated in 2016 and dedicated to pharmacovigilance, responsible for reviewing serious adverse events and toxicity and safety summaries.

- **Office of Clinical Research Finance (OCRF)** – [CRF organizational chart](#)
  o OCRF provides support for the financial aspects of clinical research studies. OCRF develops a detailed coverage determination for all clinical and lab protocols with patient care charges to assist clinical researchers in negotiating adequate clinical trial funding. OCRF also ensures compliance with institutional internal controls, reviews all research-related patient care charges to maintain regulatory compliance, facilitates clinical research billing and invoicing, and assists clinical departments in reconciling sponsor-paid charges in a timely manner. Previously housed within the Finance division, OCRF was moved to within the OCRA in 2016 to centralize all functions under one reporting line, thus enhancing efficiencies.

### Institutional Review Boards (IRBs)

MD Anderson’s Institutional Review Boards (IRBs) perform many of the core functions of the HRPP. The Vice President, Clinical Research Administration appoints the chairs and the members of the IRBs and assigns their authority and responsibility in the “charge” to the Chairs, Vice Chairs, and members. See Charges to the [Institutional Review Board on Human Subjects in](#)
Medical Research, Institutional Review Board on Human Subjects in Non-Medical Research, and Executive IRB by the Vice President, Clinical Research Administration. The charge emphasizes that the IRBs are functionally independent (e.g., of the individuals who are conducting the research and MD Anderson), autonomous, and have ready access to the highest officials of MD Anderson and covered organizations, if needed, to ensure protection for human research participants.

MD Anderson has three medical IRBs, one non-medical IRB, and one IRB Policy on IRB Committee Determinations for Reviewing Research Non-Compliance, Suspending or Terminating Research. MD Anderson IRBs authority, membership requirements, and responsibilities are described in Chapter 6. MD Anderson’s IRBs are responsible for the initial and continuing review of research, review of modifications, approval of all research subject to the HRPP, determining serious or continuing noncompliance, requiring modification (to secure approval), disapproving research, and applying applicable ethical standards.

MD Anderson also participates in Adult and Pediatric Central Institutional Review Board (CIRB) Initiative of the National Cancer Institute (NCI). The CIRBs are the IRB of record for certain adult and pediatric national multi-center cooperative oncology group cancer treatment trials.

MD Anderson’s IRB may agree to rely on a single IRB (sIRB) for multisite protocols to provide initial and ongoing regulatory reviews. The reliance terms are outlined in an IRB Authorization Agreement (IAA) (e.g., MD Anderson has signed on to SMART IRB), which supports IRB reliance across the nation. The sIRB is responsible for reviews required by federal regulations at 45 CFR 46, and 21 CFR 50 and 56 (initial review, continuing review, modifications, reportable events). When MD Anderson IRB relies on a sIRB, MD Anderson’s local IRB still retains responsibility to ensure investigator compliance with the protocol, the sIRB's determinations, applicable federal and state regulations, and MD Anderson policy. MD Anderson's IRB bears responsibility for the local conduct of these protocols, e.g., managing noncompliance and unanticipated problems, ensuring training, and protocol monitoring. In addition, local ancillary requirements, managing reliance agreements, and handling protocol specific issues that arise are MD Anderson's responsibility. For more information, see Utilizing a Single or External IRB Mechanism and NIH Policy on Single IRB Review for NIH Funded Research.

The Principal Investigator (PI) is required to submit the protocol, informed consent document from the IRB who will be the IRB of record that includes the MD Anderson local context language including HIPAA language, other protocol documents. In addition, a PDOL PI Generic Memo will need to be submitted that includes a request for the MD Anderson IRB to rely on the single IRB and the rationale for the request. Protocols submitted using the Standard Protocol Form will need to undergo review by the Scientific Review Committee unless the PI submits a request and rationale why the scientific review should be bypassed. The request to bypass the scientific review process can be completed by making the selection in PDOL on the protocol page. Below is the selection that the PI can pick in order to bypass the scientific review process:

- No patients will be enrolled at MD Anderson – Data Analysis Only
- Expanded Access Protocol
Humanitarian Use Device
Focus Group Project – IRB approval times for focus group projects may be extended due to the need for an initial PBHSRC review
Protocol conducted per 2001 TCH/Baylor agreement (patients receiving radiation treatment only at MD Anderson)
Patients receiving standard of care procedure at MD Anderson as part of enrollment on a non-MD Anderson protocol at an external site
Other

Office of Human Subjects Protection (OHSP) staff: The OHSP staff is responsible for supporting the daily operations of the IRBs, and the education program. The IRB staff (Managers and Associates) in OHSP review protocol applications for accuracy and completeness and act as liaisons between the protocol principal investigators (PIs) and the IRBs. The IRB Education staff is responsible for the training of all individuals who are affected by the Human Research Protection Program. OHSP ensures periodic evaluation and strengthening of the HRPP. Additionally, each staff member of OHSP is a subject matter expert and may be called upon to provide educational in-services to research departments as needed, including presentations on consent document requirements, modifications, continuing review, IRB, and DSMB. Outside of OHSP, general research education is provided by educational specialists in Office of Protocol Support and Management.

Upon request, Office of Clinical Research Administration component departments in consultation with Institutional Compliance Office will review and comment on proposed regulations dealing with human subjects research. When appropriate, these offices will formulate and recommend draft policies and procedures for approval by the IRB or appropriate MD Anderson office.

Researchers

Principal Investigator: The MD Anderson individual ultimately responsible for a protocol is the Principal Investigator (PI). Most (but not all PIs) have faculty appointments at MD Anderson. At MD Anderson, an investigator must be a licensed physician and MD Anderson faculty member in order to serve as the PI of a clinical research protocol. Non-faculty may not serve as the PI of a clinical research protocol, though they may be eligible to serve as the PI of a lower risk protocol if determined appropriate by the IRB. The IRB determines the eligibility of the PI for all research conducted at MD Anderson. PI responsibilities are specified in the HRPP Manual, ensuring that:

- All MD Anderson human subjects research has received initial prospective review and approval by an authorized IRB
- Continuing review and approval of the research has been accomplished within the time frame stipulated by an authorized IRB
- The research is conducted at all times in compliance with all applicable regulatory requirements and the determinations of an authorized IRB
Other Members of the Research Team: Every member of the research team is responsible for protecting human participants. Co-investigators, collaborators, protocol coordinators, nurses, data and research coordinators, students, and all other research staff have the following strict obligations to:

- Comply with all IRB determinations and procedures
- Adhere rigorously to all protocol requirements
- Inform the PI, and thus IRB, of unanticipated problems
- Ensure the adequacy of the informed consent process
- Take necessary measures to ensure adequate protection for protocol participants.

See Chapter 14 for more PI responsibilities and duties under the HRPP.

Sponsored Research

A sponsor can be a company, institution, individual donor or organization that provides funding, investigational agent, or other support for human subjects research and may receive access to research information or the results of the research. A supporter typically only provides funding or access to the investigational agent only, and does not expect to have access to research information or rights to the results of the research. In the event the sponsor has any access to any PHI of the participants in the research project, the sponsor has obligations to protect such PHI. Additionally, if the sponsor provides investigational agents for the research project, the sponsor is responsible for only providing investigational agents that meet the manufacturing requirements under applicable law.

Participant Outreach

Participants in a research project also have responsibilities. These include telling the truth, asking for clarification, following the protocol, notifying protocol personnel of their non-compliance, and telling investigators if they wish to withdraw from the protocol.

HRPP Organizational Components and Other Organizational Components that Play a Role in Protecting Human Research Participants

In addition to the Vice President, Clinical Research Administration and OHSP, human research protection responsibilities are shared by the following MD Anderson HRPP and other MD Anderson components:

Scientific Review Committee (SRC): The SRCs are officially constituted committees of The University of Texas MD Anderson Cancer Center that report to the Vice President, Clinical Research Administration. MD Anderson has four SRCs that each meet monthly to evaluate the scientific content and prioritization of all clinical protocols, including investigator-initiated, pharmaceutical and biotechnology company-sponsored; multi-institutional; and other clinical investigation protocols deemed as high-risk. Each SRC has two Co-Chairpersons and at least 12 members appointed to each of the SRCs with representation from the majority of the Institutional Divisions. Committees will also have multidisciplinary members from Diagnostic
Imaging, Pharmacy, Nursing, Pathology and the Quantitative Sciences Division. In addition, each SRC committee has one member from the Houston community.

**Psychosocial, Behavioral, and Health Services Research Committee (PBHSRC):** The PBHSRC is an officially constituted committee of The University of Texas MD Anderson Cancer Center that reports to the Vice President, Clinical Research Administration. The purpose of the PBHSRC is to evaluate the scientific content of research that addresses areas related to psychosocial, behavioral and health services research involving human subjects. The PBHSRC meets on a monthly basis. This committee has three Chairpersons who share Chair responsibilities on a rotating monthly basis and at least 12 members appointed with representation from the different areas (i.e. Behavioral Science, Health Disparities, Palliative Care, etc.) and a representative from the Department of Quantitative Science.

**Electronic Protocol Accrual and Auditing Committee (ePAAC):** The ePAAC is comprised of the Chairs of the SRC/PBHSRC and Institutional Clinical Leadership. The committee is responsible for monitoring protocol accrual on a biannual basis. Reports are generated from the institution’s centralized registration system for categories of “IRB Approved but Not Yet Activated”, “No (Zero) Accrual” or “Low Accrual”. Investigators with protocols falling into one of these categories are queried and a formal written response with a corrective action plan is requested. An ePAAC subcommittee consisting of Institutional Clinical Leadership meets prior to each convened ePAAC meeting to review protocols that are IRB-approved but have not been activated for 6 months or longer from the date of IRB approval, or that have demonstrated consistent post-activation challenges in meeting accrual goals, to further enhance the quality of the ePAAC review process.

**Data Safety Monitoring Board (DSMB):** The DSMB reports to the President, or his designee, as the on-campus representative of The University of Texas Board of Regents. This board consists of clinical faculty and biostatisticians from both MD Andersons as well as clinical faculty from other educational institutions. The DSMB meets 10 times in a year and oversees the data and patient safety issues for the following categories of trials: Phase II or higher randomized and/ or blinded clinical trials that originate at MD Anderson; trials that are coordinated or analyzed by MD Anderson and are not being monitored by any other DSMB; or trials that have been designated as requiring DSMB monitoring at the request of the IRB or institution.

**External Data and Safety Monitoring Board (EDSMB):** The EDSMB reports to the President, or his designee, as the on-campus representative of The University of Texas Board of Regents. This board consists of non-MD Anderson clinical faculty and non-MD Anderson biostatisticians. Currently, the EDSMB meets once a year but more meetings may be held as more protocols come under EDSMB oversight. EDSMB oversees the data and patient safety issues for trials where MD Anderson has an Institutional Conflict of Interest (ICO).

**Institutional Conflict of Interest Committee (ICOI Committee):** MD Anderson’s ICOI Committee serves as an advisory committee to The University of Texas System and is responsible for reviewing MD Anderson’s Significant Financial Interests and MD Anderson’s Institutional
Decision Makers’ Financial Interests to determine if those interests constitute an Institutional Conflict of Interest (ICOI), and for addressing identified ICOIs through reduction, management, or elimination of such ICOIs. The ICOI Committee’s responsibilities are set forth in the Institutional Conflict of Interest Policy for The University of Texas Cancer Center and its Institutional Decision Makers. See the Institutional Conflict of Interest Policy for the University of Texas MD Anderson Cancer Center and Its Institutional Decision Makers (ADM1273) for more information.

**Conflict of Interest Committee (COIC):** MD Anderson’s COIC reviews financial relationship disclosures from all investigators, faculty, trainees, and institutional decision makers and determines if such relationships constitute an individual conflict of interest, and requires such individuals to reduce, manage, or eliminate the conflict of interest. The IRBs have the authority to determine additional measures as it deems necessary for the protection of human research subjects. See Chapter 3.7 and the Conflict of Interest Policy for Faculty Members, Trainees, Faculty Supervisors, Institutional Decision Makers, and Investigators UTMDACC (ACA0001) for more information.

**Environmental Health and Safety (EH&S website):** The MD Anderson EH&S program ensures low impact of hazardous pollutants to air, water, and land through compliance with federal, state, and local environmental regulations and operations to reduce pollution and promote environmental stewardship. EH&S works with investigators to promote a safe laboratory environment. Under EH&S, Laboratory Safety, identifies the basic principles employees should apply to protect themselves against all work hazards, including those related to environmental protection, laboratory safety, radiation safety, business continuity, emergency management, food safety, product recalls, operations and facilitates management, zone inspection, fire and life safety, construction safety, and occupational health safety. Compliance with the institutional Laboratory Space Policy (ADM0169) and safety training is required.

**Radiation Safety Committee (RSC website):** MD Anderson has established a Radiation Safety Committee (RSC), which is qualified through the experience and expertise of its members to oversee the institution’s radiation program, facilities and procedures. The President of MD Anderson appoints the Members, Chair, and Vice-Chair of the RSC. The President delegates authority to the RSC to ensure the safe handling of radioactive material, radioactive sources, and radiation-producing machines. The committee reports to the President of MD Anderson (see Radiation Safety Committee By-Laws).

**Clinical & Translational Research Center (CTRC website):** The CTRC serves an on-site resource for MD Anderson investigators performing early clinical trials and where patients received intensive monitoring for complex, early-phase clinical trials. CTRC facilities and services include:
- Coordination of multidisciplinary research
- Intensive, time-sensitive monitoring of patients
- Phlebotomy team and adjoining laboratory for prompt specimen processing
- Storage, tracking and shipment of specimens
- Coordination and communication with referring physicians
**Internal Audit:** MD Anderson’s Internal Audit department (IA) is established under the authority of, and in accordance with the Texas Internal Auditing Act and The University of Texas System Board of Regents. IA, with strict accountability for confidentiality and safeguarding records and information, is authorized full, free, and unrestricted access to any and all of MD Anderson’s records, physical properties, and personnel pertinent to carrying out any engagement. The scope of internal auditing carried out by IA includes MD Anderson’s HRPP. For more information see The University of Texas MD Anderson Cancer Center Internal Audit Activity Charter.

**Institutional Compliance Program:** The Mission of MD Anderson's Institutional Compliance Program is to support MD Anderson's Mission, Vision, and Core Values and to help the institution fulfill its responsibilities to the people of Texas in an environment based upon ethical behavior and compliance with applicable laws, rules, and guidelines. The Institutional Compliance Program consists of the Chief Compliance and Ethics Officer, the Executive Institutional Compliance Committee and other compliance committees, the Institutional Compliance Office, and Institutional Compliance – Compliance Program. It addresses general compliance issues, as well as issues related to research compliance, billing and reimbursement compliance, privacy and information security compliance, and corporate ethics and compliance. In addition, we respond to reported compliance concerns and those identified through ongoing auditing and monitoring activities.

The Institutional Compliance Program maintains a Compliance Hotline (1-800-789-4448) that is available for reporting compliance concerns on a confidential basis. Such reports may also be made on an anonymous basis. To maintain MD Anderson’s culture of compliance and achieve its Mission, the Institutional Compliance Program provides all workforce members with regularly scheduled and specifically requested trainings on state and federal legal and regulatory matters, as well as Institutional Policies and Procedures.

**Research Compliance Program:** Research is key to achieving MD Anderson’s Mission to eliminate cancer and is driven by our Core Value of Discovery. In pursuit of its Mission, MD Anderson is committed to providing a research compliance program that works in concert with our academic research endeavors. The goal of the program is to ensure that all research (including clinical, behavioral, and translational research) is conducted according to the highest ethical standards and in compliance with all applicable laws, rules, guidelines, and institutional policies. In addition, MD Anderson’s Senior Legal Officer & Director, Research Compliance, provides serves as institutional legal and regulatory counsel, and provides legal research and analysis for complex research compliance-related legal issues, including issues regarding human subjects research and participant protection, to MD Anderson, its researchers, its IRBs, and the Vice President, Clinical Research Administration. For more information about the Research Compliance Program see MD Anderson’s Research Compliance Plan.

**Privacy and Information Security Compliance Program:** MD Anderson is committed to safeguarding the privacy of our patients and workforce members, as well as safeguarding state
resources. To such end, the protection of private and confidential information is an institutional priority. MD Anderson is committed to providing a privacy compliance program that ensures all patient Protected Health Information (PHI), as well as other confidential business and proprietary information, is managed and protected in accordance with the highest standards and in compliance with all applicable laws, rules, guidelines, and institutional policies. In addition, MD Anderson’s Senior Legal Officer & Director, Privacy & Information Security Compliance, provides regulatory counsel, and provides legal research and analysis for complex privacy and information security compliance-related legal issues, including issues regarding human subjects research and privacy and confidentiality of human research participants, to MD Anderson, its researchers, its IRBs, and the Vice President, Clinical Research Administration. For more information about the Privacy and Information Security Compliance Program see MD Anderson’s Privacy Compliance Plan and Information Security Compliance Plan.

**Legal Services department:** The Legal Services department is responsible for addressing legal issues arising out of the activities of MD Anderson. In the human subjects research context, Legal Services is responsible for preparing and negotiating sponsored research agreements, such as clinical trial agreements, material transfer agreements, technology license agreements, and strategic development agreements.

**Leadership for research including research administration** at MD Anderson is jointly shared between the Chief Medical Executive and the Chief Academic Officer who both report to the President.

### 1.6 Ethical and Legal Principles Governing Human Subjects Research

**Ethical Principles**

The primary ethical principles applied to research covered by the HRPP, including protocols “exempt” under federal regulations pertaining to human subjects research, are those set forth in The **Belmont Report:** Ethical Principles and Guidelines for the Protection of Human Subjects of Research of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (Belmont Report).

The three main principles are:

- **Respect for persons** (e.g., applied by obtaining informed consent, giving consideration to privacy and confidentiality, and adding protections for vulnerable populations)
- **Beneficence** (e.g., applied by weighing risks and benefits)
- **Justice** (e.g., applied by the equitable selection of subjects)

All parties involved in the conduct of research are expected to also adhere to the principles of expertise (“competent to do the work”) and integrity (“faithfully adhere to professional principles”). Ethical principles from other sources (e.g., International Conference on Harmonization) may also be applied to research covered by the HRPP, for example:
• To an individual protocol because its particular circumstances raise a type of ethical issue that most other protocols do not
• When they are recognized by the federal or other funding source or the state or country where the research will occur
• When they have been developed for specific areas or types of subjects (e.g., embryos and fetal tissue, illiterate subjects).

Investigator training on the ethical principles governing human subjects research and investigator responsibilities is provided via various online training modules including Principal Investigator Responsibilities at MD Anderson, and International Conference on Harmonization (ICH) E6 Good Clinical Practice Guidelines v2.0. These principles are also covered in the Human Subjects Protection Training (HSPT) for investigators and research team members. IRB Members, and IRB Staff also attend an annual IRB orientation.

With respect to sponsored clinical research, MD Anderson addresses the protection of research participants by including in the negotiation process a provision that MD Anderson will conduct the research in accordance with MD Anderson’s policies. MD Anderson’s policies as related to the execution of contracts and agreements, as part of human subjects research are located on the Legal Services website, Office of Sponsored Programs, Office of Clinical Research Administration and in the HRPP Manual (see Chapters 15, 16, and 17).

Legal Principles
The basic legal principles governing human subjects research, covered by the HRPP and applicable to individual protocols are:
• Federal Policy for Protection of Human Subjects (Common Rule) in 45 CFR Part 46
• Food and Drug Administration Regulations for the Protection of Human Subjects in 21 CFR Parts 50 and 56
• Food and Drug Administration Regulations in 21 CFR Parts 11, 312, and 812.
• Standards for Privacy of Individually Identifiable Health Information (HIPAA Privacy Rule) in 45 CFR Parts 160 and 164.
• Applicable Texas law.

These and other legal principles are addressed when applicable in individual chapters of this manual.

Additional Requirements
Depending on the source of support for research, regulations from other agencies such as DoD, etc. might apply (see Other Federal Agencies - Additional Requirements).

MD Anderson has and follows written policies and procedures setting forth the ethical standards and practices of the Human Research Protection Program. Relevant policies and procedures are
1.7 Scientific and Scholarly Validity Review and Ethics Review

Scientific and Scholarly Validity Review

When evaluating the scientific and scholarly validity of a protocol, the IRB relies on the review provided by different entities, as follows:

- For federally sponsored research, the peer review process by the sponsoring agency (e.g., NIH, NCI, DoD) provides scientific and scholarly review, and the IRB may require review the Scientific Review Committee.
- For research subject to FDA review, the FDA conducts a rigorous scientific design review during IND or IDE evaluation. Most industry-sponsored research falls within this category. An important exception is Non-Significant Risk (NSR) device research, where the IRB serves, in a sense, as the FDA’s surrogate with respect to review and approval of NSR protocols.
- The Scientific Review Committee (SRC) provides a peer review of local, national, and international research protocols involving cancer patients treated at MD Anderson. The review primarily focuses on the scientific merit of the protocol and applies to all phases of clinical therapeutic intervention, tissue and body fluid research, and diagnostic protocols, which impact medical decision making for the treatment of cancer patients. The process is described in the SRC website. All cancer protocols are required to undergo SRC review with the exception of the following protocols:
  - Phase II Expansion Protocol (Phase I and II components were reviewed and approved by the MD Anderson SRC and IRB)
  - No patients will be enrolled at MD Anderson – Data Analysis Only
  - Expanded Access Protocol
  - Focus Group Projects
  - Patients receiving standard-of-care procedures at MD Anderson as part of enrollment on a non-MD Anderson protocol at a non-MD Anderson site

Department Chair Protocol Review and Prioritization Memo

Research protocols that are submitted to the SRC or PBHSRC for review must fill out and submit the Department Chair Protocol Review and Prioritization Memo as a required document. If the Department Chair is submitting a protocol for SRC or PBHSRC review, then his/her one up will need to complete this memo. The Department Chair / Designee will need to address the following topics:

- Potential innovation, clinical impact of the medical/scientific question; preclinical and/or clinical data underlying the clinical hypothesis
• Specific preclinical or prior clinical work by MD Anderson investigators that support this protocol
• Accrual feasibility, e.g. past accrual to similar protocols, approximate size of potentially eligible patient population seen annually
• Current and/or planned funding for protocol (i.e. Does this protocol have a sponsor?)
• Departmental priority of the protocol (and of how many protocols, e.g., “#2 of 8 current or pending protocols”) within this specific disease site/section: [Department Chair Protocol Review & Prioritization Memo](#).
• List all competing protocols in the disease site/section and indicate status (anticipated closure date, current accrual, and overall accrual)

The Department Chair/Designee will need to answer the questions that are in the Department Review Option section before electronically signing off on the document. At the bottom of Department Chair Protocol Review and Prioritization Memo, an attestation statement has been added.

**Departmental Review Option Description:**

Departments with an established internal department review process for all new concepts and/or protocols may designate a Content Expert Reviewer (disease-specific departmental reviewer) as part of the Departmental Review Option. This review must be submitted by a non-collaborating faculty member who has participated in the departmental review process and has agreed to submit a summary of the departmental level critiques and approval decisions regarding the new concept and/or protocol. The non-collaborating faculty member should be a faculty member who is not currently listed on the Collaborators page and is not directly involved in the protocol development and/or data analysis aspects of the clinical protocol. The department must also ensure that this reviewer does not have a financial conflict of interest involving the sponsor or supporter of the protocol.

Departments with an established internal department review process for all new concepts and/or protocols may qualify for the departmental review option. To qualify, clinical departments must have a structured internal review process for all new concepts and/or protocols that includes a faculty meeting presentation and an evaluation of the following review criteria: protocol design and rationale, feasibility and accrual, and priority and impact.

Clinical departments approved to utilize this option will receive an [Institutional Approval to Utilize Department Review Option for SRC Studies](#) verifying their qualifying status, which must be included along with their request. All requests must be submitted via the Department Chair Protocol Review and Prioritization Memo at the time of SRC or PBHSRC submission. Departments utilizing this option will not be required to appoint additional faculty reviewers for this protocol submission and, in some instances, the Principal Investigator may also be exempt from the review of another protocol during the SRC submission cycle (see [Psychosocial, Behavioral, and Health Services Research Committee Bylaws](#), [Scientific Review Committee Bylaws](#), [Scientific Review Committee Procedures](#), [Data Safety Monitoring Board Bylaws](#).
External Data and Safety Monitoring Board (EDSMB) By-Laws, Psychosocial, Behavioral, and Health Services Research Committee Procedures, Data Safety Monitoring Board (DSMB) Standard Operating Procedures (SOP), External Data and Safety Monitoring Board (EDSMB) for Standard Operating Procedures (SOP), and ePAAC Procedures).

**MD Anderson has and follows written policies and procedures for reviewing the scientific or scholarly validity of a proposed research study. Such procedures are coordinated with the ethics review process. (AAHRPP Element I.1.F)**

For all research, the IRB evaluates, in accordance with federal research regulations [45 CFR 46.111(a) and 21 CFR 56.111(a)] whether the following requirements are satisfied:

- Risks to participants (physical, psychological, social, legal and economic) are minimized (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose participants to risk; and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
- Risks to participants are reasonable in relation to anticipated benefits, if any, to participants, and the importance of the knowledge that may be expected to result.

If the requirements noted above are not satisfied, the protocol may not be approved as written. IRB reviewer(s) may consider other scientific reviews, as noted above, (e.g., NIH peer review, or other Non-MD Anderson SRC review) in their evaluation as long as documentation has been submitted in the electronic system. For protocols where the protocol design is unusual or novel, in addition to the protocol being assigned to primary reviewer(s) with relevant expertise, input from *ad hoc* consultants may also be obtained. For further information, refer to guidance **Evaluating Sound Study Design**.

**Ethics Review**

IRB review of the protocol procedures, risks, and benefits includes the identification, evaluation, and resolution of the ethics issues presented in the protocol in accordance with the ethical principles outlined in **Chapter 1**. Each IRB includes a Clinical Ethicist as a voting member. If necessary, the IRB may seek *ad hoc* assistance from ethical consultants, both internal and external (e.g., members of other hospital’s ethics committees).

- Ethics consults are also available for researchers, via the MD Anderson Clinical Integrated Ethics Department. Initial ethics consultations for protocol design, bedside consultations are available services.
Chapter 2. Resources Supporting the HRPP

MD Anderson ensures that the Human Research Protection Program has resources sufficient to protect the rights and welfare of research participants for the research activities that MD Anderson conducts or oversees. *(AAHRPP Standard 1-2)*

2.1 Sufficient Human and Fiscal Resources

The provision of adequate human and fiscal resources facilitated through the budgeting process results in a well-functioning and effective HRPP.

Human Resources: MD Anderson demonstrates a high level of institutional commitment to its HRPP in terms of human resources. The HRPP is led by the Vice President of Clinical Research Administration (VPCRA), pursuant to the authority delegated by the President of MD Anderson (see Delegation of Authority for the Human Research Protection Program). The VPCRA oversees the Division of Clinical Research Administration (CRA).

Fiscal Resources: MD Anderson demonstrates a high level of institutional commitment to its HRPP in terms of fiscal resources provided to the OCRA and its component offices, and MD Anderson’s committees including the IRBs, DSMBs, SRCs and PBHSRC that are an integral part of MD Anderson’s HRPP.

Resource Allocation in support of HRPP: The OCRA funding is provided by MD Anderson on an annual basis with some support from industry sponsored studies. The budget process is as follows:

- Each Director in OCRA provides input regarding priorities and resources needed for the new academic year. This information is consolidated into the annual budget for the division.
- The annual budget for the division is reviewed and approved by the VPCRA, Vice President, Clinical & Interdisciplinary Research, and the Office of the Chief Academic Officer. This budget is then submitted to the Office of the Chief Financial Officer and integrated in the overall budget for the institution that is then provided to the UT Board of Regents for approval. It takes effect on September 1 of each year.
- Once approved, the division level budget is divided by department and disseminated to the respective director. Each director is responsible for managing their areas within the approved budget. When unanticipated expenses arise, the director presents the request to expend the unbudgeted item to the Executive Director. They work with the VPCRA to determine if the unbudgeted item should be approved.

MD Anderson ensures that the Human Research Protection Program has resources sufficient to protect the rights and welfare of research participants for the research activities that MD Anderson conducts or oversees. *(AAHRPP Standard 1-2)*
2.2 Matching IRBs to Volume and Types of Human Research

Scientific Review

All protocols involving human subject’s research must be approved by the Institutional Review Board (IRB) prior to activation. Before a protocol goes to IRB however, it must first be reviewed by a committee that focuses on the science of that protocol. In this regard, the Scientific Review Committees (SRCs) and the Psychosocial, Behavioral, and Health Services Research Committee (PBHSRC) are the scientific reviewing agents for the IRB.

The SRC will evaluate the scientific content of all investigator-initiated protocols (sponsored or non-sponsored), as well as protocols sponsored by pharmaceutical and biotechnology companies, whether those are single center or large multi-center protocols. The clinical protocols involve investigational drug(s), device(s), surgery, and/or radiation therapy. There are four SRCs that meet on specific days within a month. Each SRC reviews the same types of clinical protocols. To ensure timely acceptance of newly submitted protocols to the next available SRC meeting, the Principal Investigator will need to meet the pertinent deadlines for the submission cycle.

All protocols that are primarily psychosocial, behavioral, or health services research (e.g., quality of life [QOL] questionnaires or surveys, symptom and pain research, social work, thesis / dissertation projects, health disparities research, and population based protocols) are submitted to the PBHSRC, which meets monthly, for review of scientific merit.

SRC and PBHSRC submission and meeting dates are established a year in advance and are published on the Office of Protocol Review and Reporting website.

IRB Review

The clinical IRBs meet twice a month, the psychosocial behavioral science IRB meets once a month along with the Executive Session IRB (see Executive IRB By-Laws). Protocols are randomly assigned to an IRB based on research type, volumes, and expertise available on the IRB.

The medical IRBs review interventional drug, surgical and radiotherapy protocols. The medical IRBs also routinely review device protocols, although depending on the type of device used, these may be assigned to the non-medical IRB.

The non-medical IRB reviews research conducted in the field of human behavioral and population-based research, education, and other similar areas. This IRB generally will not review protocols that include clinical interventions.

The OHSP assesses the level of IRB activity at least annually in order to optimize the workflow and IRB load. It considers the ratio of protocols to staff, the number of transactions generated by each protocol, the type of protocols (regular, expedited or exempt), and any other appropriate elements. Input from the IRB Chairs regarding the level of activity and other IRB-
related matters is gathered in the IRB annual report that is presented to the VPCRA. When adjustments are necessary, the financial implications of the workload are considered during the budget process outlined above in Chapter 2.

New IRBs or new staff positions are created on an as needed basis to meet the demands of the workload. The Scientific and Clinical IRB Schedules are posted on the OHSP website. Submitted protocols are assessed for completeness before assignment to an IRB. Once a protocol is assigned to an IRB, the review process starts and includes a detailed pre-meeting review phase that ensures that substantive issues and compliance requirements that were identified during the SRC or pre-review process have been addressed. See Chapter 7 for information on the review process.

MD Anderson ensures that the Human Research Protection Program has resources sufficient to protect the rights and welfare of research participants for the research activities that MD Anderson conducts or oversees. (AAHRPP Standard I-2)

The IRB has and follows written policies and procedures for identifying and analyzing risks and identifying measures to minimize such risks. The analysis of risk includes a determination that the risks to participants are reasonable in relation to the potential benefits to participants and to society. (AAHRPP Element II.3.A)

2.3 Human Research Protection, Care of Participants, and Safety
To approve research, the IRB must determine that, where appropriate, there are adequate resources to ensure the care and safety of participants, from the screening and recruitment phases throughout the project. During review of the submitted protocol, the IRB assesses the information in the PDOL Application and as necessary asks for additional details. See Chapter 7 for information about the review process. If the protocol does not provide adequate protection, it will not be approved.

Investigators are required to indicate in their protocol whether they:
- will have access to a population that will allow recruitment of the required number of participants;
- will have sufficient time to conduct and complete the research;
- will have adequate numbers of qualified staff;
- will have adequate facilities;
- will have a process to ensure that all persons assisting with the research are adequately informed about the protocol and their research related duties and functions;
- will have medical or psychological resources available that participants might require as a consequence of the research when applicable.

The Department Chair or Division Head assesses each protocol for feasibility to ensure that the department and investigator have adequate resources to conduct the protocol.
Investigators are required to continually monitor the resources allocated for their research and notify the IRB if any change in the availability of resources may adversely impact the rights and welfare of participants.

**MD Anderson has and follows written policies and procedures setting forth the ethical standards and practices of the Human Research Protection Program. Relevant policies and procedures are made available to Sponsors, Researchers, Research Staff, research participants, and the Institutional Review Board, as appropriate. (AAHRPP Element I.1.D)**

### 2.4 Communication and Interaction

#### Communication

The central office components within OCRA coordinate closely to ensure that all institutionally required communications and information in the PDOL Application are provided. The process consists of sign offs from various central offices, research services, various central support offices, and financial departments to ensure that all institutional, financial and operational signoffs are captured prior to protocols being activated and participants enrolling onto those protocols.

- **The Radiation Safety Committee (RSC)** is qualified through the experience and expertise of its members to oversee the institution’s radiation program, facilities and procedures. The Radiation Safety Committee must certify that it has reviewed a protocol using radioisotopes or radiation machines and recommends it for approval. Without this approval, a protocol which employs these modalities will either be tabled to a future convened meeting, or will be approved contingent on Radiation Safety Committee recommendation for approval. If a modification involves review by Radiation Safety, the IRB will hold its approval until Radiation Safety forwards its approval to the IRB. Radiation Safety is given access to the protocol information by the IRB. The President of MD Anderson appoints the Members, Chair, and Vice-Chair of the RSC. The President delegates authority to the RSC to ensure the safe handling of radioactive material, radioactive sources, and radiation-producing machines. The committee reports to the President of MD Anderson.

- **Protocols involving biosafety materials** and requiring review by the Biosafety Panel must be reviewed by this Panel and receive an approval letter in addition to review by the IRB. A new protocol generally will not be presented at an IRB convened meeting until the Biosafety Panel has approved it. If a modification or continuing review involves review by Biosafety, the IRB will hold its approval until Biosafety forwards its approval to the IRB. The HRPP Associate Director and the IRB Manager are ex-officio members of the Biosafety Panel. A member of the IRB staff attends the Biosafety Panel meetings and receives communications directly from the Panel regarding submitted protocols. The Biosafety Officer and Biosafety Specialist (from the Environmental Health & Safety department) are ex officio members of the medical IRBs and IRB/SCRO and attend medical IRB and IRB/SCRO Panel meetings.
Protocols that also involve the use of human embryonic stem cells and human induced pluripotent stem cells must be reviewed and approved by the Human Embryonic & Induced Pluripotent Stem Cell Research Oversight (HEIPSCRO), in addition to having an IRB approval for the protocol, prior to activity commencement.

**Good Manufacturing Practice (GMP) Laboratory (SRC Protocols Only):** Prior to SRC, investigators are required to confirm if the protocol requires the services of the Cell Therapy Lab Good Manufacturing Practice (GMP) facility or products to be manufactured using the GMP facility.

**Patient related equipment using electricity** must meet the standards established by the Hospital Instrumentation and Electrical Safety Committee. For protocols using such equipment, the investigator is referred to Clinical Engineering.

**Investigator Conflict of Interest disclosures:** All investigator and institutional conflicts of interest are managed via the Conflict of Interest Committee (COIC) and its associated Institutional Conflict of Interest Committee (ICOIC). The Manager of Human Research Regulations in OHSP serves on the COIC. IRB will not approve a protocol until any disclosed COI has been reviewed and resolved by the COIC/ICOIC, and as appropriate, a plan or strategy to adequately eliminate, mitigate, or manage the conflict has been determined by the COIC/ICOIC (see Chapters 3, 6, and 14).

- An FDA investigational drug or biologic that is not under the control of the hospital or investigational pharmacy services: The PI must have a security and controlled access plan for the drug or biologic (see Chapter 5).
- Blood, tissue, or data (slides, X-rays, etc.) that are being transferred in or out of the institution, and there is no contract in place: The PI must coordinate with the Legal Services and/or Research Administration about a Material Transfer Agreement (MTA) or Data Use Agreement (DUA).
- **Funding status:** Inquiries may be made of the Office of Research Administration, Clinical Research Finance, and Office of Sponsored Programs to verify whether there is active funding.

The following communications and interactions between various components occur during the SRC and PBHSRC Review Process here are MD Anderson. If concerns are brought forth during the review process, it is the Principal Investigator’s responsibility to respond and make any agreed upon changes before the protocol can be placed on the next SRC meeting agenda. If the Reviewer/PI cannot agree on outstanding concerns, then the committee will weigh in on the matter.

**VP, Clinical Research Administration (VPCRA) Review (SRC Protocols Only):** The VPCRA conducts a review of the Department Chair Protocol Review and Prioritization Memo and makes a determination if the protocol can begin the SRC review process. If so, then the protocol is processed by the SRC Meeting Coordinator. If not, then the protocol is rejected back for additional corrections before proceeding forward.
Medical Reviewers (SRC and PBHSRC): Two medical reviewers are selected to review a newly submitted protocol for the SRC unless the Principal Investigator’s (PIs) department has been approved to participate in the Department Review Option. If approved, then the Content Expert Reviewer will override the two Medical Reviewers. The Reviewers are given Scientific Reviewer Guidelines for Preparing Written Comments to use when completing their scientific review. Topics include but not limited to: discuss the strengths and weaknesses of the protocol; is the protocol clearly written; has sufficient considerations been given to the statistical aspects of the protocol as well as provide any suggestions that might improve the protocol.

Content Expert Reviewer (only if Departments have been approved to participate in the Department Review Option – SRC Protocols Only): This individual is required to complete a medical/scientific review of the newly submitted protocol. Like the Medical Reviewers listed above, the Content Expert Reviewer is given the Scientific Reviewer Guidelines for Preparing Written Comments to use when completing their scientific review. During their written review, the reviewer will also be asked to summarize comments and/or critiques from the department review process that supported the protocol’s approval. Please also include overall results of scoring, vote tally and/or prioritization ranking within the department.

Psychosocial Based Reviewer, if applicable (SRC Protocols only): This reviewer is responsible for reviewing the questionnaires that have been attached to the clinical protocol. Items to be considered when reviewing: is the questionnaire appropriate for the protocol population; is the schedule for administration of the questionnaire appropriate for its use; do the questionnaires place undue and unnecessary burden on protocol subjects or are they likely to lead to errors of multiplicity, and is the proposed statistical plan for analysis of the questionnaires appropriate.

Biostatistical Review (SRC and PBHSRC): This review is performed to ensure that the protocol objectives can be successfully met given the stated protocol design, protocol endpoints and number of planned patients or participants. The reviewer looks at the protocol with regard to the rationale for the protocol and the target population, treatment alternatives for the target population, and any other protocols evaluating the experimental treatment to date. The statistical considerations is reviewed to make sure sufficient details of the protocol design, sample size justification, statistical methodology, and plans/rules for futility, efficacy and safety monitoring are provided. Specifically, the group assess whether the primary objective and corresponding primary endpoint(s) are clearly defined and evaluate whether they are harmonious with statistical design and analysis plan, while also making sure patients are protected against excessive toxicity or ineffective treatments.

Pharmacy (SRC Protocols Only): Conducts scientific pharmaceutical reviews for the newly submitted protocols to the SRC for review. This group looks at the drug(s) that will be given for the protocol, drug formulas, route of administration, as well as other pharmacologic aspects. This group is also responsible for responsible for the administrative management of all investigational drugs used at MD Anderson. Specific operational responsibilities would include but are not limited to drug acquisition, inventory control and investigational drug accountability.
Radiology - Diagnostic Imaging (SRC Protocols Only): The Diagnostic Imaging reviewer identifies protocols with imaging as an endpoint to ensure compliance, representation from DI if needed, feasibility, appropriate budgeting is in place, and assist with operations and logistics of protocols impacting DI, as a downstream division.

Radiology – Interventional (SRC Protocols Only): For Interventional Radiology reviewer looks for procedures such as biopsies, vaccine protocols, etc. to get their operations in place and to ensure collaborators/Co-Investigators are involved with the content expertise. The reviewer wants to make sure that the amount of core samples involved is amenable for IR to acquire, etc. Based on patient safety/risk profile of the patients which present. For protocols involving response criteria, then the IR group we onboard them to QIAC to assist. For protocols involving image de-identification services for 3rd party radiological review, the group ensures that certain groups are involved from the beginning to assist. For protocols involving investigational radiopharmaceuticals, we have the appropriate NM/Imaging Physics faculty involved (if we are expected to manufacture this agent, there are people who make sure that our cyclotron facility is aware and capable, or if a 3rd party vendor is involved, then the group will need to make sure that they receive it on time per protocol design). For protocols involving radiology services w/o a collaborator, or for protocols which may speak of using equipment we don’t have at MD Anderson, this group will need to make sure the PI/sponsor is aware.

Nursing (SRC Protocols Only): When the nursing reviewers conduct their review, they are reviewing form points that would impact the care of the patient while in the care of the clinical nurse. Here are some points that they look for when reviewing the protocols from a clinical nurse’s perspective: Is the location of protocol treatment administration site feasible based on the frequency of lab, vital signs, EKG, etc.? Are the type of equipment, supplies, etc. required for the protocol available in the institution for nursing administration of protocol? The administration instructions (IV, PO, Intrathecal, etc.) and what supplies are needed to administer the medications. The route, time, dose, and medication to be delivered along with the inclusion and exclusion criteria. Where the protocol medication will be administered (inpatient vs. outpatient vs. in OR, etc.). If the protocol medication is cardiotoxic, how often will the EKGs be ordered or will the patient be continuously monitored during the administration. In addition, if the protocol medication is harmful to the other organs, how often lab work will be performed to monitor the status of those organs. Is the protocol medication FDA approved for another type of cancer and why was it chosen for the protocol cancer studied.

IND Admin Review (SRC Protocols Only): Protocols are reviewed as to whether or not they may need to be conducted under IND. Protocols noted as being IND exempt are evaluated and may be referred to the Institutional IND Review Committee or the FDA as needed. Device protocols are deferred to IRB for review and are noted as “Device Study”.
If the protocol is slated to go to the Institutional IND Review Committee (IIRC) for review, an official notification with the committee’s determination will be sent to the PI/ Additional Contacts through the electronic system.

**Multicenter (SRC and PBHSRC):** This group reviews all newly submitted protocols submitted to the SRC to see if they are multicenter protocols, that the correct sponsor/supporter is identified, who the lead site is vs industry/CRO, and that there is language guiding protocol and data management. We then offer support to the department who may need it regarding contingencies that are found.

**OPR&R Administrative Review (SRC and PBHSRC):** This person serves as the liaison between the Office of Protocol Review and Reporting (OPR&R), the SRC or PBHSRC Committee, as well as the Principal Investigator / Regulatory Staff. The review that is conducted from this person is capturing administrative issues as well as looking to make sure all required documents have been attached in the electronic system. While the SRC / PBHSRC review process is underway, this individual is gathering documents and conducting quality assurance checks to make sure that the agreed upon changes have been corrected to the protocol documents. All pertinent information is then bundles up in a PDF document for the committee to review.

**Pathology – CLIA (SRC Protocols Only):** The reviewer is looking at newly submitted protocols to the SRC. If the PI has stated YES the CLIA question in the electronic system, then the reviewer is looking to see if the PI has adequately addressed the other questions pertaining to CLIA.

**MD Anderson DSMB, if applicable (SRC and PBHSRC):** During the DSMB ancillary review, OHSP staff look to see if the following criteria are met: Randomized and/or blinded; Phase II or higher; Accrual (to make sure it will not be completed within one year); Is MD Anderson the lead site. If these criteria are met, then the MD Anderson DSMB will be chosen as the monitor.

**Environmental Health and Safety (E. H. & S.) (SRC and PBHSRC):** OHSP staff screen human protocols on behalf of Institutional Biosafety Committee (IBC) and Radiation Safety Committee (RSC) to identify the protocols that are subject to, but have not been submitted to, IBC and/or RSC for approval. In addition to the protocol and its abstract, the Investigator’s Brochure and Pharmacy Manual are used to determine whether a protocol is subject to IBC and/or RSC.

The following are notified of new protocol submissions but do not provide written comments to the SRC or PBHSRC.

**Scientific Editors (SRC and PBHSRC):** This group is notified of newly submitted protocols to the SRC and PBHSRC. The editors assist the principal investigators (PIs) and research staff in creating an informed consent document (ICD) that includes all of the federally required elements at the appropriate reading level.

**Clinical Research Finance (SRC and PBHSRC):** Clinical Research Finance will develop a detailed coverage determination for all clinical protocols with patient care charges to enhance the
financial processes that support the efforts of the clinical researchers and assure adequate clinical protocol funding. This group also assists with contract and budget review, research charge review and completing the circle by monitoring the research charges.

Research Quality Nurse Specialist (Research Protocol Fact Sheet) (SRC Protocols Only): This group is notified of newly submitted protocols to the SRC. They are responsible for reviewing the Research Protocol Fact Sheet. At the time of SRC submission, this is not a required document but the Fact Sheet will need to be completed and finalized before the protocol can be activated. Research Protocol Fact Sheets are electronic information sheets that will provide a quick reference guide on protocol requirements. The Fact Sheet will include basic information needed to take care of the patient and follow the protocol as outlined. The document would also include protocol requirements for drug administration, potential toxicities, contraindications and protocol specific equipment.

Primary / Secondary Discussant Reviewers (SRC Protocols Only) (Confidential to SRC and IRB Committees Only): This reviewer is selected from the upcoming SRC committee roster. The reviewer is charged with completing the Clinical Trial Assessment and Prioritization Scoring Sheet. This assessment looks at the following areas: Importance of Medical/Scientific Question (potential significance/impact); Background and Rationale (strength of preclinical/early clinical data, MD Anderson contribution); Approach and Statistical Design (strength of the protocol design and statistical plan); Strength of Correlative Science (potential to provide insight into cancer biology and/or treatment response, toxicity, or resistance); Patient Population/History of Similar Protocol Accrual/Competing Protocols; as well as the Economic Feasibility/Budget Review. Once all areas have been scored, then the discussant will be asked to provide an overall impact score. All of this information is taken into consideration before the committee votes on the protocol at the SRC meeting.

The SRC and PBHSRC discussion notes are transcribed and then handed over with the protocol for the IRB to make a final determination.

Policies Available to all Parties to Research

The HRPP Manual and other relevant policies and procedures are available to the sponsors and to the entire MD Anderson research community, including researchers, research staff, IRB staff, IRB members, employees, and students through the Office of Human Subjects Protection website and various other sources as described in Chapter 3.
Chapter 3. Compliance Monitoring

**MD Anderson has and follows written policies and procedures setting forth the ethical standards and practices of the Human Research Protection Program. Relevant policies and procedures are made available to Sponsors, Researchers, Research Staff, research participants, and the Institutional Review Board, as appropriate. (AAHRPP Element I.1.D)**

### 3.1 Policies, Procedures, and Resources Available to Investigators and Research Staff

The Office of Human Subjects Protections (OHSP) has primary responsibility for ensuring the HRPP Policy Manual and related materials are available to the entire MD Anderson research community, including:

- Investigators
- Research staff
- IRB staff
- IRB members
- Employees
- Students
- Trainees
- Sponsors
- Research Participants

The Office of Clinical Research Administration maintains the Office of Human Subjects Protection (OHSP) website, which provides access to:

- The Human Research Protections Program Manual
- Links to pertinent governmental regulations and guidelines
- Links to human research protection related MD Anderson policies
- IRB forms, including checklists, consent and HIPAA authorization templates
- Protocol submission instructions and information
- Frequently Asked Questions for investigators regarding human subject research protections and the IRB review process
- Organizational Charts
- Human subject determination information and forms to assist investigators in identifying which protocols involve human subject research requiring IRB review. For example, the following might not be research under 45 CFR 46, or 21 CFR 50, 56: QA/QI, pilot projects, and case studies (see [IRB Policy on Preparation and Publication of Case Reports and Case Series](#)) (see [Does My Project Need IRB Review?](#)) (see [Authorization for the Use and Disclosure of Protected Health Information](#)).
- New alerts highlighting the posting of new information or changes in existing policies and procedures
- IRB education presentations
The IRB staff is readily available by telephone and in-person to assist investigators and research staff on human subject research matters, particularly IRB applications and review questions.

IRB member education is provided on a quarterly basis, or more frequently depending on their responsibilities on the IRB (e.g., IRB Chair or Vice Chair). OHSP staff including the IRB staff are required to attend monthly Informational Meetings to discuss changes in regulations or institutional policies that may impact their specific responsibilities. Each quarter, at the beginning of IRB meetings, the IRB Chair or IRB Manager provides an educational presentation on any new or revised policy or procedures governing human subject research. Each quarterly education presentation will also be made available to all IRB members on the Office of Human Subjects Protection website. There is also a monthly IRB Chairs meeting where experts on varying topics will be invited to attend and provide a focused educational training to the IRB leadership (e.g., Institutional Official, IRB Chairs, IRB Vice-Chairs, IRB Associate Chairs, IRB staff and OCRA Directors and Managers)

The identification of new information involving human research participant protection such as new organizational policies, or emerging ethical and scientific issues is a shared responsibility between the components of the Office of Clinical Research Administration. Information about new or modified laws are also identified by legal and regulatory counsel from MD Anderson’s Institutional Compliance Office. New information is posted on the Office of Human Subjects Protection website as well as other websites in the division and is disseminated to the IRB staff, IRB members and the MD Anderson research community via other distribution sources, including monthly research newsletters that detail new policies, procedures, and regulations. Employee Notes articles are also disseminated when necessary.

MD Anderson’s institutional policies are available on Institutional Compliance Program – Institutional Policies and maintained and managed by MD Anderson’s Institutional Compliance Office.

**MD Anderson has and follows written policies and procedures that allow the Institutional Review Board to function independently of other organizational entities in protecting research participants. (AAHRPP Element I.1.C)**

### 3.2 Independence of IRBs

**Organizational Structure that Provides Independence**

The President of MD Anderson has delegated the authority and responsibility to establish, maintain and oversee the HRPP to the Vice President for Clinical Research Administration as specified in the President’s [Delegation of Authority for the Human Research Protection Program](https://example.com).

The Vice President for Clinical Research Administration reports to the Vice President and Deputy Chief Academic Officer, Clinical & Interdisciplinary Research and does not have a direct reporting relationship to any part of MD Anderson that carries out research or to any of the
other organizations covered by the HRPP. MD Anderson IRB members are MD Anderson faculty members and their IRB duties are carried out independently of their other departmental or divisional reporting relationships (see Memo for Vice-Chair, Memo for IRB Member, Memo for IRB Associate Member, Memo for IRB Associate Chair, and Memo for Chair Appointment). The duties of the Vice President for Clinical Research Administration and the Office for Clinical Research Administration all relate to establishing, implementing, and helping with adhering to policy for human participant research.

Delegation to the IRB

The Vice President for Clinical Research Administration delegates independence and authority to the IRBs (Charge to the Institutional Review Boards on Human Subjects In Medical Research, Charge to the Institutional Review Board on Human Subjects in Nonmedical Research, and Charge to the Executive Institutional Review Board on Human Subjects in Medical and Nonmedical Research) through this Chapter 3 and the Charge to each IRB Chair and member at the time of their appointment. The IRBs have authority to:

- Review, approve, disapprove, or require changes in research involving human participants
- Suspend or terminate research involving human participants or an investigator’s privilege to conduct such research (e.g., in situations where research is not being conducted in accordance with IRB requirements, or where the research has been associated with unexpected serious harm to participants)
- Observe, or have a third party observe the consent process
- Observe, or have a third party observe the conduct of research.

Prohibition against Others Usurping IRB Approval Authority or Using Undue Influence

MD Anderson officials, investigators, and employees, and sponsors contracting with MD Anderson for research are prohibited from:

- Maintaining or claiming IRB approval of research that has been disapproved or not yet been reviewed by the IRB
- Attempting to use or using undue influence with the IRB, any of its members or staff, a PI or any other member of the research team to obtain a particular result, decision or action.

“Undue influence” means attempting to interfere with the normal functioning and decision-making of the IRB or to influence an IRB member or staff, a PI or any other member of the research team outside of established processes or normal and accepted methods, in order to obtain a particular result, decision or action by the IRB or one of its members or staff.

In addition, to avoid undue influence of IRB members, the IRB preserves the anonymity of members assigned as reviewers to specific protocols or protocol events, and does not publish IRB membership lists.
An individual who believes he or she has been subjected to such undue influence should make a report of non-compliance under Chapter 3 (e.g., to the Institutional Compliance Office or Vice President for Clinical Research Administration). Such reports to the Vice President for Clinical Research Administration will be reviewed in the same manner as possible non-compliance by an IRB Chair or the OHSP Director along with the Vice President for Clinical Research Administration as described in Chapter 3. Reports to the Institutional Compliance Office will be reviewed in accordance with the Institutional Compliance Program policies and procedures.

MD Anderson employees are encouraged to report compliance concerns by directly contacting the Chief Compliance and Ethics Officer via the page operator at 713-792-7090 or through the Institutional Compliance Office at 713-745-6636. A compliance hotline, 1-800-789-4448, is available 365 days a year, 24-hours a day, for reporting compliance concerns, suspected violations, or questionable conduct. The types of response to attempts to unduly influence the IRB are determined as appropriate to the situation, by either the Vice President for Clinical Research Administration or the Institutional Compliance Office.

**MD Anderson has and follows written policies and procedures for determining when activities are overseen by the Human Research Protection Program (AAHRPP Element I.1.A)**

### 3.3 Regulatory Definition of Human Subject Research

Human subject research is defined under 45 CFR §46.102, and 21 CFR §50.3. Human subjects research\(^\dagger\) is defined as any of the following: (a) research that involves a living individual about whom an investigator conducting research obtains (i) data through intervention or interaction with the individual, or (ii) identifiable private information; (b) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; (c) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens; (d) research that involves the use or disclosure of Protected Health Information; (e) an experiment involving one or more human subjects, in which a drug is administered or dispensed to, or used; or (f) a clinical investigation or research that involves one or more human subjects to determine the safety or effectiveness of a device. Thus, human subjects research includes research on disease mechanisms, biomarker protocols, therapeutic interventions, clinical protocols, prevention protocols, epidemiological and behavioral protocols, tissue, and data banking, outcomes research, and health services research.

See also MD Anderson’s Standards of Conduct: [Do The Right Thing](#) publication for additional information on human subjects research.

The IRB retains ultimate authority to determine whether an activity meets the definition of human subject research. Upon receipt of a Protocol Application Form (minimal risk research) in PDOL, the IRB makes this determination in a timely manner, and communicates to the PI the decision on whether the activity meets the definitions as defined in the HRPP Policy Manual.

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\(^\dagger\) The term clinical research is sometimes used synonymously for human subjects research.
The IRB will receive the Standard Protocol Form from the Scientific Review Committee or directly from the PI if there is a request to bypass scientific review. Depending upon the risk level of the research that has been submitted, the IRB will determine if expedited or convened board is required. Please refer to Chapter 7.

Chapter 1 describes the types of human subject research conducted at MD Anderson. All protocols involving both "research" and "human subjects" (other than those determined to be exempt) must be reviewed and approved by the IRB before recruitment and/or data collection may start. See:

- Office of Human Subjects Protection website
- Does My Project Need IRB Review?
- What Qualifies as Human Subject Research

Depending on the source of support for research, regulations from other agencies such as DoD, etc. might apply (see Other Federal Agencies - Additional Requirements).

The IRB has and follows written policies and procedures for determining when activities are exempt from applicable laws and regulations, when permitted by law or regulation and exercised by the IRB. Such policies and procedures indicate that exemption determinations are not to be made by Researchers or others who might have a conflict of interest regarding the studies. **(AAHRPP Element II.2.A)**

### 3.4 Exempt Research Determinations

Categories of exempt research are stipulated in the Common Rule, Subpart A of 45 CFR Part 46. See 45 CFR §46.101(b), and 21 CFR 56.104 (FDA), and guidance Exempt Review Categories Common Rule, FDA, and MD Anderson Policy.

**Exempt status shall not be granted when:**

- Research involves prisoners as participants, pursuant to subpart C (45 CFR §46.305 (a))
- Categories (1) through (5) apply and research is subject to FDA regulations
- Category (b)(2) applies and research involves children as participants, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed, pursuant to subpart D (45 CFR 46.401 (b).
- The project involves significant physical invasions or intrusions upon the privacy of participants.

The IRB s refers to guidance Exempt Review Categories Common Rule, FDA, and MD Anderson Policy and use the IRB Research Determination and Exempt Review Form to verify that the PI has requested an appropriate exemption under the appropriate category.

Confirmation of exempt status is made by IRB members or designated IRB staff who have the knowledge and authority to confirm exemption. If a protocol meets the criteria for exemption,
a New PA Protocol Exempt Memo is generated and available for the PI. This notice indicates category(ies) under which the exemption is granted.

Emergency use of a test article is exempt from prospective IRB review under 21 CFR 56.104. See Chapter 5 for more information on this topic.

Making Exemption Determinations without Conflict of Interest
Those IRB members, staff, and consultants involved in reviewing and approving the exempt determination of protocol applications must not participate in the review of protocols in which they have a conflicting interest – see Chapter 6 for policies prohibiting such situations.

OHSP staff will check for conflict of interest (COI) before sending to the IRB Chair, IRB Vice-Chair or designee selected to review the Protocol Application. IRB Chair, IRB Vice-Chair or designee cannot be in the same department as the study PI, cannot be a study Co-Chair/Collaborator, or have any financial interest.

IRB Chair, IRB Vice-Chair or designees have the authority to review research that may be considered exempt from the regulations. The IRB Research Determination and Exempt Review Form will be used to document the IRB Chair, IRB Vice-Chair or designees determination.

The IRB determinations will be documented in the electronic databases and will be provided to the PI and research teams via an IRB memo.

Emergency use of a test article is exempt from prospective IRB review under 21 CFR 56.104. See Chapter 5 for more information on this topic.

The IRB has and follows written policies and procedures for addressing protection of participants in research that is exempt from applicable laws and regulations. These functions may be delegated to an entity other than the IRB. (AAHRPP Element II.2.B)

3.5 Policies and Procedures for Exempt Research
MD Anderson requires protocols qualifying for exempt review to be submitted for IRB review and confirmation of exempt status. While such research is exempt from the regulations set forth in 45 CFR 46.101(b), and 21 CFR 56.104 (FDA), the research must meet MD Anderson HRPP ethical standards governing the conduct of research (see Chapter 1).

The IRB ascertains that exempt protocols provide appropriate protection of privacy and confidentiality interests (see Chapter 1).

If there are interactions with participants, authorization requirements under the Privacy Rule may apply to exempt research, such as providing the following information:

- The activity involves research
- A description of the procedures
• Participation is voluntary
• Name and contact information for the investigator.

Exempt Review Process

PIs are required to submit the Exempt Application Form in the Protocol. In reviewing the application, IRB staff refer to guidance Exempt Review Categories and use the IRB Research Determination and Exempt Review Form to verify:
• Whether the PI has requested an appropriate exemption, and
• That exemption, if granted, is assigned under the appropriate category.
• The review is performed by IRB staff or IRB members who have the knowledge and authority to confirm exemption, or refer the protocol for expedited or regular review.

If a protocol meets the criteria for exemption, a New PA Protocol Exempt Memo is generated and is available for the PI.

If a protocol does not meet criteria for exemption, it is returned to the PI with notification of failure to meet the criteria. As appropriate, the application is converted to a Protocol Application for expedited or regular review.

Once a protocol is determined to be exempt, it is not reviewed again unless a modification application is submitted. There is no continuing review process for exempt research, as long as the criteria for exemption remain satisfied.

Policy for Not for Human Subjects Research (Quality Improvement)

The Quality Improvement Assessment Board (QIAB) is established by Institutional Policy, Quality Assessment Improvement Board Policy (ADM1080) and reviews all MDACC Quality Improvement (QI) projects to: assure patient safety; optimize the potential benefits being sought; and discern which projects may be more appropriately designed or categorized as research studies requiring Institutional Review Board (IRB) oversight.

[boxed text]

MD Anderson has and follows written policies and procedures that identify applicable laws in the localities where it conducts human research, takes them into account in the review and conduct of research, and resolves differences between federal or national law and local laws.

(AAHRPP Element I.1.G)

3.6 Federal and State of Texas Requirements

The IRB requires that Principal Investigators (PIs) comply with the local, federal, and state laws that are applicable to their research.

MD Anderson legal and regulatory counsel in the Institutional Compliance Office and Legal Services department provide advice to investigators, MD Anderson’s IRBs, IO, and DSMBs about such laws, including compliance with state laws while acting in accordance with the Common
Rule, FDA regulations, and HIPAA, and to assist in resolving any conflicts among applicable laws.

As needed, and in consultation with MD Anderson legal and regulatory counsel if necessary, IRB staff develop educational materials for investigators and IRB members and staff relating to new state laws.

**Texas Health and Safety Code, Texas Family Code, and Texas Administrative Code.**

See MD Anderson institutional Informed Consent Policy (CLN0547) that is in accordance with Texas law regarding the informed consent for care, treatment, services, medications, interventions, and procedures performed as part of standard of care or research, and decision-making capacity requirement and provisions related to lack of capacity.

**Texas Revised Uniform Anatomical Gift Act**

See MD Anderson institutional Policy on Postmortem Biospecimen Collection for Research (ACA1271) in accordance with Texas law in addition to applicable federal laws.

**Laws of Other States (Research Outside of Texas)**

MD Anderson investigators conduct research in states other than Texas. As each state has different laws, MD Anderson investigators are expected to adhere to the laws of the state in which research is being conducted as well as those of Texas.

When necessary other attorneys in MD Anderson’s Institutional Compliance Office, Legal Services department, or outside attorneys retained by MD Anderson provide direction and interpretation of Texas and laws of other states.

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**MD Anderson has and follows written policies and procedures to identify, manage, and minimize or eliminate individual financial conflicts of interest of Researchers and Research Staff that could influence the conduct of the research or the integrity of the Human Research Protection Program. The Organization works with the Institutional Review Board in ensuring that financial conflicts of interest are managed and minimized or eliminated, when appropriate. (AAHRPP Element I.6.B.)**

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### 3.7 Investigators’ Conflicts of Interest (COI)

**Conflict of Interest Policies**

MD Anderson has the following policies regarding conflict of interest (COI) for research carried out at MD Anderson or elsewhere:

- MD Anderson institutional policies:
  - Conflict of Interest Policy for Faculty Members, Trainees, Faculty Supervisors, Institutional Decision Makers, and Investigators of The University of Texas MD Anderson Cancer Center (ACA0001), and
MD Anderson’s Chief Compliance and Ethics Officer is responsible for ensuring implementation of the above-listed conflict of interest policies.

**Disclosure of Financial Interests**

As specified in [Conflict of Interest Policy for Faculty Members, Trainees, Faculty Supervisors, Institutional Decision Makers, and Investigators of The University of Texas MD Anderson Cancer Center (ACA0001)](https://example.com), faculty members, Faculty supervisors, trainees, investigators, and Institutional Decision Makers must disclose on an annual basis all financial relationships that reasonably appear to be related to their institutional responsibilities. This is done through MD Anderson’s electronic conflict of interest database portal (COI database). In addition, these individuals can access their disclosures to update previously reported activities or financial relationships, or to enter new activities.

Identification of conflicts of interest (individual and institutional) is carried out by the institutional designated conflict of interest official with assistance from the Conflict of Interest Committee (individual conflict of interest) and the Institutional Conflict of Interest Committee.

The IRB office receives a memo from the conflict of interest committee (COIC) detailing new disclosures from investigators. These memos detail the protocols that may be affected by the disclosure.

A member of the OHSP will review the memo for the following information:

- The role of the investigator in each protocol listed in the COI memo.
- The amount of money the investigator has received in the past 12 months from the entity and any of the partners of the entity.
- The state of the protocol (i.e., active, closed to new patient entry, if there are patients on protocol).
- If any disclosures already exist in the informed consent.

If a disclosure is needed, a memo will be sent to the protocol staff by a member of the IRB staff. If the protocol staff requests the consent to be updated, this request should be sent to the original OHSP staff member who reviewed the disclosures for the meeting.

If not action is needed, a copy of the original memo will be signed by a representative of OHSP and filed in the hard copy of the protocol.

A summary of OHSP’s recommendations will be presented to IRB3 and voted on before an action is taken.

**Management of Investigator Conflict of Interest Disclosures**
If one of the investigators on a protocol has answered “yes” to one of the screening questions, the case is managed in accordance with University policies.

All investigators’ conflicts of interest are managed via the Conflict of Interest office and its associated Conflict of Interest Committee (COIC). Points of contact are listed on the Conflict of Interest website.

Conflict disclosure in the informed consent process may be an important part of the management strategy, but will not necessarily be the only strategy used. It is the responsibility of the COIC and at times the Institutional Conflict of Interest Committee (ICOIC), to determine what strategy or strategies are appropriate to eliminate, mitigate, or manage conflict that has the potential to harm subjects or compromise the objectivity of the research, or are likely to be perceived as having that potential.

Role of the IRB

Review of Potential Conflicts of Interest with Initial Approval

When a potential conflict of interest has been identified, the IRB communicates closely with the appropriate COI point of contact and the investigator throughout the protocol review process. When appropriate, a plan or strategy to adequately eliminate, mitigate, or manage the conflict must be determined by the COIC and accepted by the IRB. See Chapter 14.1. The COI Manager fills out a Transaction Assessment Report that informs the IRB of the ICOIC evaluation including any management plan. The IRB has the final authority to decide whether the potential conflict of interest and its management, if any, allows the research to be approved.

- When there are non-substantive outstanding COI matters, a protocol may be approved contingent upon the matters being resolved (e.g., requiring that the investigator modify the informed consent document to include verbatim language).
- When there are substantive outstanding COI matters, a protocol will either be tabled or precluded from activation until matters are resolved.

As stated in the Conflict of Interest Policy for Faculty Members, Trainees, Faculty Supervisors, Institutional Decision Makers, and Investigators UTMDACC (ACA0001), no faculty member may be the principal investigator (PI) or co-PI of a clinical trial when that faculty member:

- owns stock in the sponsor of that study;
- has stock options in the sponsor of that study;
- is on the Board of Directors of the sponsor of that study;
- has an ongoing consultation agreement with the sponsor of that study that involves receipt of anything of value in excess of $25,000.00 in any twelve month period within the previous 12 months; or
- received anything of cumulative value in excess of $25,000.00, except for reimbursement of actually incurred reasonable and customary travel expenses, from the sponsor of that study in any twelve month period within the previous 12 months.
If a faculty member has a disclosed conflict that involves receipt of anything of value less than $25,000 in any twelve month period within the previous 12 months with the sponsor of the study, he/she may serve as the PI so long as this information is listed in the informed consent document for the study, along with a listing of any conflicts between co-investigators and the sponsor of the study. If study collaborators, the UT System, The University of Texas MD Anderson Cancer Center (MD Anderson), the President of MD Anderson, or an Executive Vice President of MD Anderson have a financial interest in the sponsor of a study, that too will be disclosed in the informed consent document for that study.

**Record keeping**

Records on all disclosures of financial interests and all decisions to manage, reduce, or eliminate conflicts of interest are maintained in the COIC database. This information will be made available to DHHS upon request, while maintaining the confidentiality of all records of financial interest. The IRB decisions on COIs are maintained in the OHSP protocol file.

**Additional requirements**

Additional requirements might apply, depending on the source of support/funding (e.g., Cancer Prevention Research Institute of Texas, Department of Defense), or particular requirements regarding financial disclosures and agency notifications (e.g., if the research must follow Public Health Service [PHS]) (see Other Federal Agencies - Additional Requirements).

**MD Anderson has and follows written policies and procedures to identify, manage, and minimize or eliminate financial conflicts of interest of the Organization that could influence the conduct of the research or the integrity of the Human Research Protection Program. (AAHRPP Element I.6.A)**

### 3.8 Institutional Conflict of Interest

Organizational conflict of interest is handled in accordance with Institutional Conflict of Interest Policy for The University of Texas Cancer Center and its Institutional Decision Makers (ADM1273). MD Anderson’s ICOI Committee serves as an advisory committee to The University of Texas System and is responsible for reviewing MD Anderson’s Significant Financial Interests and MD Anderson’s Institutional Decision Makers’ Financial Interests to determine if those interests constitute an Institutional Conflict of Interest (ICOI), and for addressing identified ICOIs through reduction, management, or elimination of such ICOIs. The ICOI Committee’s responsibilities are set forth in the Institutional Conflict of Interest Policy for The University of Texas Cancer Center and its Institutional Decision Makers, and include submission of MD Anderson and Institutional Decision Makers institutional conflict of interest management plans to UT System and the UT System Executive Vice Chancellor for Health Affairs (EVC), for approval. All research including human subjects research that is such institutional conflict of interest management plans must be in compliance with the plan requirements including oversight by an external IRB and external data safety monitoring board. In addition, MD Anderson will educate all MD Anderson members of research teams carrying out research subject to an institutional conflict of interest management plan, including those responsible for
identification and enrollment of protocol participants, about MD Anderson’s financial conflict of interest and the requirements of such plan.

See the Institutional Conflict of Interest Policy for the University of Texas MD Anderson Cancer Center and Its Institutional Decision Makers (ADM1273) for more information.

**MD Anderson has and follows written policies and procedures setting forth the ethical standards and practices of the Human Research Protection Program. Relevant policies and procedures are made available to Sponsors, Researchers, Research Staff, research participants, and the Institutional Review Board, as appropriate. (AAHRPP Element I.1.D)**

**MD Anderson has and follows written policies and procedures for addressing allegations and findings of non-compliance with Human Research Protection Program requirements, and works with the Institutional Review Board, when appropriate, to ensure that participants are protected when non-compliance occurs. Such policies and procedures include reporting these actions, when appropriate. (AAHRPP Element I.5.D)**

### 3.9 Non-Compliance with HRPP Requirements

Any situation of perceived or actual serious or continuing non-compliance jeopardizes the MD Anderson commitment to human subject research protection. Receiving information about possible non-compliance is essential for accountability and education purposes, correcting non-compliance, deterring it from occurring again, and attempting to mitigate any adverse effects on research participants. Please see MD Anderson IRB Policy on IRB Committee Determinations for Reviewing Research Non-Compliance, Suspending or Terminating Research and Process for Internal and External Reporting.

**Definitions**

**Non-compliance:** An action or activity in human subject research at variance with the approved IRB protocol, other requirements and determinations of the IRB, the HRPP Policy Manual and other applicable policies of MD Anderson or relevant state or federal laws.

**Serious non-compliance:** Non-compliance that affects the rights or welfare of human subject research participants, including failure to obtain IRB approval for human subjects research.

**Continuing non-compliance:** A pattern of non-compliance that continues to occur after a report of non-compliance and a corrective action plan has been reviewed and approved by the IRB, after an investigator has been warned to correct errors or noncompliance, or a circumstance in which an investigator fails to cooperate with investigating or correcting non-compliance.

**Obligation to Report Non-Compliance**
• Principal investigators, researchers, and other MD Anderson workforce members are encouraged to self-report non-compliance with the HRPP to the IRB or the Vice President for Clinical Research Administration.
  o Vice President for Clinical Research Administration, Aman Buzdar, M.D., 713-745-7139
  o OHSP Director, Wanda Quezada, 713-563-5445
  o IRB Manager, Marion Olson, 713-792-1809
  o IRB Office, 713-792-OHSP
• MD Anderson’s Institutional Compliance Program and Institutional Code of Conduct require MD Anderson workforce members to report compliance concerns. Such reports can be made by directly contacting the Chief Compliance & Ethics Officer via the page operator at 713-792-7090 or through the Institutional Compliance Office at 713-745-6636.

Additionally, MD Anderson has established the following compliance telephone hotlines to report suspected violations or questionable conduct:
  • The Fraud and Abuse Hotline (1-800-789-4448).
  • The Privacy Hotline (1-888-337-7497).

All discussions and reports to the Institutional Compliance Office or the compliance telephone hotlines are treated confidentially and may be made on an anonymous basis. Each report is reviewed, and the Chief Compliance & Ethics Officer initiates any needed investigations, corrections, and/or follow-up.

Alternatively, alleged wrongdoing may be reported to the UT Systemwide Compliance Office:
  • Compliance Hotline at 1-888-228-7786 or e-mail systemwidecomp@utsystem.edu.
  • Chief Compliance and Risk Officer, Phillip Dendy, at 512-499-4389.
  • Vice Chancellor, General Counsel and UT System Ethics Officer, Daniel H. Sharphorn, at 512-499-4462.
  • Chief Audit Executive, J. Michael Peppers, at 512-499-4390.

Individuals may also report suspected fraud, waste, and abuse involving state resources to the State Auditor’s Office’s Hotline at 1-800-TX-AUDIT (1-800-892-8348). The State Auditor’s Office provides additional information on its website.

Research participants and individuals not directly involved with conducting or overseeing the research are also encouraged to report suspected non-compliance. Information about various reporting methods is provided on MD Anderson’s Institutional Compliance Office’s intranet website as well as MD Anderson’s intranet site.

Possible non-compliance or evidence of non-compliance might also be discovered by Office of Clinical Research Administration and its components during the course of their normal duties.
and are required to be reported to the IRB and the Vice President for Clinical Research Administration.

**Non-Compliance – Allegations or Findings**

Generally, self-reported instances by investigators on the Report Form are reviewed by the IRB and will be accepted as a finding of non-compliance. IRB determinations are reported to the Vice President for Clinical Research Administration and reported to appropriate enforcement agencies such as the Office for Human Research Protections and the FDA.

**Review of Allegations or Findings of Non-Compliance**

All reports of non-compliance are initially evaluated by the IRB staff. A report will either be designated as not requiring further action, or will be escalated for review by the OHSP Director or their delegate.

For non-compliance that is potentially serious or continuing, the OHSP Director in consultation with the IRB Chair and the Vice President for Clinical Research Administration, will ensure that immediate action is taken as necessary to prevent unacceptable risk to research participants or others.

All reports of non-compliance are required to be reviewed by the IRB Chair. The IRB Chair may determine that a report requires no further review if the non-compliance is:

- A factual assertion of non-compliance (generally self-reported by the investigators);
- Neither serious nor continuing; and
- Addressed by the investigator through a corrective action plan to remedy the problem.

If a report of non-compliance does not require further action, the incident and corrective action plan will be documented in writing and stored in appropriate files. The PI will receive a written final determination report from the IRB. Findings of possible serious or continuing non-compliance are referred to the convened IRB for review and, in the event that the IRB requests further investigation will be carried out by the Institutional Compliance Office.

If a report is an allegation of non-compliance, the OHSP Director or delegate will review the report (see *Addressing Allegations and Findings of Non-Compliance*).

**Investigation**

The OHSP Director or delegate reviews the report and takes one or more of the following courses of action for non-compliance allegations:

- Conducts an initial review in coordination with the IRB Chair with support from IRB staff
- Requests that legal and regulatory counsel in the Institutional Compliance Office provide advice.
- Requests assistance from others departments at MD Anderson, *e.g.* Institutional Compliance Office, Risk management, Patient Advocacy.
During the fact-finding process, the OHSP Director or delegate communicates as appropriate with the PI or representative about the progress of the review and investigation. A factual and objective written record of findings and evidence is made by the OHSP and stored in the appropriate files.

Allegations which, in the opinion of the OHSP Director or delegate and the IRB Chair, as supported by the information gathered and reviewed are determined to be findings of non-compliance.

Findings of non-compliance are assessed by the OHSP Director or delegate and the IRB Chair as to whether they are either serious or continuing.

If the non-compliance is neither serious nor continuing, the OHSP Director or delegate, alone or with the IRB Chair, examines whether the PI understands the non-compliance and has an adequate corrective action plan. If so, the decision and corrective action plan are documented and filed, otherwise the report is referred to the IRB (the convened IRB, the IRB Chair, or their delegate) for review (see Process for Internal and External Reporting).

**Serious or Continuing Non-Compliance Referred to the IRB**

Serious or continuing non-compliance is referred for review and determination by the convened IRB. The report with other relevant portions of the protocol is made available to the reviewer(s). The IRB considers all information (e.g. new risks, history of non-compliance, FDA black box warnings), in determining whether changes are needed in the protocol or consent and authorization form.

As a result of this review, the following actions may be taken:

- The IRB determines that additional information is needed and requests that such information be obtained before further action is taken.
- The IRB determines that non-compliance did not occur or that non-compliance occurred but was neither serious nor continuing, and either takes no action or requires or recommends an appropriate corrective action plan.
- The IRB determines that non-compliance occurred and that it was serious or continuing. This is referred to as a “Reportable Decision” (see Chapter 3), and the IRB:
  - Takes action appropriate to the situation (see possible actions below)
  - Follows the internal reporting procedure required in Chapter 3 concerning determinations of serious or continuing non-compliance.
- For concerns not within the IRB’s purview, the IRB refers the matter to the appropriate official at MD Anderson.
- IRB determinations and actions are recorded, and communicated as appropriate to the relevant, involved individual(s), normally including the PI.
- IRB determinations of serious or continuing non-compliance are reported internally and externally as described in Chapter 3.
Possible IRB Actions for Serious or Continuing Non-Compliance

In considering actions for serious or continuing non-compliance, the IRB seeks to:

- Correct the non-compliance
- Deter it from occurring again (e.g., hold the relevant individuals accountable for their actions and provide education on how to comply), and
- Attempt to mitigate any adverse effects on participants.

The IRB must consider:

- Suspension or termination of the protocol pursuant to Chapter 9. Suspension or Termination of IRB Approval and the MD Anderson IRB Policy on IRB Committee Determinations for Reviewing Research Non-Compliance, Suspending or Terminating Research.
- Notification of current participants (required when such information may relate to participants’ willingness to continue to take part in the research)

Other possible IRB actions include but are not limited to the following:

- Monitoring of the research
- Monitoring of the consent process
- Referral to other organizational entities (e.g., legal counsel, risk management, institutional official)
- Changes to previously approved protocol and consent forms
- Modification of the information disclosed during the consent process
- Provision of additional information to past participants
- Requiring re-consent of current participants for continued participation
- Modification of the continuing review schedule
- Participation by research team members in additional training or education
- When appropriate, applying any corrective action to all similar protocols
- Referral to the IO for referral to institutional leadership for possible institutional disciplinary or action

If the IRB action will affect participants in the protocol (e.g., requires withdrawal of participants), the IRB utilizes a process that takes into account the impact on their health and safety as described in Chapter 9.

Additional Requirements - Other Federal Agencies

See Other Federal Agencies - Additional Requirements for requirements depending on the source of support/funding (e.g., Department of Defense).

IRB-related Non-Compliance Involving an IRB Chair, IRB Member or OHSP Staff

IRB Chairs, IRB Members, or OHSP Director

The Vice President for Clinical Research Administration is primarily responsible for investigating and reviewing IRB-related non-compliance involving an IRB Chair, IRB member or the OHSP
Director. If a fact-finding review of an allegation is necessary to assess the evidence, it could include the Vice President for Clinical Research Administration acting alone, empaneling a review committee requesting that legal counsel provide advice and conduct the review, or requesting assistance from others. If the Vice President for Clinical Research Administration makes a finding of serious or continuing non-compliance, the report is referred to the IRB for review and other institutional offices as appropriate.

**OHSP Staff**

The OHSP Director is primarily responsible for reviewing non-compliance involving OHSP staff. The OHSP Director may delegate the initial review or fact-finding to others, such as the supervisor of the staff member. If the non-compliance is deemed to have merit the OHSP Director in consultation with the Vice President for Clinical Research Administration is ultimately responsible for determining the action via MD Anderson policies and procedures:

**Possible IRB Actions for Non-Compliance Involving an IRB Chair, IRB Member or Staff**

Possible actions as determined by the Vice President, Clinical Research Administration, include but are not limited to the following:

- As appropriate: Evaluation of the IRB Chair’s or member’s ability to serve on the IRB, or evaluation of the staff member’s ability to support the IRB
- Other actions as appropriate to MD Anderson Human Resources institutional policies
- Referral to the appropriate department chair or division head for action in accordance with institutional policies and procedures.

**Reporting to AAHRPP**

MD Anderson’s HRPP is seeking accreditation by the Association for the Accreditation of Human Research Protection Programs (AAHRPP). In addition to the information that MD Anderson is required to provide to AAHRPP in annual reports and the re-accreditation application, AAHRPP requires that any of the following are reported to AAHRPP after the organization or any researcher (if the researcher is notified rather than the organization) becomes aware:

- Any negative actions by a government oversight office, including, but not limited to, OHRP Determination Letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated, FDA Restrictions Placed on IRBs or Investigators, and corresponding compliance actions taken under non-US authorities related to human research protections;
- Any final resolution of litigation, arbitration, or settlements related to human research protections under the auspices of MD Anderson; and/or
- Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding MD Anderson’s HRPP.

As part of the institution’s commitment to the human subjects research accreditation program, the Institutional Official is responsible for ensuring these incidents are monitored and reported to federal agencies, institutional officials and AAHRPP as soon as feasible, and in compliance
with federal, state and local laws. The Institutional Official maintains standard procedures for monitoring, tracking and resolving these types of events.

With assistance from MD Anderson’s Legal Services Department and Institutional Compliance Office, the Institutional Official will submit a quarterly summary report to AAHRPP that includes information on the following in relation to human subjects protection:

- Any negative actions by a government oversight office, including, but not limited to, OHRP Determination Letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated, FDA Restrictions Placed on IRBs or Investigators, and corresponding compliance actions taken under non-US authorities related to human research protections;
- Any final resolution of litigation, arbitration, or settlements related to human research protections such as lack of informed consent and research conducted without IRB approval.

Additionally, a summary of any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding MD Anderson’s HRPP will be reported to AAHRPP within 48 hours of the Institutional Official becoming aware of such coverage. The Institutional Official will obtain assistance from MD Anderson’s Public Relations Office for fulfilling this reporting.

**MD Anderson has and follows written policies and procedures for addressing allegations and findings of non-compliance with Human Research Protection Program requirements, and works with the Institutional Review Board, when appropriate, to ensure that participants are protected when non-compliance occurs. Such policies and procedures include reporting these actions, when appropriate. (AAHRPP Element I.5.D)**

**The IRB has and follows written policies and procedures for addressing unanticipated problems involving risks to participants or others, and for reporting these actions, when appropriate. (AAHRPP Element II.2.F)**

### 3.10 Unanticipated Problems Involving Risks to Participants or Others (UPs), and Other Reportable Information

Principal Investigator responsibilities for reporting unanticipated problems involving risks to research participants or others, and other reportable information, are outlined in Chapter 14.

**Events and Information – Required Reporting to the IRB**

Events and information that must be reported to the IRB, along with the timelines for reporting, are listed in the guidance MD Anderson IRB Policy on Reporting Protocol Deviations, Protocol Violations, and Unanticipated Problems. Protocol deviations are reported on a Protocol Deviation Log and submitted with the continuing review form in CORe. Violations are submitted on a Protocol Violation Tracking Form. Unanticipated problems are submitted on an
Unanticipated Problem Form via PDOL Generic Memo. All of these forms are reported to the IRB online Lotus Notes based system called “PDOL” and a web-based system called PDOL.net.

### Serious Adverse Events
- **Internal SAE Form**
- **Internal SAE Addendum Form**
- **Departmental External SAE Form**

#### Additional reporting requirements
Additional requirements might apply, depending on the source of support/funding (e.g., Department of Defense) (see Other Federal Agencies - Additional Requirements).

#### Optional reporting
The IRB Report Form may also be used to report other items (see MD Anderson IRB Policy Reporting Protocol Deviations, Protocol Violations, and Unanticipated). The IRB will review any information submitted by the PI, but information that is not required to be reported to the IRB by federal regulations or institutional policies, may be returned to the PI.

### 3.11 Review of Reports
See the flowchart Process for Handling Reports. At any point during the review process, the IRB staff, the IRB member, the IRB, the IRB designee or the convened IRB may seek additional expertise if needed.

#### IRB staff evaluation
The IRB staff evaluates reports, checking whether reports have been appropriately completed (e.g., correct report category has been indicated; for events reported as UPs it is indicated that the event was unexpected, related and harmful; supporting documents have been submitted with the report). A report that does not satisfy initial IRB staff evaluation will be returned to the PI with an explanation and, as necessary, request for additional information.

#### IRB member review
Reports which appear to be UPs, and reports of other reportable events and information will be assigned for review by an IRB member with adequate expertise.

The IRB member reviews the report and materials from the protocol file, (e.g., protocol, investigator’s brochure, continuing reviews, modifications, and other reports) and assesses whether the report constitutes a UP or other information that should be presented at an IRB convened meeting.

#### IRB convened meeting review
Prior to the meeting, the IRB staff provides all voting members with a copy of the report and supporting documents.
At the convened meeting, the IRB discusses and votes on whether the report qualifies as a UP or other reportable information. The vote is recorded in the minutes for the meeting. The IRB considers whether any action is necessary, and the decision is documented in the minutes and in the protocol file.

### Possible actions by the IRB

The IRB has a range of available actions it can take if an event is deemed to be a UP or other reportable information. Depending on the severity of the event and the potential for continuing risk to participants, the IRB determines what further action will be required, including:

- Suspending the research
- Terminating the research
- Requiring participants to be notified of the event, especially if the event may relate to the participant’s willingness to continue in the protocol
- Requiring a modification to the research (either as soon as possible or at continuing review). The modification can include a change to the protocol procedures, informed consent process or written informed consent document
- Requiring current participants to be re-consented
- Providing additional information to past participants
- Requiring monitoring of the research or consent process
- Modification of the continuing review schedule
- Referral to other organizational entities (e.g., legal counsel, risk management, institutional official)
- Other actions as deemed appropriate. If the convened IRB:
  - Determines that an unanticipated problem involving risks to participants or others (UP) or some other reportable event has occurred, or
  - Suspends or terminates the approval of a protocol (see Chapter 9), or
  - Determines that serious or continuing non-compliance has occurred (see Chapter 3),

If this is designated a “Reportable Decision”, and internal and external reporting proceeds as outlined in Chapter 3.

Any action taken by the IRB is communicated to the PI, and depending on the severity of the event, the Department Chair and/or Division Head. If the IRB action will affect participants in the protocol (e.g., requires withdrawal of participants), the IRB considers the impact on their health and safety (see Chapter 9).

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**MD Anderson has and follows written policies and procedures for addressing allegations and findings of non-compliance with Human Research Protection Program requirements, and works with the Institutional Review Board, when appropriate, to ensure that participants are protected when non-compliance occurs. Such policies and procedures include reporting these actions, when appropriate. (AAHRPP Element I.5.D)**
The IRB has and follows written policies and procedures for addressing unanticipated problems involving risks to participants or others, and for reporting these actions, when appropriate.

(AAHRPP Element II.2.F)

The IRB has and follows written policies and procedures for suspending or terminating IRB approval of research, if warranted, and for reporting these actions, when appropriate.

(AAHRPP Element II.2.G)

3.12 Internal and External Reporting

Reportable Decisions

If the convened IRB:

- determines that serious or continuing noncompliance has occurred as specified above under Chapter 3, or
- determines that an unanticipated problem involving risks to participants or others (UP) or some other reportable event has occurred as specified in Chapter 3, or
- suspends or terminates the approval of a protocol pursuant to Chapter 9

The IRB sends the Reportable Decision to the Vice President, Clinical Research Administration (see Process for Internal and External Reporting flow chart). Written procedures for reporting unanticipated problems, noncompliance, suspension and termination follow the OHRP and FDA regulations (45 CFR 46.103(5); 21 CFR 56.108(b)).

Additional reporting requirements

Additional requirements might apply, depending on the source of support/funding (e.g., Department of Defense) (see Other Federal Agencies - Additional Requirements).

Time-Line For and Content of Report

The Vice President for Clinical Research Administration will provide a written report to internal departments and external agencies within 30 days from the date of the IRB’s determination.

The report will cover the IRB findings and any applicable actions. The relevant supporting documents may be transmitted with this report.

Distribution

The report is sent to:

- For non-federally or federally-sponsored research, the relevant Department or Agency head, any applicable regulatory body, and OHRP;
- For research that is subject to the Food and Drug Administration regulations regarding human subjects (any activity that involves an approved or unapproved drug or medical device except for activities that involve the use of an approved drug or medical device in
the course of medical practices, and any activity in which data is reported to or held for inspection by FDA), the sponsor and the FDA; and

This written report will be sent as soon as possible, but generally not longer than 30 days after the IRB determination. For more serious incidents, the Vice President for Clinical Research Administration will make a preliminary written report as soon as possible and will follow-up with a final report as soon as additional information becomes available.

For any non-federally or federally sponsored research, the report will include:

- The name(s) of the relevant MD Anderson organization(s) conducting the research
- The title and number of the IRB protocol and of any federal proposal or award in which the Reportable Decision occurred
- The name of the Principal Investigator (PI) on any applicable federal award if different from the PI
- A detailed description of the Reportable Decision
- The actions taken or planned to be taken to address the circumstance(s) and underlying factors leading to the Reportable Decision.

For multicenter research projects, only the institution at which the participant(s) experienced an adverse event determined to be an unanticipated problem (or the institution at which any other type of unanticipated problem occurred) must report the event to the supporting agency head (or designee) and OHRP (45 CFR 46.103(b)(5)).

### 3.13 Assurance of Compliance

MD Anderson as covered by the HRPP maintains a Federalwide Assurance under OHRP (45 CFR 46.103), available to investigators and others involved in human subject research.

MD Anderson has a Federalwide Assurance through the Office for Human Research Protections (OHRP), federalwide assurance number FWA00000363. The MD Anderson Institutional Review Boards (IRBs) are organized and operate in compliance with DHHS regulations as described in 45 CFR part 46, 21 CFR Parts 50 and 56, and the guidelines resulting from the International Conference on Harmonization (ICH) E-6 Good Clinical Practice guidelines, as appropriate.

As per the regulations, each of MD Anderson’s 5 IRBs are registered with OHRP under IRB Organization #0000083 with an expiration date of October 17, 2024. The IRB registration numbers are listed below:

- IRB0000121 U of Texas MD Anderson Cancer CT IRB#1-Clinical
- IRB00002203 U of Texas MD Anderson Cancer Ctr IRB#2-Clinical
- IRB00003869 U of Texas MD Anderson Cancer Ctr IRB#3-Executive Session
- IRB00005015 U of Texas MD Anderson Cancer Ctr IRB#4-Psychosocial/Behavioral
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IRB00006023  U of Texas MD Anderson Cancer Ctr IRB#5-Clinical

The Organization conducts audits or surveys or uses other methods to assess compliance with organizational policies and procedures and applicable laws, regulations, codes, and guidance. The Organization makes improvements to increase compliance, when necessary. (AAHRPP Element I.5.A)

The Organization conducts audits or surveys or uses other methods to assess the quality, efficiency, and effectiveness of the Human Research Protection Program. The Organization identifies strengths and weaknesses of the Human Research Protection Program and makes improvements, when necessary, to increase the quality, efficiency, and effectiveness of the program. (AAHRPP Element I.5.B)

3.14 HRPP Quality Improvement Activities

OCRA component departments and the Institutional Compliance Program are designed to:

• Evaluate and monitor the effectiveness of the HRPP,
• Assess compliance with HRPP policies and procedures,
• Identify areas and implement measures for improvement.

This is accomplished by working with the various components of the HRPP to design, recommend, and implement improvements to promote the protection of human subject research participants.

Compliance Monitoring

The component offices of the OCRA are collectively responsible for monitoring the HRPP. The Office of Protocol Support and Management and the Institutional Compliance Program conduct periodic compliance reviews and for-cause assessments to evaluate adherence to applicable federal regulations, state and local laws and MD Anderson policies and procedures, and to verify that research is conducted in accordance with the IRB approved protocols. Other periodic assessments as related to research finance, IRB operations and IND management may be conducted by Clinical Research Finance, IND Office or the Office of Human Subjects Protection.

• Periodic Compliance Reviews: Periodic compliance reviews are conducted using systematic methods to assess investigator and IRB compliance with federal regulations, state and local laws, and MD Anderson policies and procedures. Periodic compliance reviews include but are not limited to:
  o Examinations of executed informed consent forms
  o Reviews of IRB meeting minutes;
  o Detailed examinations of protocol files;
  o Observations of the informed consent process.
• **For-cause assessments**: The IRB or the Vice President for Clinical Research Administration may direct HRPP staff to conduct an assessment in response to a particular concern. Concerns that may prompt a for-cause assessment include but are not limited to:
  o Failure of routine reviews;
  o Complaints or concerns initiated by a research participant, family member, or research team/workforce member;
  o Reports of serious or repeated non-compliance;
  o Results of reviews or monitoring conducted by other clinical protocol monitors that reported to designated HRPP staff.

**Additional Requirements**

See [Other Federal Agencies - Additional Requirements](#) for other requirements depending on the source of support/funding.

**Reporting of Compliance Monitoring Results**

Results of compliance monitoring activities are documented and reported to the IRB, Institutional Officials and other units within MD Anderson as appropriate. These results, supplemented by other review results when available, provide a quantitative and qualitative measurement of compliance with the HRPP.

**Other Review Activities**

Depending on the results of annual risk assessments conducted by MD Anderson’s Internal Audit Department or Institutional Compliance Office, such department/office may conduct additional reviews of the IRBs and the various departments or offices within MD Anderson that conduct or review human subject research activities.

**Research Community Feedback**

HRPP staff track comments, questions and issues received from the MD Anderson investigators and participants to identify areas for potential improvement in the effectiveness of HRPP policies and procedures and for ensuring the protection of human subject research participants. The principal investigator and key protocol personnel receive a request to respond to a survey after approval of each event by the IRB.

**IRB Performance Metrics**

HRPP staff produce periodic metrics and analysis of the IRB operations and functions, including detailed measurements of activity volume and processing times.

*MD Anderson conducts activities designed to enhance understanding of human research by participants, prospective participants, or their communities, when appropriate. These activities are evaluated on a regular basis for improvement. (AAHRPP Element I.4.B.)*
MD Anderson promotes the involvement of community members, when appropriate, in the design and implementation of research and the dissemination of results. *(AAHRPP Element I.5.A)*

### 3.15 Continuous Quality Improvement (CQI)

Based on the results of the aforementioned assessments and feedback received from the communities served by the HRPP, the CQI Team partners with other components of the MD Anderson HRPP to identify root causes of problems, recommend action plans to correct issues, and provide education, tools and outreach to promote effectiveness of improvements.

Significant changes to the Human Research Protection Program (HRPP) that are implemented as a result of quality assessment and quality improvement activities are monitored to ensure effectiveness and consistency.

This leads to the continuous improvement of the HRPP and the protection of human subject research participants.

**Evaluation**

Evaluations take place in an ongoing manner. The various organizations cited in the previous sections of this chapter evaluate their impact on an ongoing basis. For instance, course evaluations or surveys regarding public opinion on clinical research may be used to facilitate the evaluation process. Survey results are made available as appropriate to the Institutional Official and other institutional departments as
appropriate. If the evaluations indicate that a change in procedures, policies are practice are needed, the appropriate institutional department would be contacted.

All IRB staff, members and Chairs are requested to report both positive and negative feedback about all HRPP outreach activities, (wherever the feedback originates), to the IRB staff, who track this input in order to make changes to improve outreach activities. IRB staff, members and Chairs also submit self-evaluations at the end of each fiscal year. The evaluations are reviewed by the OHSP Director, the IRB Manager and the Institutional Official. Feedback regarding recommended changes to procedures or policies is also shared with the IRB Chairs.

**MD Anderson has and follows written policies and procedures so that Researchers and Research Staff may bring forward concerns or suggestions regarding the Human Research Protection Program, including the ethics review process. (AAHRPP Element I.5.C.)**

### 3.16 Investigators’ Input to the HRPP

There are a variety of mechanisms available for contacting relevant individuals to bring concerns and suggestions, including:

- Reporting possible non-compliance as described in [Chapter 3](#).
- Reporting possible unanticipated problems as described in [Chapter 3](#).
- Making general comments and suggestions and expressing concerns about other matters, issues or processes involving the HRPP, including IRB review and operations to the Office of Human Subjects Protection, the IRB Chairs, the Vice President for Clinical Research Administration, the Vice President & Deputy Chief Academic Officer in Clinical and Intramural Research, or the Chief Academic Officer.
- Participating in institutional surveys regarding the IRB or any component of the HRPP
- Institutional Compliance Program: MD Anderson’s Institutional Compliance Program and Institutional Code of Conduct require MD Anderson workforce members to report compliance concerns. Such reports can be made by directly contacting the Chief Compliance & Ethics Officer via the page operator at 713-792-7090 or through the Institutional Compliance Office at 713-745-6636.
- Additionally, MD Anderson has established the following compliance telephone hotlines to report suspected violations or questionable conduct:
  - Ombuds Office 713-792-4896 or 866-610-7841
  - The Fraud and Abuse Hotline (1-800-789-4448)
  - The Privacy Hotline (1-888-337-7497)
- All discussions and reports are treated confidentially and may be made on an anonymous basis. Each report is reviewed, and the Chief Compliance & Ethics Officer initiates any needed investigations, corrections, and/or follow-up.
- Alternatively, alleged wrongdoing may be reported to the UT System wide:
  - Compliance Hotline at 1-888-228-7786 or e-mail [systemwidcomp@utsystem.edu](mailto:systemwidcomp@utsystem.edu).
  - Chief Compliance and Risk Officer, Phillip Dendy, at 512-499-4389.
  - Vice Chancellor and General Counsel and UT System Ethics Officer, Daniel H. Sharphorn, at 512-499-4462.
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- Chief Audit Executive, J. Michael Peppers, at 512-499-4390.
- Individuals may also report suspected fraud, waste, and abuse involving state resources to the State Auditor’s Office’s Hotline at 1-800-TX-AUDIT (1-800-892-8348). The State Auditor’s Office provides additional information on its website.
Chapter 4. Knowledge of Human Research Protection Requirements

**MD Anderson has an education program that contributes to the improvement of the qualifications and expertise of individuals responsible for protecting the rights and welfare of research participants. (AAHRPP Element I.1.E)**

### 4.1 Education of Individuals Responsible for Human Research

Education and training are provided to all individuals involved with the HRPP. The HRPP Policy Manual specifies education requirements for IRB members, IRB staff, and key personnel on the research team (see Chapter 4). The Office of Protocol Management and Support works with MD Anderson departments and other institutions to offer comprehensive education to the MD Anderson research community.

Education is offered in many areas of research, including ethical standards, related both to research and to professional conduct, MD Anderson policies and procedures, and applicable federal, state, and local law. The foundation of ethical training at MD Anderson is the Belmont Report, which is made available at training sessions and on the Human Subjects Research website.


OHSP has a full-time Quality Assurance Specialist dedicated to developing and providing education for IRB members and IRB staff. The OPSM is dedicated to the development of online educational modules and classroom training sessions that serve the research community regarding human research protections.

**Evaluation of Qualifications**

In addition to receiving training on human subject research protections (described in Chapter 4.2), IRB members and IRB staff are reviewed periodically to evaluate their understanding of the HRPP (ethical principles, policies and procedures, and regulations).

IRB staff qualifications are reviewed during the hiring process and annually or as needed to ensure a high level of commitment to the HRPP.

IRB member qualifications are reviewed by the OHSP Director and the IRB Manager during the recruitment process, and IRB members are formally appointed by the Vice President of Clinical Research Administration.

IRB members, including IRB Chairs, are evaluated yearly to ensure that their service on the IRB contributes to the ethical and regulatory review of research at MD Anderson. Members are re-appointed based on these evaluations.
The Continuous Quality Improvement (CQI) program (described in Chapter 3.15) evaluates the effectiveness of the education provided. Results of the CQI evaluations are used to adjust the content of educational materials, improve delivery methods and identify appropriate audiences, and to communicate with the other components of the HRPP about updating their education and training.

**Contributing to the Improvement of Expertise**

New IRB members and IRB staff receive orientation to the MD Anderson HRPP. All IRB members and IRB staff receive regular, ongoing training at convened meetings and continuing education. Opportunities for continuing education in human research protections are announced on a regular basis. IRB member and IRB staff attendance is encouraged at regulatory and professional meetings and conferences both locally and nationally, and for web broadcasts and seminars at MD Anderson and in the greater community. Additionally, the OHSP supports and encourages professional certification for qualified IRB staff.

Before IRB members can review protocols according to expedited review procedures, they must meet additional training and participation requirements. Members who review protocols using the expedited procedure are appointed by an IRB Chair. In addition, the OHSP and IRB consult with other institutional offices for specific training tailored to the review of certain protocol types, e.g. protocols involving pediatrics, stem cells or gene transfer materials. IRB members’ expertise is considered when assigning primary reviewers (see Chapter 7).

**Educational Materials and Resources**

The MD Anderson research community, IRB members, IRB staff and other individuals responsible for the protection of human research participants have access to a wealth of educational material, available online and in printed format, or offered as courses or workshops. These include, among others:

- The Office of Human Subjects Protection, with links to the MD Anderson HRPP Manual, instructional information, FAQs, educational material, document templates, forms, and guidance documents.
- Access to required training through the interactive online Human Subjects Protection Training (HSPT).
  - Regular ad hoc communications via the Clinical Research Bulletin.
- The PDOL electronic protocol submission system, providing instructional text and explanation as part of the application
- HIPPA Training _ Protecting Patient Privacy
- **Conflict of Interest (COI) _ Annual Certification**
Additional education is provided through classes, training courses, workshops, and seminars offered by the various offices as part of the HRPP component.

**Education Planning**

Senior HRPP staff members meet regularly to discuss the education provided to IRB staff, IRB members, and investigators. They incorporate input received from IRB members, IRB staff and investigators, and from CQI monitoring and evaluation activities. Trends in research at MD Anderson are considered, and new federal, state or local regulations (or published guidance documents) are integrated. Compliance activities (e.g., internal and external audits) also provide input.

**MD Anderson has and follows written policies and procedures setting forth the ethical standards and practices of the Human Research Protection Program. Relevant policies and procedures are made available to Sponsors, Researchers, Research Staff, research participants, and the Institutional Review Board, as appropriate. (AAHRPP Element I.1.D)**

**Researchers and Research Staff recruit participants in a fair and equitable manner. (AAHRPP Element III.1.E)**

### 4.2 Required Training in Human Research Protections

Completion of human subject training by all staff working on a research project (all investigators and other protocol personnel, including all persons who are responsible for the design, conduct, data analysis or reporting) is one of the requirements for protocol approval by the IRB.

MD Anderson provides access to the required training through an interactive online tutorial - Human Subjects Protection Training (HSPT). HSPT offers required training that has been customized for different learner groups (medical and non-medical investigators and members of the research team).

Upon completion of the required modules, the learner can download, save and print a certificate of completion from the online learning management system, Education Center. Individual investigators must maintain their own training records. It is the responsibility of the Principal Investigator to ensure completion of the required training by all protocol personnel, including all persons who are responsible for the design, conduct, data analysis or reporting, and to have all certificates of completion available for inspection.

Training records of IRB Staff, IRB Members and Institutional Officials are maintained in the OHSP.

**OHSP Staff (to include IRB Staff) Required Training**

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### Training

<table>
<thead>
<tr>
<th>Training</th>
<th>IRB Staff/CQI Staff</th>
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<tbody>
<tr>
<td>OHSP orientation for new staff (onboarding checklist)</td>
<td>Required</td>
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<tr>
<td>HRPP Training for new staff</td>
<td>Required</td>
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<tr>
<td>HRPP Information Meeting for new and current staff</td>
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<tr>
<td>Human Subjects Tutorial (HSPT)</td>
<td>Required</td>
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<tr>
<td>HIPAA training as included in <em>Employment, Law, and Practices Training</em> (ELPT) and Employee Education Event (EEE)</td>
<td>Required</td>
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<tr>
<td>Continuing HRPP education such as PRIM&amp;R webinars, SoCRA webinars</td>
<td>Required</td>
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For newly hired OHSP staff involved in the HRPP:
- **HRPP Training** is an on-going process managed by the CQI Staff. New employees are assessed from 6-month of hire date.
- **HSPT training** must be completed within 180 days of employment in OHSP.
- **HIPAA training** required for all employees through ELPT and EEE.

See MD Anderson general policies [Human Resources - New to MD Anderson](#) regarding New Employee Training.

### IRB Members Required Training

<table>
<thead>
<tr>
<th>Training</th>
<th>Medical IRB Members and Chairs</th>
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<tr>
<td>IRB orientation for new and ongoing members</td>
<td>Required</td>
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<td>Human Subjects Tutorial (HSPT)</td>
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### Institutional Official Required Training
The institutional official for human subjects research at MD Anderson must take HSPT training and also participates in the annual IRB Member training.

**Investigator Required Training**

MD Anderson requires that Principal Investigators and other key personnel involved in the design or conduct of a project, including those projects that may be deemed exempt under 45 CFR 46, provide evidence of training and qualifications by submitting relevant documentation as requested by the sponsor, IRB, or regulatory authorities (see Chapter 14).

The IRB-required training of investigators and other key personnel must be completed prior to IRB protocol approval.

**Key personnel**: all investigators and other protocol personnel, including all persons who are responsible for the design, conduct, data analysis or reporting of research that involves human subjects. Key personnel may include faculty, staff, students, or visiting or contract personnel, persons who obtain informed consent, administer surveys, or collect private or personal information from individuals.

In the event that individuals from other institutions (“third-party” or contract employees) conduct research under the oversight of the MD Anderson IRB, they must complete human subjects protections training at MD Anderson. Third-party individuals may be required to take the MD Anderson HSPT modules. All IRB-required training completion records are maintained in the Clinical Oncology Research (CORE) system. For third-party individuals, the IRB will require written documentation confirming that the individual has completed an acceptable HSPT course, and this documentation will be maintained in the IRB’s protocol record. The investigator should also maintain a copy of this documentation in their regulatory binder.

<table>
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<tr>
<th>Training</th>
<th>MD Anderson Investigators</th>
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<tbody>
<tr>
<td>Human Subjects Tutorial (HSPT)</td>
<td>Required Group 7 (medical) Group 2 (nonmedical)</td>
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<tr>
<td>MD Anderson HIPAA training</td>
<td>Required</td>
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</table>

- Examples of investigator training required or recommended per other MD Anderson, non-IRB policies, typically prior to engaging in research are listed below. Refer to individual entities and departments for more information.
  - Information Security Compliance website.
  - Use of Information Technology Policy (ADM0263)
Electronic Confidential and Restricted Confidential Information Access and Storage Policy (ADM1187)

- **GCP training**: available through HSPT for all researchers
- **Integrated Ethics in Cancer Care** - Ethics Education courses and resources (MD Anderson Center for Biomedical Ethics, or Program for Ethics in Society) training; Integrated Ethics - Policies and Procedures
- **Sponsored Projects Administration** Overview (Office of Research Administration, Grants and Contracts Office of Sponsored Programs)
- **Environmental Health and Safety** training (Environmental Health and Safety)

All IRB-required training completion records are maintained in the Clinical Oncology Research (CORE) system. For third-party individuals, the PI is expected to maintain written documentation in their regulatory binder confirming that the individual has completed an acceptable HSPT course. The investigator should also maintain a copy of this documentation in their regulatory binder.

The Office of Protocol Support and Management is a resource for any questions regarding HRPP education for the research community.
Chapter 5. Investigational or Unlicensed Test Articles Research with Drugs, Devices, or Biologics

When research involves investigational or unlicensed test articles, MD Anderson confirms that the test articles have appropriate regulatory approval or meet exemptions for such approval. (AAHRPP Element I.7.A)

5.1 Research with Test Articles

Research with FDA-regulated test articles may commence only after the IRB has approved the protocol and:

- receives documentation that the research will be conducted under an applicable Investigational New Drug Application (IND) or Investigational Device Exemption (IDE);
  The IND goes into effect generally 30 days after the FDA assigns the IND, unless the sponsor receives earlier notice from the FDA; or
- formally determines and documents that the proposed use of any investigational device satisfies the FDA criteria for non-significant risk devices; or
- formally determines that satisfactory justification has been provided by the investigator as to why an IND or IDE is not required.

The IRB collaborates with the Investigational New Drug (IND) Office to support MD Anderson clinical investigators who conduct non-industry sponsored FDA-regulated research.

Definitions

Biologic: A biological or related product, regulated by the FDA, including blood, vaccines, allergies, tissues, and cellular and gene therapies. Biologics, in contrast to drugs that are chemically synthesized, are derived from living sources (such as humans, animals, and microorganisms). Studies of unlicensed biologics are regulated according to the IND regulations, except in some cases when the biologic is in a combination product with a medical device. FDA regulates biologics general use and licensing under 21CFR Parts 600 and 601 (42 U.S.C 262 of the Public Health Service Act).

Clinical investigation: Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the Federal Food, Drug and Cosmetic Act (FD&C Act), or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that must meet the provisions of 221 CFR Part 58, regarding nonclinical laboratory studies. The terms research, clinical research, clinical study, study, and clinical investigation are deemed to be synonymous for purposes of this part (see 21 CFR 56.102).
Combination product: A product containing a combination of a drug, a device, or a biological product. Studies of combination products are regulated according to the IND or IDE regulations, depending on the components of the product. The FDA determines which of its organizational components has primary jurisdiction for the premarket review and regulation of products that are comprised of any combination of a drug, device, and/or biological (see 21 CFR 3.2[e]).

Human subject: An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient (see 21 CFR 56.102).

Off-Label: Use of an approved drug, an approved or cleared device, or a licensed biologic for an indication not in the approved labeling. Most research involving off-label uses requires IND or IDE applications (see FDA Off-Label” and Investigational Use of Marked Drugs, Biologics and Medical Devices).

Test article: Any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 or 354-360F of the Public Health Service Act (see 21 CFR 56.102).

5.2 Research with Drugs

Clinical investigations of drugs are subject to the Investigational New Drug Application (IND) regulations, 21 CFR 312.

An investigational new drug application (IND) is synonymous with “Notice of Claimed Investigational Exemption for a New Drug.” An investigational drug must have an IND before it can be shipped, unless one of the exemptions outlined in 21 CFR 312.2 is met.

Applications for research on the use of a drug, unless that research is exempt from the IND regulations, must be accompanied by documentation from the FDA that includes a valid IND number. The IND number must either match the number on the sponsor protocol with the same title as the proposed research, or be listed on communication from the sponsor specific to the proposed research, or on communication with the FDA. IND numbers may not be validated with an Investigator Brochure (which may serve multiple INDs). The IND number will be required prior to the activation of the protocol.

As stated in 21 CFR 312.2(b), clinical investigation of a drug is exempt from the IND regulations if the drug is lawfully marketed in the United States and all of the following are true:

- The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug;
• If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product;
• The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
• The investigation is conducted in compliance with the requirements for institutional review set forth in part 56 and with the requirements for informed consent set forth in part 50; and
• The investigation is conducted in compliance with the requirements of 21 CFR 312.7 and 21 CFR 312.8 (Promotion and charging for investigational drugs).

Additionally, a clinical investigation involving use of a placebo is exempt from the requirements of 21 CFR 312 if the investigation does not otherwise require submission of an IND. Clinical investigations that are exempt from IND regulations still require IRB review and approval.

Even when there is no immediate intent to change product labeling or advertising, investigators who are planning rigorous, carefully controlled clinical investigations of off-label uses of approved drugs or biologics should contact the IND Office regarding obtaining an IND before submitting a protocol to the IRB. See the FDA guidance for FDA’s current thinking on exemptions from IND regulations for oncology combination protocols. See the FDA guidance IND Exemptions for Studies of Lawfully Marketed Drug or Biological Products.

Drug studies involving Oncology Drugs may be considered IND Exempt based on additional criteria noted in Guidance for Industry IND Exemptions for Studies of Lawfully Marketed Drug or Biological Products for the Treatment of Cancer.

5.3 Research with Devices

Clinical investigations of devices are subject to the Investigational Device Exemptions (IDE) regulations, 21 CFR Part 812.

An approved investigational device exemption (IDE) permits a device that is not approved (via premarket authorization, PMA) or cleared to market (via 510(k)) by the FDA to be shipped to conduct clinical investigations of that device. Significant risk investigational devices must have an IDE issued by FDA before they can be shipped. Sponsor’s Responsibilities for Significant Risk Device Investigations (Nov. 1995) General Duties (21 CFR 812.40) Submitting the IDE application to FDA Obtaining both FDA and IRB approvals for the investigation and submitting certification of IRB approval to FDA before shipping the device to any investigator.

Research with devices falls into three categories:
• Investigations of significant risk devices to determine safety and effectiveness of the device.
• Investigations of nonsignificant risk devices to determine safety and effectiveness of the device
• Investigations exempted from the IDE regulations:
  o Significant Risk (SR) and Nonsignificant Risk (NSR) Medical Device Studies
  o Frequently Asked Questions Medical Devices (FDA)
  o Significant Risk and Nonsignificant Risk Medical Device Studies (FDA)

Studies that include medical device use in an incidental way, where the device or the use of the device is not the focus of the research, are generally not considered to be FDA-regulated research or subject to 21 CFR 812, and in some instances are eligible for IRB review according to the expedited procedure.

**Significant Risk Device Research**

Applications for research on the use of a significant risk device must be accompanied by documentation from the FDA that includes a valid IDE number. The IDE number must either match the number on the sponsor protocol with the same title as the proposed research, or be listed on communication from the sponsor specific to the proposed research, or on communication with the FDA. The protocol may include a pending IDE number as long as an application to the FDA has been submitted, and there is documentation from the FDA indicating that they have received the application. IDE numbers may not be validated with a device manual (which may serve multiple IDEs). Protocols will not be activated until a valid IDE number has been submitted.

**Nonsignificant Risk Device Research**

When research is conducted to determine the safety or effectiveness of a nonsignificant risk device, both the PI and the IRB are responsible for confirming that the device fulfills the requirements in 21 CFR 812.2(b)(1):

• The device is not a banned device;
• The sponsor labels the device in accordance with 21 CFR 812.5;
• The sponsor obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval;
• The sponsor ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator’s care, consent under 21 CFR 50 and documents it, unless documentation is waived;
• The sponsor complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations;
• The sponsor maintains the records required under 21 CFR 812.140(b) (4) and (5) and makes the reports required under 21 CFR 812.150(b) (1) through (3) and (5) through (10);
• The sponsor ensures that participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 21 CFR 812.150(a) (1), (2), (5), and (7); and
• The sponsor complies with the prohibitions in 21 CFR 812.7 against promotion and other practices.

For protocols that do not have a Sponsor, the PI is responsible for fulfilling the Sponsor obligations listed above.

If the investigator applies to the IRB for a nonsignificant risk determination for a device study, but the IRB determines that the device is a significant risk device, the IRB shall notify the investigator and the sponsor, if any.

**Device Research that is exempt from the IDE regulations**

Clinical investigations that are exempt from IDE regulations still require IRB review and approval. An investigation of a medical device in human subjects research that is exempt from the IDE regulations must fall into one of the following categories (Criteria in 21 CFR 812.2(c)):

- A device legally marketed in the US that is used or investigated in accordance with the indications in the FDA-approved labeling.

- A diagnostic device (that is, an in vitro diagnostic device) if the testing:
  - Is noninvasive
  - Does not require an invasive sampling procedure that presents significant risk,

- Does not by design or intention introduce energy into a subject, and

- Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

- A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk.

- A custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

- A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time.

- A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantialequivalence.

**In Vitro Diagnostic Device Research**

In vitro diagnostic (IVD) device investigations may be exempt from the IDE requirements of 21 CFR 812 if the devices are properly labeled and meet the criteria set forth in 21 CFR 812.2(c)(3). However, such studies are still subject to the FDA regulations and IRB review requirements if the research is to support an application for research or marketing of the device (see 21 CFR 50.1). This is true regardless of whether the samples to be used are individually identifiable or not. The FDA regulations define a subject to include a human on whose specimens an
investigational device is used (21 CFR 812.3(p)). Thus, an IVD study to support a premarket submission to the FDA is considered a human subject investigation and is subject to IRB review under 21 CFR parts 50 and 56. IVD research may be eligible for expedited review and without informed consent if the study involves leftover human specimens and as long as subject privacy is protected by using only specimens that are not individually identifiable, when appropriate.

In addition to the above, FDA Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable makes clear that IRB review is one of several criteria for IVD studies using leftover specimens that are not individually identifiable.

5.4 Radiology Devices and Radioactive Materials

Oversight of radiologic devices and radioactive materials at MD Anderson is handled by the Radiation Safety Committee (RSC). Most research involving radiation is covered by an IND or an IDE, and must be reviewed and approved by the IRB. The RSC, in compliance with State regulation, reviews applications from persons requesting use of any radioactive material at MD Anderson Cancer Center. No one may order or receive radioactive material until he/she has been approved as an Authorized User by the RSC.

The protocol includes the necessary radiological safety questions, which are reviewed by both the IRB and the RSC. In addition, the RSC provides feedback for Principal Investigators designing studies with radiation.

The Radiation Safety Committee functions to provide compliance with State regulations, and address safety concerns for patients, staff, and visitors regarding the use of radioactive materials. The Radiation Safety Committee regulates the use of all radioactive material and ionizing radiation-producing equipment in all areas of the institution. The Radiation Safety Committee establishes policy relating to the acquisition, use, storage, and disposal of radioactive material. Authorization requests to use specific isotopes are reviewed and approved by this committee before they may be purchased.

5.5 Research with Biologics

Clinical investigations of biologics are regulated in the same way as clinical investigations for drugs, and require an IND, unless the biologic is part of a combination product that the FDA has assigned for premarket approval to the Center for Devices and Radiological Health (CDRH). In such cases, the biologic/device combination product would require an IDE prior to research approval by the IRB.

Generally, protocols using biological agents or recombinant DNA vectors are reviewed by IRBs 1, 2, and 5. Information about use of biohazardous agents and recombinant DNA at MD Anderson is located on the Institutional Biosafety Committee webpage.
5.6 Institution-held INDs and IDEs for Significant Risk Devices

The University of Texas MD Anderson Cancer Center has worked to initiate an institutional program to provide investigators with support, while at the same time ensuring compliance with sponsor federal regulatory requirements. As a result, MD Anderson takes the obligations of Investigational New Drug (IND) and Investigational Device Exemption (IDE) sponsorship off the investigator and assumes this responsibility at a centralized level.

MD Anderson is the sponsor of record for all investigator-initiated studies that are conducted under IND or IDE and are not sponsored by another entity. The Vice President for Clinical Research is the Official Sponsor representative and the IND Office serves to represent the sponsor on a day-to-day basis.

See:
- Standard Operating Procedure – IND/IDE Information for Supporting Companies
- Standard Operating Procedure – Guidelines for Monitoring MD Anderson IND Sponsored

5.7 Internal Handling of Test Articles

The Department of Investigational Pharmacy Services (IPS) is responsible for the administrative management of all investigational drugs used at MD Anderson. Specific operational responsibilities of this office include but are not limited to drug acquisition, inventory control and investigational drug accountability in compliance with state and federal regulations. An equally important function is the provision of drug information of these agents and protocols for health care professionals within the institution. The IPS serves as the liaison between researchers, IND sponsors, and the Division of Pharmacy in addition to ensuring pharmacy compliance with protocol requirements.

See:
- Investigational Pharmacy Updated Site Initiation Packet
- Standard Operating Procedure – Study Drug Accountability

5.8 Expanded Access to Investigational Drugs and Devices for Treatment Use

Expanded access to investigational drugs and devices requires prior IRB review and approval (with the exception of Emergency Use, Chapter 5).
5.8.1 Drugs

Definitions

**Expanded access**: Use of investigational new drugs and approved drugs where availability is limited by a risk evaluation and mitigation strategy (REMS) when the primary purpose is to diagnose, monitor, or treat a patient’s disease or condition. The aim of this subpart is to facilitate the availability of such drugs to patients with serious diseases or conditions when there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the patient’s disease or condition (21 CFR 312.300 [Subpart I]).

**Expanded Access Programs (EAPs)**: The FDA uses this term to refer to the various types of allowable expanded access use.

**Immediately life-threatening disease or condition**: A stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.

**Serious disease or condition**: A disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one.

There are 3 categories of expanded access program (EAP) for investigational drugs:
- Single patients (CIND), including for emergency use (see Chapter 5.9) (see IRB Policy Single Patient Use of an Investigational Agent or Device _Compassionate Use of an Investigational or Label Drug) (21 CFR 312.310).
- Intermediate-size patient populations (21 CFR 312.315)
- Treatment IND or “treatment protocol” for widespread treatment use (21 CFR 312.320)
(see Expanded Access to Investigational Drugs and Devices)

5.8.2 Devices

The FDA may make an unapproved device available under several mechanisms:
- Emergency Use (see Chapter 5.9)
- Compassionate Use (or Single Patient/Small Group Access) (see IRB Policy Single Patient Use of an Investigational Agent or Device _Compassionate Use of an Investigational or Label Drug)
- Treatment Use (Larger Group/More Widespread Use)
- Continued Access

For more information, see Expanded Access to Investigational Drugs and Devices.
MD Anderson has and follows written policies and procedures for compliance with legal and regulatory requirements governing emergency use of an investigational or unlicensed test article. ([AAHRPP Element I.7.C](#))

5.9 Emergency Use of a Test Article

**Emergency Use**: Use of a test article on a human participant in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval ([21 CFR 56.102(d)](#)).

Specific additional requirements apply, see Emergency Use of a Test Article.

5.10 Humanitarian Use Device (HUD); Orphan Drugs

**Humanitarian Use Device (HUD)**

A Humanitarian Use Device (HUD) is a device intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the United States per year. The regulations under [21 CFR 814 (Subpart H)](#) were designed to promote the development of devices for diseases affecting these populations.

For more information, see Humanitarian Use Device.

**Orphan Drugs**

The Orphan Drug Designation program provides orphan status to drugs and biologics which are defined as those intended for the safe and effective treatment, diagnosis or prevention of rare diseases/disorders that affect fewer than 200,000 people in the U.S. These drugs are not expected to recover the costs of developing and marketing as treatment drugs.

5.11 Planned Emergency Research

**Planned emergency research**: Planned research in life-threatening emergent situations where obtaining prospective informed consent has been waived ([21 CFR 50.24](#)).

- The research plan must be approved in advance by the FDA and IRB. The IRB will follow the HHS and FDA harmonized criteria for review set forth in [21 CFR 50.24](#) and in the flow-chart in FDA’S Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors Exception from Informed Consent Requirements for Emergency Research, Appendix C. The research plan must also be disclosed to the communities where the research will be conducted and from where participants will be drawn, including presentation of the risks and expected benefits of the research. An independent data monitoring committee (DMC) must be established to exercise oversight of the research.

When the research is not regulated by the FDA, advance notice of these protocols will be provided to the Office for Human Research Protections pursuant to federal regulation 45 CFR 46.101(i). PI’s who wish to conduct planned emergency research should consult with IRB staff prior to submission of the protocol to the IRB.
- Planned emergency research is usually not eligible for emergency use approvals.
- Please reference the [IRB SOPs for Evaluating and Monitoring Planned Emergency Research](#) for additional information.
Chapter 6. Structure and Composition of the IRB

6.1 Scope of IRB Authority

The IRB derives its authority from both federal statutory and regulatory, and institutional sources. Institutional authority is conveyed by the Vice President, Clinical Research Administration (VPCRA), and the Deputy Chief Academic Officer & Vice President of Clinical and Interdisciplinary Research, through approval of this chapter and other chapters of the Human Research Protection Program (HRPP) Policy Manual. Additionally, the VPCRA issues a direct, written delegation of authority under an institutional Charge to IRB members upon their appointment to the IRB (see Charge to IRB members [Charge to the Institutional Review Boards on Human Subjects In Medical Research and Charge to the Institutional Review Board on Human Subjects in Nonmedical Research]). The VPCRA in turn has the authority Delegation of Authority for the Human Research Protection Program to him or her by the President of MD Anderson (President). On an as needed basis and as it relates to the HRPP, the IRB communicates with the VPCRA, directly or through the Office of Human Subjects Protection (OHSP) Director. However, in extraordinary circumstances, as warranted, an IRB Chair, an IRB member, or the convened IRB may refer a matter directly to the President.

The IRB has the statutory and regulatory, and institutional authority to take any action necessary to protect the rights and welfare of human research participants involved in research. For example, the IRB assesses suspected or alleged protocol deviations, participant complaints, or violations of external regulations or MD Anderson policies. The IRB has the authority to suspend or terminate the enrollment or ongoing involvement of research participants in research as it determines necessary for the protection of those participants. The IRB also has the authority to observe or monitor any human research to whatever extent it considers necessary to protect research participants (45 CFR 46.109, and 46.113).

Upon request, the IRB shall review and comment on proposed external regulations dealing with human research. When appropriate, the IRB will formulate draft policies and procedures for approval by the appropriate MD Anderson bodies and promulgation by the VPCRA.

The HHS regulations at 45 CFR part 46, subpart E, require all IRBs to register with HHS if they will review human subjects research conducted or supported by HHS and are to be designated under an assurance of compliance approved for federalwide use by OHRP (see MD Anderson's Federalwide Assurance).

The MD Anderson IRBs are registered with the Office for Human Research Protections by an OHSP staff designated by the OHSP Director. Each IRB is registered electronically through http://ohrp.cit.nih.gov/efile/. If there are changes to the IRB membership during the year, the IRB registration is updated and submitted to OHRP (see Statement of IRB Compliance).

Decisions of the IRB
IRB approval is always required before a research project involving human research participants may begin. An IRB decision to not approve a human research project, or require modifications as a condition for approval, may not be overturned by any MD Anderson official or MD Anderson committee (45 CFR 46.112).

The IRB must provide the investigator with a written statement of the reasons for not approving proposed research and must give the investigator an opportunity to respond in person or in writing. The IRB must carefully and fairly evaluate the investigator’s response in reaching a final determination.

If an investigator has concerns with respect to procedures or decisions of the IRB, the investigator may discuss his/her concerns with the VPCRA with the understanding that neither the VPCRA, the Deputy Chief Academic Officer & Vice President of Clinical and Interdisciplinary Research, nor any other MD Anderson official or committee may approve a protocol that has not been approved by decision of one of the Boards, nor apply undue pressure on the Board to reverse a decision (45 CFR 46.112).

At the time an investigator seeks to discuss his or her concerns with the VPCRA, those concern(s) must be in writing, and the VPCRA will use his or her sole discretion to determine the process for responding to the concern, included but not limited to:

- Notifying the IRB of the concern and requesting a response and relevant information from its records
- Appointing a fact-finder to review the matter and report back to the VPCRA
- Seeking assistance from consultants or internal administrative units such as the Institutional Compliance Office, Internal Audit, Legal Services, Risk Management, or Information Security.

However, all such reviews are subject to the fundamental principle that no one at MD Anderson can approve a human subjects protocol that has not been approved by an IRB, nor apply pressure on the Board to reverse a decision. Thus, policies clearly state that no other review or person at MD Anderson can overturn the decision of an IRB.

**Reporting Obligations within MD Anderson**

The OHSP provides administrative support to MD Anderson’s IRBs, and is a component of the Office of the VPCRA. The VPCRA is the institutional official responsible for assuring compliance with MD Anderson policies and external regulations as it relates to human research participants, and is the head of the MD Anderson HRPP. The OHSP Director and the IRB Manager provide annual reports to the Vice President, Clinical Research Administration, summarizing the nature and volume of MD Anderson’s IRBs’ activities and resources needed for the new fiscal year.

**Responsibilities to Regulatory Agencies**
The IRB must comply with the requirements of all relevant federal regulatory and compliance enforcement agencies or offices, including OHRP and FDA, as well as relevant agencies of the State of Texas.

6.2 Relationships Between the IRB and Others

The IRB is required at times to coordinate its approvals with other programs or research compliance committees at MD Anderson that also have responsibility for the ethical oversight of research within the HRPP. In some cases, the approval of another MD Anderson body may be required prior to or in addition to, but not in lieu of IRB review. Such cases include:

Radiological Safety: If a protocol involves any radioisotopes or radiation-producing machines, the Radiation Safety Committee (RSC), in compliance with State regulation, reviews applications from persons requesting use of any radioactive material at MD Anderson. No one may order or receive radioactive material until he/she has been approved as an Authorized User by the RSC.

The Radiation Safety Committee functions to provide compliance with State regulations, and address safety concerns for patients, staff, and visitors regarding the use of radioactive materials. The Radiation Safety Committee regulates the use of all radioactive material and ionizing radiation-producing equipment in all areas of the institution. The Radiation Safety Committee establishes policy relating to the acquisition, use, storage, and disposal of radioactive material. Authorization requests to use specific isotopes are reviewed and approved by this committee before they may be purchased.

Protocols involving biohazardous materials and requiring review by the Institutional Biosafety Committee must be reviewed by this committee and receive an approval letter in addition to review and approval by the IRB.

Investigator Conflict of Interest disclosures: All investigator conflicts of interest and financial disclosures are managed in accordance with MD Anderson’s Conflict of Interest Policy for Faculty Members, Trainees, Faculty Supervisors, Institutional Decision Makers, and Investigators UTMDACC (ACA0001) and Conflict of Interest Committee (COIC). The IRB will not approve a protocol until any disclosed COI has been reviewed and resolved by the COIC, and as appropriate, a plan or strategy to adequately eliminate, mitigate, or manage the conflict has been determined by the COIC (see Chapters 3.7, 6.2, and 14.2).

Clinical and Translational Research Center (CTRC): Depending upon the nature of the research, for any human research supported by the CTRC, in addition to IRB approval, CTRC approval must be obtained prior to enrolling participants in the protocol.

The Scientific Review Committees (SRCs): The SRCs are officially constituted committees of The University of Texas MD Anderson Cancer Center that report to the Vice President of Clinical Research Administration. The four SRCs each meet monthly to evaluate the scientific content and prioritization of all clinical protocols, including investigator-initiated, pharmaceutical and biotechnology company-sponsored; multi-institutional; and other clinical investigation
protocols deemed as high-risk. Each committee has two Co-Chairpersons and at least 12 members appointed to each of the SRCs with representation from the majority of the Institutional Divisions. Committees will also have multidisciplinary members from Diagnostic Imaging, Pharmacy, Nursing, Pathology and the Quantitative Sciences Division. In addition, each SRC committee will have one volunteer member from the community.

**Psychosocial, Behavioral, and Health Services Research Committee (PBHSRC):** The PBHSRC, which is an officially constituted committee of The University of Texas MD Anderson Cancer Center that reports to the VPCRA. The purpose of the PBHSRC is to evaluate the scientific content of research that addresses areas related to psychosocial, behavioral and health services research. The PBHSRC meets on a monthly basis. This committee has three Chairpersons who share Chair responsibilities on a rotating monthly basis and at least 12 members appointed with representation from the different areas (i.e. Behavioral Science, Health Disparities, Palliative Care, etc.) and a representative from the Department of Quantitative Science.

**The Data & Safety Monitoring Board:**

**Data Safety Monitoring Board (DSMB):** The DSMB reports to the President, or his designee, as the on-campus representative of The University of Texas Board of Regents. This board’s membership consists of clinical faculty and biostatisticians from both MD Andersons as well as clinical faculty from outside of the institution. The DSMB convenes 10 months of the year and oversees the data and patient safety issues for the following categories of trials: Phase II or higher randomized and/or blinded clinical trials that are PI initiated at MD Anderson; trials that are coordinated or analyzed by MD Anderson and are not being monitored by any other DSMB; or trials that have been designated as requiring DSMB monitoring at the request of the IRB or institution.

**External Data and Safety Monitoring Board (eDSMB):** The eDSMB reports to the President, or his designee, as the on-campus representative of The University of Texas Board of Regents. This board’s membership consists of clinical faculty and biostatisticians from outside of MD Anderson. Currently, the EDSMB holds one annual meeting, but more meetings will be added as more protocols come under EDSMB oversight. EDSMB oversees the data and patient safety issues for trials where MD Anderson has a Significant Financial Interest and it has been determined if those interests constitute an Institutional Conflict of Interest (ICOI).

**The IND Office:** Regulatory and monitoring oversight for investigator-initiated IND protocols is provided by the IND Office on behalf of the Vice President for Clinical Research, the official IND sponsor. Services include assisting the PI in the preclinical concept stage, arranging a pre-IND meeting with the FDA, formatting the initial IND submission, and facilitating all communications with the FDA and the Recombinant DNA Advisory Committee (RAC) throughout the life of the trial. Clinical Research Monitors review these IND trials for compliance every 8-12 weeks based on protocol-specific, risk-based monitoring plans. Medical Affairs/Safety, within the IND Office, is a new group initiated in 2016 and dedicated to pharmacovigilance, responsible for reviewing serious adverse events and toxicity and safety summaries.
The Cell Therapy Laboratory: The Cell Therapy Laboratory specializes in cell processing procedures, such as high-speed cell sorting, cord blood expansion, and gene modification, and supports researchers throughout MD Anderson in performing complex molecular protocols.

Human Embryonic and Induced Pluripotent Stem Cell Research Oversight: Any human research involving human embryonic and/or induced pluripotent stem cells must be reviewed and approved by MD Anderson’s Human Embryonic and Induced Pluripotent Stem Cell Research Oversight Committee (HEIPSCRO) as well as the IRB.

Relationships with Industry Sponsors and Other IND or IDE Holders

Unless specifically required by the FDA or requested by the sponsor, the IRB will not routinely provide written notification of IRB decisions to industry sponsors and other holders of INDs or IDEs (MD Anderson held INDs excepted). For FDA-regulated research, clinical investigators generally serve as the link between the IRB and the sponsor, as required by the FDA in compliance with their obligations as clinical investigators. This relationship is agreed to by investigators when they sign FDA Form 1572 (for drug and biologic protocols) or an investigator agreement for device protocols.

There are occasions when direct communication between the IRB and the sponsor may facilitate resolution of concerns about protocol procedures or specific wording in an informed consent document. The IRB staff may engage in such direct communication on behalf of the IRB when the IRB Chair or the OHSP Director or IRB Manager considers it desirable. The clinical investigator will be kept apprised of such communication.

The FDA indicates that direct communication between the sponsor and the IRB may be appropriate when the IRB does not accept a sponsor’s Non-Significant Risk (NSR) designation of a medical device (21 CFR 812.66). Direct communication between the sponsor and the IRB is required for the waiver of informed consent in planned emergency research relative to (a) the public disclosures required under 21 CFR 56.109(a)(7)(ii),(iii); or (b) disapproval of such a waiver under 21 CFR 50.24(e) (see Chapter 5.11).

The IRB has qualified leadership (e.g., chair and vice chair) and qualified members and staff. Membership and composition of the IRB are periodically reviewed and adjusted as appropriate. (AAHRPP Element II.1.B)

6.3 IRB Composition and Membership

Each IRB has a qualified Chair, Associate Chair, Vice-Chair, members, associate members, and staff whose membership and composition is reviewed and adjusted annually by the VPCRA in collaboration with the IRB Chair(s), OHSP Director, and the IRB Manager. This review ensures that individual IRB Chairs and members have the knowledge, skills, and abilities appropriate to their respective roles and perform their responsibilities in an acceptable manner.
MD Anderson policy requires that the IRB consists of at least 5 members according to DHHS regulations and FDA regulations (45 CFR 46.107 and 21 CFR 56.107). Additionally,

- The IRB shall include a nonscientific IRB member, educated and with experience in unambiguously nonscientific areas (see Checklist for Determining if IRB Members are Nonscientists), to represent the perspective of research participants. These individuals may not have meaningful scientific or medical training or experience. Health professionals, regardless of discipline, may not be considered nonscientists. At least one non-scientist IRB member must always be present to have a quorum. See discussion of quorum in Chapter 6.10.

**MD Anderson has and follows written policies and procedures to separate competing business interests from ethics review functions. (AAHRPP Element II.1.C)**

To avoid any possible conflicting interests or influence on IRB determinations due to competing MD Anderson business interests, individuals who are responsible for development activities (including raising funds), or are in a position to influence programmatic and budgetary decisions may not serve as IRB Members (see Chapter 6.8).

**Appointment of Members and Associates Members, Length of Service, and Duties**

IRB members and associate members are nominated from lists of faculty members submitted by Department Chairs and Division Heads, faculty members that volunteered, and faculty members suggested by the Faculty Senate, the VPCRA, and the IRB Chairs. Consideration is given to balancing race, gender, expertise, and cultural backgrounds. People with active licensure from various clinical disciplines are sought. A background knowledge of and current familiarity with affiliated institutional concerns (e.g., DoD research, Cancer Networks, Houston Area Locations, community based research) helps ensure that the local research context is brought to IRB deliberations. Sensitivity to issues such as community attitudes and international dimensions is valued. During the three months prior to September 1st (the start date for the IRB year) newly identified nominees are contacted by the IRB Manager (or delegate) about their willingness to voluntarily serve on the IRB and their availability for the coming year. When a nominee agrees to serve on the IRB, his or her curriculum vitae and any relevant correspondence are provided to the IRB staff.

After an extensive review of a potential member’s education, experience and other characteristics that might add diversity to the IRB, a new IRB member is formally appointed by the VPCRA. Members and associate members serve one-year renewable terms (from September 1 to August 31). Members and associate members may be re-appointed to new terms without a lapse in service at the end of each term. At the conclusion of the IRB year (and interim, if needed), members’ and associate members’ contributions are evaluated by the IRB Chair with assistance from the IRB Manager (see Chapter 4). If their service is satisfactory, and continued membership is mutually desired, they are eligible for reappointment. The items reviewed include but are not limited to the following: 1) Attendance at convened board
meetings, 2) Number of new protocols presented at convened board meetings, 3) Length of stay at convened board meetings, and 4) Contribution to discussions at convened board meetings. All members and associate members may be re-appointed at the end of their terms without lapse in service. An IRB member or associate member may be removed at the discretion of the VPCRA in consultation with the IRB Chair, the IRB Manager, and the OHSP Director. The removal is based upon completion of the stated criteria noted in the following paragraphs.

Members and associate members are responsible for ensuring that the rights and welfare of research subjects are protected. Members vote to approve, require modifications in, disapprove, or defer research submitted to the IRB. Associate members will vote in the place of members not in attendance, i.e. associate scientific member will vote in the place of a scientific member. Members and associate members are expected to attend IRB meetings on a regular basis, serve as primary reviewers for research within their areas of expertise, and serve as general reviewers on all research. Members and associate members may also be asked to participate in subcommittees, audits, and education, as long as there is no conflict of interest with their IRB responsibilities or their other personal or professional roles.

**Associate IRB Members**

Associate members replace regular IRB members who are unable to attend convened board meetings of the IRB. They are required to have the same qualifications and characteristics of expertise and diversity as the regular IRB members for whom they substitute. When an associate substitutes for a regular member, the IRB staff provides the associate member the same material that the regular member received or would have received.

IRB membership rosters specify which regular member each associate member is qualified to replace. The expertise or qualifications of associate members are similar to those of the regular member they replace, and in some case, associate members are able to represent similar interests or a specific vulnerable population. Terms of appointment, length of service, and duties are exactly as for regular IRB members. Associate members must adhere to the same conflict of interest standards and documentation requirements as regular IRB members.

If an associate member attends a convened meeting at which his or her regular member is in attendance, one of them does not vote.

Senior IRB staff may also be appointed as an associate member in an administrative member function. The senior IRB staff provide regulatory guidance and expertise when attending the convened board meetings.

**Appointment of IRB Chair, Associate Chair, and Vice-Chair, Length of Service, and Duties**
IRB Chairs, Associate Chairs, and Vice-Chairs are nominated from current IRB members. In addition to the characteristics sought in an IRB member, these individuals possess demonstrated skills in leadership and group process.

IRB Chairs, Associate Chairs, and Vice-Chairs are formally appointed by the VPCRA. IRB Chairs, Associate Chairs, and Vice-Chairs serve yearly renewable terms (from September 1 to August 31). At the conclusion of the IRB year (and interim, if needed) the IRB Chairs’, Associate Chairs’, and Vice-Chairs’ contributions are evaluated by the VPCRA with the OHSP Director and the IRB Manager (see Chapter 4). The items reviewed include but are not limited to the following: 1) Attendance at convened board meetings, 2) Number of new protocols presented at convened board meetings, and 3) Length of stay at convened board meetings, and 4) Contribution to discussions at convened board meetings, 5) Timely completion of specifically assigned duties i.e. continuing reviews, protocol modifications, and 6) Timely completion of assigned reviews. If their service is satisfactory, and their continued service is mutually desired, they are eligible for reappointment. An IRB Chair, Associate Chair, and Vice-Chair may be removed at the discretion of the VPCRA in consultation with the OHSP Director and the IRB Manager: this action is based on the criteria above.

In addition to the responsibilities of IRB membership, the Chair has primary responsibility for conducting IRB meetings and working with staff for completion of applicable regulatory reviews in a timely manner. The IRB Chair also will review non-compliance issues. The IRB Chair works with IRB members, institutional officials, and investigators to ensure that the rights and welfare of research participants are adequately protected. The Associate Chair will conduct the IRB meeting in the Chair’s absence. The Associate Chair and Vice-Chair have primary responsibilities assigned specific to the continuing review process, review of protocol modifications to protocols, and review of reportable new information. The OHSP Director and IRB Manager ensure effective and efficient operation of the IRB within all applicable regulatory and IRB policy requirements.

**Qualification to Perform Expedited Review**

An IRB Vice-Chair may be assigned responsibility for performing protocol review according to the expedited review procedure when the IRB Chair, in consultation with the IRB Manager, determines that the member is "experienced" with regard to this purpose. There are several ways a member may achieve sufficient experience, including attendance at IRB meetings, targeted education, working with a mentor, independent protocol, and previous IRB service. See Chapter 7 and Policy on Designated Individuals for more information.

**Compensation of IRB Members**

IRB Chairs receive a $24,000 annual stipend to offset the time dedicated to IRB duties. IRB Associate Chairs receive $15,000 annual stipend, and IRB Vice-Chairs receive $12,000 annual stipend; these stipends are paid by MD Anderson from the Clinical Research Administration budget. IRB members generally do not receive monetary compensation for their service on the
IRB. IRB members who are clinicians do receive risk management credits. It is recognized that service on the IRB requires a significant investment of time for all members.

Ex Officio IRB Members
An ex officio member is designated as an IRB member by virtue of that individual’s institutional title/role. For example, if the Executive Director, Clinical Research Administration changes, that ex officio IRB membership changes hands accordingly and does not remain with the individual who has left that role. Some ex officio members serve on other MD Anderson oversight committees and may provide expertise to the IRB. Ex officio members may participate in IRB deliberations to provide information and expertise as requested by the IRB. Ex officio members are expected to adhere to the same conflict of interest and confidentiality standards and documentation requirements as regular IRB members and associate members. Ex officio members may not vote on any IRB action or determination, and for this reason are sometimes referred to as “non-voting” members.

The medical IRBs may designate permanent ex officio representatives from the following areas:
- Office of the Vice President, Clinical Research Administration
- Office of Clinical & Interdisciplinary Research
- Institutional Compliance Office
- Legal Services Department

The nonmedical IRB may designate permanent ex officio representatives from the following areas:
- Office of the Vice President, Clinical Research Administration
- Office of Clinical & Interdisciplinary Research
- Institutional Compliance Office
- Legal Services Department

The IRB may designate additional permanent ex officio members with the agreement of the IRB Chair, the OHSP Director, and the IRB Manager.

Support of IRB Membership
The IRB has a qualified staff, dedicated to supporting the IRB in its mission to protect human participants in research. The IRB staffing model is reviewed at least annually by the OHSP Director, the IRB Manager, and the VPCRA to ensure sufficient administrative support for the IRB. The IRB staff who directly support the IRB have knowledge, skills, and abilities appropriate to their respective roles. The OHSP Director oversees the IRB Manager, the IRB Supervisors, and is responsible for the overall management of OHSP.

For policies on qualifications, education and periodic evaluation of IRB staff, see Chapter 4.
6.4 Scientific and Scholarly Expertise of IRB Members

Wide-ranging scientific or scholarly expertise among IRB members allows the IRB to review the broad variety of research in which MD Anderson investigators are engaged. These policies and procedures require IRB members to be knowledgeable about all relevant regulatory requirements, and to strive to remain impartial and objective during protocol review, deliberation, and voting. The IRB includes several members who are particularly knowledgeable about research ethics and the vulnerable research participants included in MD Anderson research.

The IRB uses a “presenter reviewer” system. The IRB Manager, in consultation with the IRB Chair where appropriate, assigns protocols to presenter reviewers, based on each individual’s scientific, scholarly, professional, or clinical expertise. Presenter reviewers must have the relevant expertise to conduct an in-depth review of the protocols assigned. If the IRB Manager cannot identify a presenter reviewer with the appropriate scientific or scholarly expertise, the IRB Manager arranges for expert consultation and will not place the protocol on an agenda until appropriate expertise is made available. Presenter reviewers are expected to conduct an in-depth review, and it is the responsibility of presenter reviewers to notify the IRB Chair or IRB staff should they feel unqualified or unable to do so. In such cases, the IRB Chair will assign presenter review responsibilities to another member who is appropriately qualified or obtain consultation from one or more experts outside the IRB (see below).

When the IRB reviews research that involves categories of participants vulnerable to coercion or undue influence, the review process includes one or more individuals who are knowledgeable about or experienced in working with such participants (children, pregnant women, adults unable to consent, students, etc.). The IRB staff reviews each set of submitted protocol documents to determine whether it involves participants vulnerable to coercion or undue influence, and considers the participant population when assigning primary reviewers.

The IRB is constituted to possess and make use of collective knowledge of applicable regulatory and legal requirements; knowledge of professional standards and practices; knowledge of the local research context and research sites, and their capabilities and limitations; knowledge of community standards and attitudes; scientific, scholarly, clinical, and professional expertise; racial, ethnic, and cultural diversity; and representation of participants’ perspectives.

6.5 Obtaining Additional Expertise

The IRB Chair or IRB Manager reviews the proposed convened meeting agenda and determines whether the IRB has the required expertise to review upcoming research. If not:

- The IRB Manager, in consultation with the IRB Chair, will invite individuals with competence in the specific areas needed to assist in evaluating issues that require expertise beyond or in addition to that available on the IRB.
- On an as-needed basis, an IRB presenter reviewer, in consultation with the IRB Chair or IRB Manager, may invite individuals with competence in special areas to assist in evaluating specific issues.
Reasons for seeking additional or special competence from outside experts may include (but are not limited to) the need for additional scientific, clinical, or scholarly expertise; the need for particular knowledge and understanding about potentially vulnerable populations of subjects; the desire to ensure appropriate consideration of race, gender, language, cultural background, and sensitivity to such issues as community attitudes.

Additional expertise may be obtained through a member of another IRB, or individuals from various departments/offices within MD Anderson, such as:

- Institutional Compliance Office
- Legal Services Department
- Office of Research Administration
- Office of Protocol Management & Support
- MD Anderson IND Office
- MD Anderson Clinical and Translational Research Center
- Various specialty Clinical Departments at the affiliated institutions
- Experts from other institutions
- Representatives from the community
- Representatives from specific subject populations

The IRB Manager or the IRB Chair makes initial contact with a proposed consultant and notifies the consultant of the IRB member conflict of interest policy (See Chapter 6.6). When a consultant is used, that fact and the pertinent information gained from the consultant’s assessment is documented at the time of the protocol discussion, and recorded in the IRB minutes. In some cases, a consultant may provide the IRB with a written report of his or her assessment, which is kept with the protocol file. The IRB staff can assist in making the consultation arrangements and in obtaining the required conflict of interest documentation.

All consultants, internal or external to MD Anderson, must comply with the Guidelines for IRB Members on Conflicting Interest. They are not considered ad hoc IRB members, and are not permitted to vote.

The Guidance for Obtaining Additional Expertise or an Expert Consultant addresses the use of consultants in further detail.

The IRB has and follows written policies and procedures so that members and consultants do not participate in the review of research protocols or plans in which they have a conflict of interest, except to provide information requested by the IRB. (AAHRPP Element II.1.D)

6.6 IRB Member, IRB Staff, and Consultant Conflicting Interest

See 45 CFR 46.107(e); 21 CFR 56.107(e).
Guidelines for IRB Members on Conflicting Interest includes definitions of conflicting interest and outlines procedures for recusal. This guideline applies:
- When protocols and reports are first received by members assigned to review
- During discussion and voting in convened meetings
- When consultants are asked to advise the IRB

This guideline applies to all protocols reviewed by the IRB, regardless of whether the protocol is exempt or considered during full, expedited, or continuing review. This guideline also applies to reviews of non-compliance reports and unanticipated problems involving risks to participants or others.

IRB intake procedures take into account conflicts of interest when assigning new protocols to an IRB, such as when any IRB member is named in the research protocol or has a spousal relationship with any research personnel.

IRB Member’s Disclosure of a Conflicting Interest

IRB members who realize they have a conflicting interest when they are first assigned a protocol or report for review are required to notify the IRB staff or IRB Chair immediately so that the protocol can be reassigned.

IRB members review the draft Agenda List before a convened meeting with conflicts of interest in mind. Any conflicting interest for protocols to be voted on must be reported to the IRB Chair or IRB Manager before the meeting whenever possible.

The IRB Chair begins each meeting with a reminder that proceedings are confidential. This is followed by a reminder of the requirement that each member must disclose any conflicting interest and recuse him or herself from the discussion of, and vote on, the protocol by leaving the room, except if the member is providing information at the IRB’s request. If an IRB member realizes at a meeting that he or she may have a conflicting interest with regard to a protocol, then that should be disclosed to the IRB Chair immediately, orally and in writing on the IRB Member Conflict of Interest Declaration.

Consultant’s Disclosure of a Conflicting Interest

The definition of conflicting interest as defined in the Guidelines for IRB Members on Conflicting Interest extends to any consultant who may be asked to review a protocol. The IRB Manager who contacts a consultant to enquire about review of a project is responsible for asking if the consultant has a conflicting interest in the project. If such an interest exists, then the protocol will not be assigned to the consultant. If no conflict of interest is declared, the consultant is asked to complete a Consultant Conflict of Interest Declaration for inclusion with the minutes of the meeting.
If a consultant with a conflicting interest is the only appropriate resource for the IRB, (e.g., is the only scientist with sufficient technical understanding of the project) and if that consultant has been asked to provide information to the IRB, then the conflict of interest must be disclosed to the IRB members reviewing the protocol or present in the convened meeting where the information is presented. Such a consultant is excluded from discussion except to provide information requested by the IRB, and must leave the meeting room during the rest of the discussion and voting.

6.7 IRB Staff and Conflicting Interest

IRB Staff must not participate in the review of research protocols, and must not make exempt determinations for research protocols in which they have a conflict of interest. IRB staff are required to identify if they have a conflicting interest when they are first assigned a protocol or a report for review, and they must notify their supervisor immediately so that the protocol can be reassigned.

The MD Anderson Conflict of Interest Policy (ADM0255) is distributed annually to IRB Staff who are involved in protocol review.

MD Anderson has and follows written policies and procedures to separate competing business interests from ethics review functions. (AAHRPP Element II.1.C)

6.8 Separating Competing Business Interests from Ethics Review Functions

To avoid any possible conflicting interests or influence on IRB determinations due to competing business interests, individuals who are responsible for development activities (including raising funds), or are in a position to influence programmatic and budgetary decisions may not serve as IRB Members.

MD Anderson recognizes that officials who administer research programs, and individuals who are responsible for development activities (including raising funds), may represent competing MD Anderson business interests, or be in a position to influence programmatic and budgetary decisions and exert undue influence on IRBs or individual IRB members. To avoid such influence on IRB determinations, the VPCRA, Senior Vice Presidents, Division Heads, Department Chairs, or other senior institutional officials defined as Institutional Decision Makers in institutional conflict of interest policies, will not serve as voting members of the IRBs.

MD Anderson’s ICOI Committee serves as an advisory committee to The University of Texas System and is responsible for reviewing MD Anderson’s Significant Financial Interests and MD Anderson’s Institutional Decision Makers’ Financial Interests to determine if those interests constitute an Institutional Conflict of Interest (ICOI), and for addressing identified ICOIs through reduction, management, or elimination of such ICOIs. MD Anderson implements ICOI management plans to (i) ensure the integrity of its research, (ii) be transparent about MD Anderson’s actual, potential, and perceived institutional conflicts of interest with respect to its research, (iii) assure that the safety of protocol subjects is paramount by ensuring that research
is conducted appropriately, and (iv) ensure that the results of research are accurately reported and unbiased. The ICOI Committee’s responsibilities, and various ICOI management approaches are set forth in the Institutional Conflict of Interest Policy for The University of Texas Cancer Center and its Institutional Decision Makers (see the Institutional Conflict of Interest Policy for the University of Texas MD Anderson Cancer Center and Its Institutional Decision Makers [ADM1273]).

Department chairs are required to review and sign off on all research proposals being submitted by faculty in their departments, divisions or institutes, including those involving human subjects research. This review occurs when the proposal is submitted for funding to an extramural sponsor (as part of the electronic submission of the Proposal Development & Routing Form, PDRF) or in meeting their obligation to provide scientific evaluation when internal funds are used to support a human subjects research project. In carrying out these duties, the department chair must identify any personal financial conflict of interest, regardless of value, that he or she has in the research sponsor or in an entity that has an interest in the investigational product that is the subject of the research.

Thus, the institutional leaders, as described above, do not:

- Serve as members on the IRB.
- Carry out day-to-day operations of the review process except as noted above.

As stated in the charges to the IRBs, “…neither the Vice President, Clinical Research Administration, nor the Deputy Chief Academic Officer & Vice President, Clinical and Interdisciplinary Research, nor any other MD Anderson official or committee may approve a protocol that has not been approved by the decision of one of the Boards, nor apply undue pressure on the Board to reverse a decision (as further provided in Chapter 3 of the HRPP Policy Manual).” See:

- Charge to the Institutional Review Boards on Human Subjects in Medical Research
- Charge to the Institutional Review Board on Human Subjects in Non-Medical Research
- Charge to the Executive Institutional Review Board on Human Subjects in Medical and Non-Medical Research

6.9 Assessment and Evaluation of the IRB

The composition and membership of each IRB is evaluated annually by the OHSP Director, the IRB Manager and the VPCRA and is adjusted as needed to ensure appropriate knowledge of applicable regulatory and legal requirements; knowledge of professional standards and practices; knowledge of the local research context and research sites and their capabilities; knowledge of community standards and attitudes; scientific, scholarly, clinical, and professional expertise; racial, ethnic, and cultural diversity; and representation of participants’ perspectives.
Due to the increased complexity of human research protocols submitted, this often results in adding members. The composition of each IRB may change annually as needed.

Education, training and periodic evaluation of IRB members, IRB Chairs, and IRB staff is discussed in Chapter 4.

**The IRB membership permits appropriate representation at the meeting for the types of research under review, and this is reflected on the IRB roster. The IRB has one or more unaffiliated members; one or more members who represent the general perspective of participants; one or more members who do not have scientific expertise; one or more members who have scientific or scholarly expertise; and, when the IRB regularly reviews research that involves vulnerable participants, one or more members who are knowledgeable about or experienced in working with such participants. (AAHRPP Element II.1.A)**

**The IRB has and follows written policies and procedures requiring research protocols or plans to be reviewed by individuals with appropriate scientific or scholarly expertise and other expertise or knowledge as required to review the research protocol or plan. (AAHRPP Element II.1.E)**

### 6.10 IRB Roster and Quorum Requirements

IRB Rosters are constituted to meet the requirements of 45 CFR 46.107 and 108; 21 CFR 56.107 and 108.

IRB Member spreadsheets is maintained by the OHSP and used as the data source for all IRB membership roster needs. The IRB Member spreadsheets include all information required under FDA and DHHS regulations and OHRP guidance (45 CFR 46.107 and 108; 21 CFR 56.107 and 108) including:

- Names of members
- Names of associate members - and regular members for whom they substitute
- Gender
- Earned degrees
- Scientific status
- Representative capacity
- Affiliation

**Representative capacity** is presented in enough detail to indicate which appropriate participants can be represented by each member (e.g., children, pregnant women, prisoners). When research protocols include vulnerable participants, a member who is knowledgeable about that population, or who has experience working with similar participants, should be assigned to the protocol review.

**Scientific status,** (including the designation of “nonscientist” – see Chapter 6.3), is determined during recruitment and annually upon evaluation of IRB members. Scientific status and area of scientific expertise (e.g., pediatrician, radiologist, psychologist, pharmacist, nursing) are
presented in sufficient detail to allow appropriate protocol assignment and in-depth protocol review.

**Affiliation** is determined during recruitment and annually upon evaluation of IRB members. An IRB member is considered affiliated if he or she, or any member of his or her immediate family, has any employment or other relationship (e.g., current employee, consultant, Board of Directors, current volunteer, trainee or student) with MD Anderson or its affiliated entities.

The role of unaffiliated members is to represent the general perspective of participants; the checklist for [Determining if IRB Members are Unaffiliated](#) is used to determine if members meet the criteria for serving as unaffiliated members.

Changes in IRB membership require reporting to Office for Human Research Protections (OHRP). The IRB Manager (or delegate) submits a revised IRB membership list to OHRP whenever membership changes occur, but at a minimum once a year and whenever a new IRB is formed.

Senior IRB staff may also be appointed as administrative members of the IRBs.

**Quorum Requirements and Voting at IRB Meetings**

The IRB Chair is a voting member of the IRB. The IRB Chair determines that quorum is established and maintained, chairs IRB meetings and calls for votes as appropriate.

Maintenance of quorum and voting at convened meetings is based on the following standards:

- A majority of the (voting) members of the IRB (or their designated associate members), including at least one member whose primary concerns are in nonscientific areas, must be present to conduct a convened meeting. In order for research to be approved, it must receive the approval of a majority of such members present at the meeting.
- **Members attending a meeting must be present in person.** Minutes shall also indicate that the members received all pertinent information prior to the meeting and were able to participate actively and equally in all discussions.
- IRB minutes shall include documentation of quorum and votes for each IRB action and determination by recording votes as follows:
  - Total number voting
  - Number for the motion
  - Number opposed
  - Number abstaining
  - Names of those abstaining
  Votes are indicated using an electronic voting system or a show of hands if the electronic voting system is not functional.
- **Members leaving the meeting room** due to a conflicting interest, or for any other reason, will not be recorded as part of the quorum for a particular protocol.
- An individual who is not listed on the official IRB membership roster may not vote.
• A non-voting ex-officio member of, or representative to, an MD Anderson IRB may not vote.
• Ad hoc consultants may not vote.
• A nonscientist IRB member must always be present for any IRB vote to be taken.
• Regular attendance of unaffiliated members is strongly encouraged. Individual members of the IRB may satisfy more than one required type of membership criterion (i.e. a nonscientific member may also be the unaffiliated member).
• Associate members are not assigned as replacements for a specific member (not a one-to-one match). Associate members may vote in place of a member wherein they are designated per the roster. For example, an affiliated, scientific associate member may vote for an affiliated, scientific member who is not present.
• Voting by proxy is not permitted.
• If the quorum fails during a meeting, such as due to lack of a majority of IRB members being present or an absence of a nonscientist member, the IRB cannot take any further actions or vote until the quorum is restored.
• The IRB Meeting Coordinator is responsible for monitoring the members present at a convened IRB meeting to ensure that at the beginning of the meeting and for each subsequent vote the meeting is appropriately convened.
• When the IRB reviews research that involves participants vulnerable to coercion or undue influence such as pediatric participants, pregnant women, handicapped, or mentally disabled persons at least one member must be present who is knowledgeable about or experienced in working with such participants.
• Research involving prisoners will be deferred to the VPCRA so as to determine which IRB will oversee the research. An MD Anderson IRB will not be the IRB of record for research involving a prisoner population.
• If there is no member with appropriate expertise on the IRB, or if a consultant with appropriate expertise has not reviewed the protocol in depth, the IRB will defer the discussion of the protocol to another IRB meeting.

See Chapter 8.4 for information about convened meeting minutes.

The IRB has and follows written policies and procedures for conducting meetings by the convened IRB. (AAHRPP Element II.2.C)

6.11 Meeting Times and Materials

Medical IRB Boards 1, 2, and 5 meet twice each month according to a regular schedule (see Scientific Review and Clinical IRB Schedule). Protocol documents are received on a weekly basis and are assigned for convened review based on the meeting schedule, if protocol documents cannot be reviewed through expedited process.

Nonmedical Board, IRB 4, meets once a month according to a regular schedule.

Executive Board, IRB3, meets once a month according to a regular schedule.
Individual meetings may be rescheduled, or additional meetings may be held, as needed by agreement of the IRB Chair and the IRB Manager.

Protocol materials are available online, via the web-based PDOLsystem: all IRB Members in attendance at a convened meeting are provided individual encrypted MD Anderson laptop computers to access the uploaded IRB agendas. A hardcopy set of the most commonly referenced guidances are available for IRB members.

6.12 Review and Preparation Time

Protocol Materials

The IRB staff assigns protocols in sufficient time for the protocols to be reviewed before the meeting, generally 5 days, but usually not later than 72 hours before an upcoming meeting. Assignment information is sent via institutional Outlook email messages. All other IRB members are granted view access to the presented protocol materials, generally 48 hours prior to the convened meeting.

Materials necessary for review may be presented to IRB members less than 48 hours prior to a meeting only where determined necessary by the IRB Chair or IRB Manager. For protocol materials provided to members, see Chapter 7.5 and 7.7.

Meeting Documents

Approximately 48 hours prior to the IRB convened meeting, all members receive:

- Minutes of the previous convened meeting
- Agenda List and Approval List, containing:
  - Protocols which will be presented at the upcoming meeting,
  - Protocols not presented at the meeting (new, minor modifications, or continuing reviews) which have been reviewed and approved by the expedited process, or reviewed by exempt review, since the prior convened IRB meeting, and
  - Other items (such as Reports, which have not required presentation at the convened meeting).

The Agenda, Agenda List containing the presented protocols, and IRB Member Conflict of Interest declaration are distributed to members at the beginning of the convened meeting. The Agenda includes the following:

- A statement on confidentiality of meetings,
- A Conflict of Interest statement, and
- Education and Information items.

A list of protocols not presented at the meeting (i.e., reviewed by the expedited process) and the minutes from the previous meeting are also available at the meeting.
Chapter 7. Systematic Review

The IRB has and follows written policies and procedures to conduct reviews by the convened IRB: (AAHRPP Element II.2.D)

Element II.2.D.1. – Initial review
Element II.2.D.2. – Continuing review
Element II.2.D.3. – Review of proposed modifications to previously approved research

The IRB has and follows written policies and procedures to conduct reviews by an expedited procedure, if such procedure is used. (AAHRPP Element II.2.E)

Element II.2.E.1. – Initial review
Element II.2.E.2. – Continuing review
Element II.2.E.3. – Review of proposed modifications to previously approved research

7.1 Protocol Review

All MD Anderson human research (as defined in Chapter 1.4) and modifications to approved research (except when the modification is necessary to eliminate apparent immediate hazards to participants) must be prospectively reviewed by the IRB. In addition, no previously approved human subject research may be continued beyond the expiration date without prospective approval (continuing review).

7.2 IRB Protocol Submissions (PDOL System)

Most submissions to the IRB are via an online Lotus Notes based system called “PDOL” and a web-based system called PDOL.net. Forms available for online submission include:

- Protocol submissions for:
  - Human Subject Research (HSR) Determinations
  - New protocols
  - Modifications
  - Reports (of unanticipated problems and events and other information requiring prompt reporting to the IRB)
  - Final Reports

Protocol submissions include sections that must be completed by the investigators, as applicable. The PDOL questions include information that will allow the IRB to assess whether or not the criteria for IRB approval have been met (45 CFR 46.111 and 21 CFR 56.111).

Investigators must select a protocol form type (Standard, Protocol Application or CIND) and protocol review type (Scientific Review Committees: Clinical Research Committee - CRC, Psychosocial Behavioral Science Research Committee - PBHSRC, or the IRB). PDOL application questions vary depending on the review type and protocol form type selected.
Projects such as case studies that do not meet the regulatory definition of human subjects research may be submitted via PDOL for an IRB acknowledgement, if the publication source requires an IRB determination (see IRB Policy on Preparation and Publication of Case Reports and Case Series).

Research that includes the use of pre-existing de-identified cell lines and cell lines purchased through a commercial source do not meet the regulatory definition of human subjects research (see Cell Line Registry).

**Protocol Submission Form**

*Standard Protocols:* Protocols conducted by personnel within, or conducted through, MD Anderson and its facilities or otherwise involving any clinical investigation involving an agent or device and use of protected identifiable health information are submitted on the Standard Protocol Form.

*Protocol Application (PA) Protocols:* Protocols for research not involving a clinical investigation with an agent or device being conducted by personnel within, or conducted through, MD Anderson and its facilities. PA protocols may use identifiable human material and identifiable protected health information as part of laboratory based procedures or use of identifiable protected health information in chart reviews. These protocols are submitted on the Protocol Application form.

*Compassionate Use Protocols (CINDs):* Protocol conducted by personnel within, or conducted through MD Anderson and its facilities involving expanded access (sometimes called “compassionate use”) of investigational drugs, biologics or medical devices outside the clinical protocol setting for treatment purposes for a single patient (see IRB Policy Single Patient Use of an Investigational Agent or Device _Compassionate Use of an Investigational or Label Drug_). CINDs are submitted using the CIND application.

**Protocol Form Types**

Before starting a Standard Protocol form, investigators must identify the appropriate form type and review type. For Protocol Application form, the investigator must select the appropriate form type (Protocol Application) and the system routes directly to the IRB.

**Other Research or Special Situations**

*Additional Requirements – Other Federal Agencies:* Depending on the source of support for research, regulations from other agencies such as DoD, etc. might apply. See Other Federal Agencies- Additional Requirements for these special considerations and for links to checklists to help ensure that all special considerations are met. IRB Staff, during pre-review, identify these requirements and confirm that they are documented.

*Protocols Using Biological Agents or Recombinant DNA Vectors:* In Lotus Notes, PDOL, investigators are required to submit a Standard Protocol form that describes the use of the
biological agent or recombinant DNA vector. In web-based PDOL.net, the investigators are expected to describe the use of the biological agent or recombinant DNA vector with the protocol body.

**Emergency Use of a Test Article:** Chapter 5.9 describes the requirements for the emergency use of an investigational drug, device, or biologic under FDA regulations at 21 CFR 56.104(c), and materials which must be submitted to the IRB.

The submitted material is received by the OHSP and the materials are provided to an IRB Chair or their designee - qualified IRB member. If the IRB staff person or the reviewer has comments they are sent to the investigator for response. Responses are reviewed and additional comments sent if needed. The reviewer documents his/her findings on the Exemption from IRB Review: Emergency Use of a Test Article.

7.3 Submission, Preliminary Review and Assignment to IRBs – New Protocols, Modifications, Continuing Review, Reports, Final Reports

**Submission and Preliminary Review - New Protocols**

Upon receipt of a new protocol documents, from either the Scientific Review Committee (Clinical Research Committee or Psychosocial Behavioral Science Research Committee) or the PI, the IRB Meeting Coordinator reviews the submission for completeness, including ensuring all required supplemental documents and information are provided. The IRB Meeting Coordinator also performs a preliminary review to confirm the PI’s selection of the form type and review type.

Protocols submitted for review that are determined to have been submitted using the incorrect submission form not appropriate are returned to the PI for conversion into the appropriate form type and review type. If an IRB staff member receives an incorrect form type, i.e., a protocol is submitted in the Protocol Application form but should be submitted in the Standard Protocol form, the protocol is returned to the PI for re-submission using a Standard Protocol form.

**Assignment to IRBs - New Protocols**

Standard Protocols: Once a new Standard Protocol submission is complete, the protocol is assigned to an IRB for review. To avoid any potential conflicting interest, new Standard Protocols are generally not assigned to an IRB where the reviewing IRB Chair of that IRB is also an investigator on the research project or the research is being conducted in the IRB Chair’s department. After taking into consideration any conflicting interest issues, assignment of Standard Protocols to IRBs is based on the order (by date) the protocol was submitted to the IRB by the SRC or PI and for protocols subject to convened board review the order of the monthly IRB meetings.
Standard Protocols that include clinical investigations and are subject to convened board review are assigned to medical IRBs 1, 2, and 5 with assignment to the next IRB starting after the preceding IRB has reached its protocol load for that meeting.

Standard Protocols that do not include medical procedures or use of a device but do include identifiable protected health information subject to convened board review or expedited review are assigned to non-medical IRB 4.

Protocol Application Protocols: Once a Protocol Application Protocol is deemed complete, the protocol is assigned to an IRB for review. To take into account any potential conflicts, members of the IRB will not be assigned research where they are the investigator or the research is being conducted by their respective department.

Protocol Application Protocols subject to convened board review, expedited or exempt review that involve laboratory based procedures using human material and protected health information are assigned to medical IRBs 1, 2, and 5. All other Protocol Applications i.e. chart reviews that use protected health information are assigned to non-medical IRB 4.

HSR Determination applications that involve laboratory based procedures are assigned to medical IRBs 1, 2, and 5. All other HSR Determination applications are assigned to non-medical IRB 4.

Special Assignment Considerations:

Protocols involving biological agents or recombinant DNA vectors (gene transfer) are assigned to medical IRBs 1, 2, and 5.

All subsequent events submitted on approved protocols are received directly by the IRB that last reviewed and approved the protocol. When necessary, protocols may be assigned to another IRB; in such instances all related reviews and event history are transferred/provided to that IRB. For example, medical IRB1 may review a protocol initially reviewed by medical IRB5.

IRB reviewers assigned to review protocols involving post-mortem collection will need to reference the Postmortem Biospecimen Collection for Research (ACA1271).

The IRB has and follows written policies and procedures requiring research protocols or plans to be reviewed by individuals with appropriate scientific or scholarly expertise and other expertise or knowledge as required to review the research protocol or plan. (AAHRPP Element II.1.E)

7.4 Assignment of Protocols to IRB Members

Reviewer assignments are made with the objective of matching reviewer expertise and experience with protocol subject matter (see Chapter 6). “Non-affiliated, Nonscientific” members assigned to review protocols are valued for the community perspective they bring to the process of ensuring the protection of research participants. For approved protocols,
subsequent submissions are assigned to the IRB Chair, IRB Associate Chair, IRB Vice-Chair or designee of the IRB of record for such the protocol.

**Protocols Subject to Convened Board Review – New, Modifications, Continuing Review and Reports**

**New Protocols:** The medical and non-medical IRBs utilize a presenter reviewer system for protocols subject to convened board review. New standard protocols are assigned by the IRB manager to an IRB reviewer to present the protocol at the convened meeting. When requested by the IRB reviewer, the IRB staff assigns other expert reviewers to protocols when applicable, (e.g., Biostatistics).

If there is not at least one person on the IRB with the appropriate scientific or scholarly expertise, or other expertise or knowledge, to conduct an in-depth review of the protocol, the IRB obtains consultation from an appropriately qualified expert.

The IRB Manager, IRB reviewer, or IRB Chair can determine whether a consultant is needed. The process by which this is done is described in Chapter 6.5.

**Modifications:** Protocol modifications are subject to convened board review as described in the Policy on IRB Revision Procedures to Previously Approved Research Protocols. IRB Chairs, IRB Associate Chairs, IRB Vice-Chairs or designees assigned to review these modifications will present the protocol at the convened meeting if the modifications require convened board review.

Protocol modifications that require convened board review will be placed on the next available IRB meeting agenda. Once approved, documentation of the IRB approved protocol modification is available in the electronic protocol system within 3-5 days of such IRB approval.

**Planned Deviations:** Any changes from the IRB approved protocol and informed consent where the IRB is notified and approval is obtained prior to the deviation occurring. For example, the enrollment of a patient who does not meet all the eligibility requirements but the physician thinks it is in the best interest of the patient (see PI Override Form).

**Continuing Review:** For all protocols initially subject to convened board review, the continuing review submission undergoes convened board review, unless it meets the criteria for expedited review (see below). Those which will undergo convened board review are assigned to a designated IRB Vice-Chair who reviews and presents the protocol at the convened board meeting (see IRB Policy on Continuing Review of Research, Continuing Review Guidance [OHRP], and Policy on IRB Revision Procedures to Previously Approved Research Protocols).

The Office for Human Research Protections (OHRP) guidance, with regards to continuing review for protocols that meet the expedited category, indicates that until the 1998 OHRP Expedited
Review Categories List (the “1998 List”) is updated to reflect the 2018 Requirements, OHRP recommends that IRBs preserve the continuing review of research (see attached link).

Reports (unanticipated problems and events and information requiring prompt reporting):


Serious Adverse Events

- Internal SAE Form
- Internal SAE Addendum Form
- Departmental External SAE Form

Additional Requirements

Depending on the type of research project, or the source of support/funding for the protocol or institution at which the protocol will be conducted (e.g., Department of Defense), other additional requirements might apply (see Other Federal Agencies - Additional Requirements).

Protocols Subject to Expedited Review – New, Modifications, Continuing Review, Reports, and Final Reports

Expedited reviews are assigned by the IRB Staff either to the IRB Chair, IRB Associate Chair, IRB Vice-Chair or designee. See Chapter 6 for reviewer qualifications, and the Annual Evaluation of IRB Members.

New Protocols: New protocols that meet expedited review criteria (see WORKSHEET - Expedited Review) are reviewed under a single reviewer process and are assigned by the IRB Staff either to the IRB Chair, IRB Associate Chair, IRB Vice-Chair or designee.

Modifications (Minor): See Policy on IRB Revision Procedures to Previously Approved Research Protocols

Minor modifications to protocols can be submitted at any time during the month, and are reviewed and approved on a first-come, first-served basis as quickly as possible. Documentation is available in PDOL upon processing of approval. The IRB reviewer makes the final determination of whether changes to the protocol require convened board review or “minor” (can be expedited) (see WORKSHEET - Expedited Review).
**Continuing Review (Protocols subject to convened board review initially):** For a protocol initially subject to convened board review, the continuing review submission undergoes expedited review:

If (expedited Category 8):
- (i) the research is permanently closed to enrollment of new subjects;
- (ii) all subjects have completed all research-related interventions; and
- (iii) the research remains active only for long term follow-up of subjects; or
- No subjects have been enrolled and no additional risks have been identified; or
- The remaining research activities are limited to data analysis,

Or (expedited Category 9):
- For continuing review of research, not conducted under an investigational new drug application or investigational device exemption where Categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

Protocols subject to expedited continuing review are assigned to an IRB Vice-Chair and are not presented at a convened board meeting.

**Continuing Review (Protocols subject to expedited review initially):** For a protocol initially subject to expedited review, the continuing review submission undergoes expedited review if:
- It does not include any modifications, or
- If modifications are included, the proposed modifications would have been eligible for expedited review had they been part of the initial protocol.

**IRB Policy on Continuing Review of Research**

Protocols subject to expedited continuing review are assigned to an IRB Vice-Chair and are not presented at a convened meeting of the IRB.

**Reports (unanticipated problems and events and information requiring prompt reporting):**

See MD Anderson [IRB Policy Reporting Protocol Deviations, Protocol Violations, and Unanticipated Problems](#) and MD Anderson [Policy on Reporting Adverse Events for Drugs and Devices](#) and [Events and Information that Require Prompt Reporting to the IRB](#)

**Final Reports:** Final reports are reports provided by the Principal Investigator, which include the following:
- Total number of participants enrolled on the protocol
- Total number of MD Anderson participants enrolled on the protocol
- Overall description of serious adverse events or toxicities that were experienced on the protocol
• Overall response for all participants enrolled on the protocol
• Conclusion/Outcomes of the research

Final Reports are acknowledged and serve as documentation of protocol closure.

7.5 Protocol Review Material and Information

Upon protocol assignment, the reviewers and IRB staff have full access to all protocol information and materials submitted. Review materials always include the relevant protocol documents submitted in PDOL (Modification, Reportable Event, or Final Report) or Continuing Review report from CORE. Depending on the protocol event under review, the protocol documents will be supplemented with a Modification, Continuing Review Report (including a status report on the progress of the research) or Final Report setting forth the dispositive information supporting the event.

In addition, reviewers have access to all documents submitted in support of the Standard Protocol Form or Protocol Application Form, which may include as applicable:

• Informed consent and assent documents
• Recruitment materials, including advertisements
• Questionnaires and surveys
• Information sheets/brochures or other protocol related materials that participants receive
• Protocol (e.g. industry sponsor or DHHS-approved protocol)
• Investigator’s brochure (drugs) (see IRB Policy on Submission of Investigator's Brochures)
• Device manual or report of prior investigations (devices)
• Relevant federal grant application
• All relevant reports, including multi-center protocol reports (at continuing review)

The IRB may request additional information to complete its review of a protocol.

7.6 Protocol Review - Pre-Review Parallel Process

General Process for All Protocol Submissions

The medical IRBs utilize a parallel process for pre-review, where the IRB staff pre-review the protocol documents submitted and associated form (Standard Protocol or Protocol Application) and the OHSP Consent Editors review the submitted informed consent document. Once the pre-review is complete, the IRB Staff assign to the IRB Chair, IRB Associate Chair, IRB Vice-Chair, or designee. The IRB Chair, IRB Associate Chair, IRB Vice-Chair, or designee will determine if the submission requires convened board review or can undergo the expedited review process.

Generally, within 3-5 days after the convened board meeting, the IRB determinations will be documented in the electronic databases and will be provided to the PI and research teams via an IRB memo. For submissions that underwent the expedited review process, generally, within 1 day of IRB Chair, IRB Associate Chair, IRB Vice-Chair, or designee determination, the IRB
determinations will be documented in the electronic databases and will be provided to the PI and research teams via an IRB memo.

If a protocol is disapproved or when the IRB has determined “serious non-compliance” other central offices (Institutional Compliance Office, Institutional Official) will be copied on the IRB determination memos.

**Approval Criteria**

All proposed research must meet MD Anderson Human Research Protection Program (HRPP) ethical standards governing the conduct of research (e.g., acceptable risk-benefit relationship, equitable selection, informed consent, protections of privacy, maintenance of confidentiality, and protections for vulnerable populations). The reviewers consider the approval criteria set forth in 45 CFR 46 and 21 CFR 50 in reviewing and approving a new protocol, continuing review, or review of a modification when the modification affects a criterion for approval.

The reviewers consider the regulations in reviewing and approving a protocol. They are aided in their consideration by regulatory guidance provided in the form of:

- WORKSHEET Criteria for Approval
- General Requirements for Informed Consent
- Reviewer Checklist

**Review of Exempt Research**

For more information, see Chapter 3.5.

**Continuing Review**

Submission of a protocol for continuing review is required on all non-exempt approved protocols. At least one IRB member is provided and reviews the complete protocol, including a status report and any protocol modifications previously approved by the IRB.

The continuing review form should also include the following:

- Number of participants accrued.
- A summary since the last IRB review of:
  - Adverse events, untoward events, and adverse outcomes experienced by participants.
  - Unanticipated problems involving risks to participants or others.
  - Participant withdrawals.
  - The reasons for withdrawals.
  - Complaints about the research.
  - Amendments or modifications.
  - Any relevant recent literature.
  - Any interim findings.
  - Any relevant multi-center trial reports.
• The researcher’s current risk-potential benefit assessment based on study results.

When continuing review of research is required by law or regulation, IRB members determine:
• Whether the protocol needs verification from sources other than the researchers that no material changes had occurred since previous IRB review.
• The current consent document is still accurate and complete.
• Any significant new findings that arise from the review process and that might relate to participants’ willingness to continue participation will be provided to participants.

The Clinical Oncology Research (CORe) system automatically identifies all protocols for which IRB approval will expire prior to the next IRB meeting date. Notices of IRB approval expiration are sent two months prior to such expiration date, a month before expiration and 2 weeks before expiration if a continuing review (renewal) form has not yet been received. IRB approval expiration Notices are sent when IRB approval of a protocol expires.

Continuing review is not required only when:
• All participants have completed all research-related interventions, and
• Collection and analysis of private identifiable information has been completed.

Modifications
No modifications to a protocol may be initiated without prior approval from the IRB, except where necessary to eliminate apparent immediate hazards to participants. Investigators are required to complete a Resubmission Cover letter in PDOL setting forth a summary of the proposed protocol modification. Modifications involving changes to previously approved or submitted documents, (e.g. consent forms, advertisements, sponsor protocol) or the addition of new documents, must be accompanied by the new documents and/or the proposed revised versions of the previously approved or submitted documents.

In the rare situation where a modification is made without prior IRB approval because it is necessary to eliminate apparent immediate hazards to subjects, the investigator must report within 5 business days this change to the IRB (see MD Anderson IRB Policy on Reporting Protocol Deviations, Protocol Violations, and Unanticipated Problems). The IRB will determine whether the change was consistent with ensuring the participants’ continued welfare (see Chapter 3.9).

If significant new findings or information are submitted as part of a modification or continuing review, the IRB may require the reporting of this information to participants if the information could reasonably affect participants’ willingness to continue participation.

Final Reports
Refer to MD Anderson IRB Policy on Human Subjects Research Termination, Termination of IRB Oversight and Activities that are not Subject to IRB Oversight.
Additional Requirements: Federally-Supported Research Involving Surveys

See Other Federal Agencies - Additional Requirements for other requirements, depending on the source of support/funding (e.g., Department of Defense).

Protocols Using Biological Agents or Recombinant DNA Vectors

The review processes described above for protocols subject to convened board review are used for protocols involving the use of biological agents or recombinant DNA vectors.

These protocols must be approved by the Institutional Biosafety Committee (IBC) prior to implementation at MD Anderson. No new research participants may be enrolled until both IBC and IRB approval is granted.

Protocols Using Radioactive Drugs

Protocols using radioactive drugs such as tracer or imaging compounds are reviewed by the MD Anderson Radiation Safety Committee. Approval from the Radiation Safety Committee must be granted prior to implementation of the protocol at MD Anderson. No research participants may be enrolled until the Radiation Safety Committee approves the protocol.

Range of Action for Decisions on Protocols Subject to Expedited Review

The IRB reviewer(s), IRB Chair, IRB Associate Chair, IRB Vice-Chair or designee, of protocols subject to expedited review act on behalf of the IRB and have the authority to approve, require modifications (to secure approval) or request convened board review of the protocols. The reviewers consider the approval criteria set forth in 45 CFR 46.111 and 21 CFR 56.111 in reviewing a protocol. The IRB determinations (e.g. Approve, disapproved, or require modifications to secure approval) will be documented in the electronic databases and will be provided to the PI and research teams via an IRB memo. The memo will include the modifications or clarifications required to secure approval.

The possible decisions are:

- **Approved:** After the reviewer(s) approves a protocol, the protocol is entered into IRB.net (database where all IRB determinations for the protocols are included) and a report is generated that is included on the next IRB meeting agenda so that all IRB members may review.

- **Approved with Contingencies (Require Modifications):** The IRB Staff informs the PI in writing via PDOL of any requested reviewer requested modifications, comments, questions, or concerns about the protocol and requests a reply within a specified time via the PDOL; the research may not proceed/commence until the responses have been reviewed and the protocol has been approved. Contingencies must be met within 60 days of IRB review or the protocol is administratively withdrawn. Withdrawn protocols must go through the entire SRC/PBHSRC and IRB review if the PI wishes to open the protocol.

- **Convened Board Review required:** The protocol raises questions that warrant convened board review, PI does not agree with the modifications required for IRB approval or if for...
research involving children, the reviewer finds that the research presents greater than minimal risk (greater than 45 CFR §46.404 (OHRP) or 21 CFR §50.51 (FDA), the reviewer will request that the protocol be presented for review at the next convened IRB meeting.

- **Decision to not approve:** A single IRB reviewer cannot reject or not approve a protocol; thus a reviewer using the expedited procedure may not disapprove research. A protocol can only be not approved (disapproved) by a vote at a convened IRB meeting. A statement of the reasons for the IRB’s decision will be included in a memo and the PI will have the opportunity to respond in person or in writing.

Protocols subject to convened board review are presented and voted on at a convened IRB meeting with a quorum of IRB members present.

### 7.7 Protocols Presented at a Convened Meeting

#### Quorum

Refer to Chapter 6.

#### Materials Available at Convened Meetings

Prior to the convened board meeting, all scheduled voting IRB members, including non-primary reviewers, are provided and notified of electronic access to all protocols to be presented. This electronic access enables reviewers to see the entire protocol submission, including the form and any reports (e.g. modification, continuing review, reportable event), all comments and responses, assent and consent form(s) and all other documents associated with the protocol (e.g. telephone script, questionnaires or surveys, advertisements). Reviewers are expected to review the information sufficiently to provide comments (if any) before the meeting and during the meeting. All materials submitted supporting a protocol are also available to voting members during the meeting.

In addition, all members are provided the Meeting Agenda, Agenda List of presented protocols, and list of protocols not presented at the meeting. Guidance documents (e.g. Additional Protections for Inclusion of Children in Research [OHRP]) for 45 CFR 46.404, 405, 406, 407 and 408; CHECKLIST: Waiver or Alteration of Consent Process and CHECKLIST: Waiver of Written Documentation of Consent for 45 CFR 46.116, 117) are made available for IRB members.

#### Meeting Deliberations
The IRB presenters are considered the lead reviewers on the IRB for protocols assigned to them. They are responsible for:

- Being thoroughly versed in all details of the research,
- Conducting an in-depth review of the research using the IRB presenter guidelines and tools as guidance.

The IRB presenter presents the protocol for discussion. All IRB members are afforded full opportunity to discuss each research protocol during the convened board meeting. The reviewers consider the approval criteria set forth in 45 CFR 46 and 21 CFR 50 in reviewing a protocol. Controverted issues that have not been resolved during the review prior to the convened IRB meeting are discussed.

**Procedure for Special Findings When Approving a Protocol**

The reviewers and voting members consider the following information and regulations to make any special findings in reviewing and approving a protocol. The IRB Supervisor and IRB Meeting Coordinator conduct a pre-review meeting to determine which forms should be made available to the Presenter Reviewer in order to assist in their consideration by providing regulatory guidance documents, including:

<table>
<thead>
<tr>
<th>Frequently Referenced Guidance</th>
</tr>
</thead>
<tbody>
<tr>
<td>WORKSHEET_Criteria for Approval</td>
</tr>
<tr>
<td>General Requirements for Informed Consent</td>
</tr>
<tr>
<td>Additional Protections for the Inclusion of Children in Research (OHRP)</td>
</tr>
</tbody>
</table>
  When the protocol involves children as participants, the IRB considers all of the regulations of 45 CFR §46.404, 45 CFR §46.405, 45 CFR §46.406, 45 CFR §46.407, 45 CFR §46.408 to make the appropriate finding(s) under which the children may be included.
  
  **Wards:** When the protocol involves children who are wards of the state the IRB considers all of the regulations of 45 CFR §46.406, 45 CFR §46.407 and 45 CFR §46.409(a) to make the appropriate finding(s).
| Additional Safeguards for Children in Clinical Investigations (FDA) |
  When the protocol involves children as participants, the IRB considers all of the regulations of FDA 21 CFR §50.51, FDA 21 CFR §50.52, FDA 21 CFR §50.53, FDA 21 CFR §50.54, and FDA 21 CFR §50.55 to make the appropriate finding(s) under which the children may be included.
  
  **Wards:** When the protocol involves children who are wards of the state the IRB considers all of the regulations of FDA 21 CFR §50.53, FDA 21 CFR §50.54 and FDA 21 CFR §50.56(a) to make the appropriate finding(s).
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Guidelines for IRB Members on Conflicting Interests

CHECKLIST: Waiver or Alteration of Consent Process and CHECKLIST: Waiver of Written Documentation of Consent

When the investigator requests waiver or alteration of informed consent in the protocol application, the rationale for the waiver or alteration is considered by the IRB as it makes any finding of waiver or alteration of informed consent as required by 45 CFR §46.116(c) or 45 CFR §46.116(d).

When the investigator requests waiver of consent documentation in the protocol application, the rationale presented for the waiver is considered by the IRB as it makes any finding of waiver of consent documentation under 45 CFR 46.117(c) and 21 CFR § 56.109(c).

Significant Risk and Non-significant Risk Medical Devices Protocols

Frequently Referenced Guidance

Research Involving Pregnant Women, Fetuses, and Neonates
When a protocol involves pregnant women, human fetuses and neonates, the IRB considers the investigator’s response to the items in 45 CFR 46.204, as well as the IRB’s review of the items, and makes a finding under 45 CFR §46.204, 45 CFR §46.205, 45 CFR §46.206, and 45 CFR §46.207.

MD Anderson will not serve as the IRB of record for any research involving prisoners.

HIPAA and PHI
Waiver of HIPAA Authorization: When the investigator requests waiver or alteration of HIPAA authorization for the protocol, or limited waiver of HIPAA authorization for activities such as recruitment, the IRB considers the rationale presented for the waiver(s) to determine if all of the requirements of 45 CFR 164.512(i)(2)(ii)(A), (B), and (C) are met, and if so, makes the required finding.

Emergency Use of a Test Article

Exempt Review Categories Common Rule, FDA, and MD Anderson Policy

Expedited Review Categories
Additionally, for protocols involving **fetal tissue transplantation**, the IRB considers the investigator’s rationale and the risks involved in order to make any finding required by 42 USC §498A (b)(1) and (2).

### Range of Actions on Regular Protocols at Convened Meetings

The IRBs must systematically evaluate each protocol to ensure the protection of research participants and reach a decision. The possible decisions are:

- **Approved**: The research is now approved by the IRB. Approval requires an affirmative vote by a majority of the convened quorum.
- **Approved with Contingencies**: Approved at a convened board meeting contingent on the investigator making minor changes. Such minor changes must be clearly delineated by the IRB at the convened board meetings and approval is contingent on the Principal Investigator (PI) accepting the IRB stipulations or making any verbatim changes to documents requested by the IRB. The research may proceed after the IRB Chair, IRB Associate Chair, IRB Vice-Chair, or designee has reviewed and accepted as satisfactory all changes to the protocol or informed consent documents, or any other responsive materials, required by the IRB from the PI. This review may be carried out via the expedited process.

If during the meeting the members decide major changes are required, the protocol is deferred.

- **Deferred**: Approvable with greater than minor changes to be reviewed by the convened IRB. The research may proceed only after the IRB has reviewed and approved the required changes to the research at a convened board meeting.
- A protocol will be deferred until it is approved (or not approved) by the voting members at a convened board meeting. If the initial IRB presenter is not available at subsequent meetings where a deferred protocol is reviewed, another IRB presenter will be assigned to review and present the protocol.

- **Disapproved**: The IRB has determined that the research cannot be conducted at MD Anderson or under the auspices of MD Anderson (e.g., the regulatory requirements, MD Anderson HRPP standards, or other stipulations have not been satisfied). The investigator is provided with a memorandum from the IRB notifying him/her that the protocol was not approved by the convened board, explaining the reason(s) the protocol was not approved, and giving the investigator an opportunity to respond in person or in writing. (Not permissible for protocols undergoing expedited review).
Contingencies must be met within 60 days of IRB review or the protocol is administratively withdrawn. Withdrawn protocols must go through the entire SRC/PBHSRC and IRB review if the PI wishes to open the protocol.

The minutes of the convened board meetings document the deliberations, actions, and votes for each protocol undergoing convened board review, and include references to the determinations made by the IRB. The IRB Staff via the PDOL system notifies the investigator about any IRB actions and determinations (e.g. Approved, Approved with Contingencies, Deferred, or Disapproved).

**Approval Date and Determination of Expiration Date**

The approval date for a protocol subject to convened board review is the date of the IRB meeting where the protocol was approved. The approval date of a protocol or protocol submission (modification or continuing review) subject to expedited review is the date the reviewer recommends the protocol or submission for approval. Approval of a modification does not alter the expiration date.

Protocols are approved for a period of no more than one year. The expiration date is the last day the protocol is approved (e.g., a protocol approved on January 1, 2010 will expire at midnight on January 1, 2011).

The IRB can approve a protocol for a shorter period if warranted by the risks presented to participants. The IRB may approve a protocol for 6 months or may stipulate the approval on further IRB review after a defined number of participants have been enrolled (e.g., review after the first three subjects receive a Phase I drug that has never been tested in humans). If any of the following are true, the IRB may perform review more often than annually: (a) novel high-risk protocol using new therapeutic modality; (b) phase I protocols of a new drug or biologic that has never been tested in humans; (c) protocols involving a novel significant risk medical device that has never been tested in humans; (d) a high degree of uncertainty regarding the risks involved; (e) the vulnerability of the subject population; (f) the experience of the investigator; (g) the IRB’s previous experience with the investigator and/or sponsor; or (h) other high-risk protocols as IRB members deem appropriate (this includes research for which the IRB determines that reports to the IRB of monitoring data should be more frequent than annually).

**Approved with Contingencies:** The protocol initial approval date is recorded as the date the convened board approved the protocol contingent on minor conditions being addressed.

However, the “effective” date of initial IRB approval is the date on which the IRB Chair, IRB Associate Chair, IRB Vice-Chair or designee has reviewed and accepted as satisfactory any documents or any other responsive materials required by the IRB; IRB Contingencies Met Letters are ‘released’ when all contingencies have been met. No research protocol activities involving human subjects may be initiated until the conditions have been satisfied in the manner set forth by the IRB and the approval becomes effective. The **expiration date** is
determined in reference to the date the protocol was approved by the convened board contingent on minor conditions being addressed.

**Research that continues after the approval period expires** is considered research conducted without IRB approval. If investigators fail to apply for continuing review and obtain IRB approval prior to the IRB approval expiration date, the designated IRB will notify the PIs that research activities -- including but not limited to recruitment, advertisement, enrollment, interventions, interactions, data collection, and data analysis -- are unapproved and must stop, unless the IRB determines that continued involvement is in the best interest of enrolled subjects who are still receiving protocol-related interventions. (The IRBs do not consider this a suspension or termination under Chapter 9.4, since it is not activity under an “approved” protocol.)

The IRB will notify the PI that the IRB approval of the protocol has lapsed and inform the PI that the IRB will need to determine if existing participants can continue research related interventions. The IRB will notify the PI in writing with this determination.

**Monitoring**

A random sample of protocols will be reviewed periodically to confirm that the funding status has not changed to federally sponsored, the level of risk has not increased to more than minimal, and that any changes made to the protocol have been reported to the IRB prior to implementation.

Notices will be sent out annually to researchers requesting that they address whether changes have occurred regarding protocol procedures, increase in risks, adverse events, or addition of a federal sponsor.
Chapter 8. Documentation of IRB Activities

The IRBs maintain documentation of their activities. IRB records include IRB protocol files, minutes for convened IRB meetings, and other documentation.

The IRB maintains a complete set of materials relevant to the review of the research protocol or plan for a period of time sufficient to comply with legal and regulatory requirements, Sponsor requirements, and organizational policies and procedures. (AAHRPP Element II.5.A)

8.1 IRB Protocol Files

The Division of Clinical Research Administration employs several electronic protocol application systems to support the human research protection program. Copies of some documents are also maintained in hard copy files, when necessary. These systems include the following:

- Lotus Notes Protocol Document On-Line System (PDOL)
- PDOL.net
- Clinical Oncology Research System (CORe)
- IRB.net
- CRO.net
- On-Base (iConsent)
- RCTS
- Click Grants
- OHSP Department Shared Drive

Electronic Protocol Systems

Lotus Notes Protocol Document On-Line System (PDOL) or Web-Based PDOL.net

The PDOL system is used to maintain electronic records of protocol documents submitted through the system for every protocol event. PDOL or PDOL.net contains a search function for locating and retrieving protocols by protocol number, protocol short title, or name of Principal Investigator (PI). Electronic copies of all materials submitted to the IRB can be accessed through these electronic protocol systems on a version by version basis, thus all documents supporting each protocol event are accessible to reconstruct the entire history of a protocol.

A protocol file contains, as applicable to the research:

- **Protocol Documents.** The protocol documents includes one or more of the following documents:
  - Standard Protocol Form or Protocol Application Form (Convened Board Review, Expedited and Exempt Review) submitted for all new research projects;
  - Abstract
  - Various Protocol Appendices
  - Resubmission Cover Letter, submitted for modifications to approved research;
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- Reports submitted for reportable events and information per policy IRB Policy on Reporting Protocol Deviations, Protocol Violations, and Unanticipated Problems and Events and Information that Require Prompt Reporting to the IRB
- Form for Requesting Termination of IRB Oversight, submitted for closing Regular review protocols.

IRB comments and investigator responses during IRB review are included with each application. Comments and responses exchanged via fax or email are also included as attachments, or are stored in the hard copy file. Below are a list of documents that the IRB may receive:

- **The IRB-approved informed consent document(s).** The protocol file includes all approved consent documents, including the currently approved consent document.
- **The IRB-approved Assent form(s).** If a protocol involves children from whom the investigators will obtain assent, the assents are imbedded in those consent documents where children will be enrolled.
- **Scientific evaluations of the proposed research.** Documentation of scientific review by a SRC or PBHRSC as applicable, is included in the protocol file. See Chapter 1.7 for information on scientific and scholarly review.
- **Sponsor Materials.** For investigational drug protocols, the Investigator’s Brochure and Sponsor’s Protocol, including current amended editions of these documents and all previous versions are included in the protocol file. For investigational devices, a report of prior investigations and the Sponsor’s Protocol.
- **Advertisements, phone screening scripts** and non-medical oral scripts, flyers, website or other subject recruitment materials.
- **Questionnaires, surveys, interview scripts, diaries** or other documents to be used in the course of conducting the research described in the protocol.
- **Participant informational** sheets, brochures and sponsor newsletters.
- **Reports submitted for reportable events and information** under the MD Anderson IRB Policy Reporting Protocol Deviations, Protocol Violations, and Unanticipated Problems and Events and Information that Require Prompt Reporting to the IRB
- **Final reports** are reports provided by the Principal Investigator (PI) to serve as study closure. The PI submits the Form for Requesting Termination of IRB Oversight, for regular protocols. The final report includes the following:
  - Total number of participants enrolled on the protocol
  - Total number of MD Anderson participants enrolled on the protocol
  - Overall description of serious adverse events or toxicities that were experienced on the protocol
  - Overall response for all participants enrolled on the protocol
  - Conclusion/Outcomes of the research
- Data and Safety Monitoring Board (DSMB) reports, Annual Progress reports.
- Conflict of Interest (COI) statement is included in the consent document, if applicable.
- **Correspondence and communication** between IRB members, IRB staff and investigators.
- Protocol Checklist. Information related to institutional requirements.
- Other IRB correspondence related to the research.
• **Documentation of all actions** including approvals, disapprovals, waivers or alterations of consents and HIPAA authorizations (as documented in the protocol application forms).
• Approval letter (or Notice of Exempt Review for research subject to exempt review.)
• **Documentation of protocol closeout** if any, including Final Report forms for regular protocols.
• Notification to PI that including date notification of IRB expiration was sent.
• IRB approvals from collaborating institutions are requested and included in the research file. IRB approval notices are requested from collaborating institutions when MD Anderson is the coordinating center for a multi-site protocol, or when data is being received at MD Anderson. If the protocol is a multi-site protocol, with MD Anderson as one of several participants, no other IRB approval is gathered or included from other participating sites.
• PDOL Revision Checklist used for the capturing of the IRB Chair, IRB Associate Chair, IRB Vice-Chair or designee’s determination for protocol modification.
• IRB determinations for proposed projects where the IRB has made the determination that the project does not meet the definition of Human Subjects Research.

**IRB determinations – Expedited Procedures**

The IRB records for initial, modifications and continuing review of research by the expedited procedure include:

• The justification for using the expedited procedure.
• Justification that the criteria for approval are met.
• Actions taken by the reviewer.
• Any findings required by laws, regulations, codes and guidance to be documented.
• Justification for exempt determinations.

Please see Section 8.4 (Determinations made by the IRB) for the links to guidance documents.

**Clinical Oncology Research (CORe)**

The CORe database system contains protocol data. CORe is used to capture patient registration data and to record accrual targets as well as progress toward those accrual targets per protocol, protocol eligibility and randomization data. It also houses SRC/IRB approval dates as well as dates of IRB approval of informed consent documents.

The Continuing Review Form completed by the PI and submitted for continuing review of research is housed in CORe. IRB correspondence related to the approval of the continuing review is housed in CORe.

**IRB.net**
The IRB.net database system contains protocol data that includes dates of IRB approval and determinations. The IRB approval dates and determinations for new protocols, modifications, and reportable new information are included in IRB.net

**On-Base (iConsent)**

The On-Base (iConsent) system houses the informed consent document and signed informed consent document. Each signed informed consent document for each participant and is part of the medical record.

**Research Contracts Tracking System (RCTS)**

RCTS is used to maintain electronic records of contracts submitted through the system. Within the system, if a protocol is related to the contract, it will be listed. RCTS contains a search function for locating and retrieving contract by the contract number, Sponsor company, or name of Principal Investigator (PI). Electronic copies of all materials submitted for the contract are in the RCTS system, thus all documents supporting the contract are accessible to reconstruct the entire history of a contract.

**Click Grants System**

The Click Grants System maintains electronic records of grant documents submitted through the system for every grant. Within the system, if a protocol is related to the grant, it will be listed. Click Grants contains a search function for locating and retrieving grants by grant number, granting agency, or name of Principal Investigator (PI). Electronic copies of all materials submitted for the grant in Click Grants system, thus all documents supporting the grant are accessible to reconstruct the entire history of a grant.

Applications for federal grant support are located in the Click Grants System. For research supported by federal funds, a copy of the grant proposal is included in the grant file. If the federal funding is subcontracted through another institution, the sub-contract with that institution is noted in the grant file.

**OHSP Shared Drive**

The OHSP shared drive on the MD Anderson network allows for the storage of template forms needed by the IRB Staff. In addition, various IRB checklists including the IRB Presenter Guidelines are included in the shared drive. Other information is maintained by IRB staff, such as correspondence between the IRB and outside agencies and institutions, IRB convened meeting documentation, minutes, agenda, information about each IRB Member including: contact information, background and experience, curriculum vitae, etc.

IRB records are retained under the MD Anderson protocol number in PDOL or PDOL.net, CORe, or in the OHSP Shared Drive. Each protocol file is organized in these research systems to allow a reconstruction of a complete history of all IRB determinations related to the review and approval of the protocol. The systems are backed up nightly at the MD Anderson Data Centers and other off-site locations that are undisclosed to the public and a complete disaster recovery
plan is required by institution policy. In the event of a disaster, the disaster recovery plan is followed to ensure that business continuity is in place. Relocating redundant critical systems affords greater geographic diversity and additional protection in the event of a level three emergency, such as a natural disaster like a hurricane.

8.2 Other Documentation Maintained

Information Specific to Certain Types of Research or Special Situations

Emergency Use of a Test Article

Research involving the emergency use of a test article under FDA regulations 21 CFR 56.104(c) is described in Chapter 5.9. Documentation of the emergency use of a test article is submitted to the IRB within five days of the use of the test article and includes the following documents:

- Emergency Use of a Test Article Notification Form
- Consent form, if applicable

The IRB Chair of a medical IRB or a IRB Vice-Chair who is a designated physician IRB member reviews the materials submitted to verify conditions of 21 CFR 56.103(c) have been met, including requirements for informed consent unless the conditions of 21 CFR 50.23(a)-(b) have been met. IRB review is documented by the Exemption from IRB Review for Emergency use of a Test Article.

The IRB maintains a complete set of materials relevant to the review of the research protocol or plan for a period of time sufficient to comply with legal and regulatory requirements, Sponsor requirements, and organizational policies and procedures. (AAHRPP Element II.5.A)

8.3 Record Retention

The Common Rule and FDA regulations (45 CFR 46.115(b) and 21 CFR 56.115[b]), require IRB records to be retained for at least three years after the completion of the research, either electronically or as hard copy. HIPAA privacy regulations, require IRB records containing protected health information (PHI) to be retained for at least six years after the completion of the research. It is MD Anderson IRB policy to retain records indefinitely. Thus, the IRB retains and makes accessible all research records at any time. This policy applies to all research protocols, whether or not participants were enrolled. Sponsored grants and contracts may require additional periods for record retention.

Other documents, such as meeting agendas and meeting minutes for the current IRB year are maintained electronically on the OHSP shared drive. Any existing hard copy files may be sent for long-term storage.

General correspondence from investigators and other documents not specific to a particular research protocol are maintained indefinitely in the OHSP shared drive.

Maintenance of and Access to IRB Records
All hard copy IRB records of active protocols are secured in closed filing cabinets in locked buildings with regular security patrols and alarms. Hard copy records of terminated protocols are sent to a MD Anderson contracted vendor for long-term storage. Access to those materials can be obtained in 48 hours, or less, if necessary. Electronic versions of terminated protocols are archived in the electronic research system, and are easily accessible by IRB staff.

The electronic research systems reside on a secured MD Anderson server, with password-protected access. Access to IRB records is routinely provided to the Vice President, Clinical Research Administration, IRB Chairs, IRB members, IRB staff, and scientific review committee members, DSMB, ePAAC, etc. to carry out HRPP operations. Research investigators are provided access to files related to their own research.

All other MD Anderson access to IRB records is limited to those with a legitimate need for access, such as the Institutional Compliance Office, Legal Services, Office of Sponsored Programs, Office of Research Administration, Clinical Research Finance, Office of Technological Licensing, or Internal Audit. In addition, the Vice President, Clinical Research Administration may allow access to IRB records by outside entities (e.g., monitors of sponsors of clinical protocols) and agencies (e.g., regulatory agencies).

The Office for Human Research Protections (OHRP) guidance, with regards to continuing review for protocols that meet the expedited category, indicates that until the 1998 OHRP Expedited Review Categories List (the “1998 List”) is updated to reflect the 2018 Requirements, OHRP recommends that IRBs preserve the continuing review of research (see attached link). At MD Anderson, we will conduct continuing review on protocols that qualify for expedited review.

Records will include the rationale for an expedited reviewer’s determination that research appearing on the expedited review list is no more than minimal risk. The rationale is documented on the Expedited Review Categories.

The IRB Authorization Agreement will include documentation specifying the responsibilities that a relying organization and an organization operating an IRB each will undertake to ensure compliance with the requirements of the Common Rule. The IRB Authorization will be included in the electronic protocol system or in the IRB shared drive.

Confidentiality of Institutional Review Board Proceedings addresses the confidentiality of IRB meetings, meeting minutes, IRB Chairs’ annual reports, research protocols and consent forms. The Vice President for Clinical Research Administration will consider the IRB confidentiality policy, and the reason for a request for access to determine whether to grant access.

The IRB documents discussions and decisions on research studies and activities in accordance with legal and regulatory requirements, Sponsor requirements (if any), and organizational policies and procedures. (AAHRPP Element II.5.B)
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The IRB or EC has and follows written policies and procedures to conduct reviews by the convened IRB: (AAHRPP Element II.2.D)

**Element II.2.D.1.** – Initial review
**Element II.2.D.2.** – Continuing review
**Element II.2.D.3.** – Review of proposed modifications to previously approved research

### 8.4 IRB Minutes

The IRB documents discussions, decisions, and findings either through the IRB minutes or for protocols subject to expedited review through documentation in the protocol file or other records.

The IRB minutes document:
- Meeting attendees and invitees
- Discussions and actions taken by the IRB and the separate deliberations for each action
- Determinations made by the IRB and the protocol-specific findings that justify those determinations
- Votes for each action recorded as numbers for, against, or abstaining
- Other issues requiring convened IRB review.

**Attendance at an IRB Convened Meeting**

Attendance at an IRB convened meeting is recorded in the minutes by documenting:
- The IRB members (voting, non-voting, and ex-officio) in attendance. Non-voting members include ex-officio members attending for informational purposes
- The IRB members not in attendance
- When an associate member replaces a primary member in attendance and voting at the convened meeting
- The continued presence of quorum for all votes, including a member whose primary concern is in a nonscientific area
- The IRB members who leave the meeting because of a conflicting interest
- The IRB members who leave the meeting briefly, are not present during a vote, and are not counted as part of the quorum
- The IRB members who arrive late or depart early from the meeting and their arrival or departure times
- OHSP staff present
- Any others present (e.g., invited guests, investigators invited to by the IRB, and consultants)

**Discussions and Actions Taken by the IRB**

- Discussions and actions taken by the IRB, and the separate deliberations and basis for each action are documented in the minutes, such as:
• Discussion of protocol submissions – new, continuing review, modifications, reports of unanticipated problems and events and information requiring prompt review
• Approval of research – including the approval period for research, at initial and continuing review, (and if appropriate to the degree of risk determination of an approval period of less than one year)
• Approval of research contingent on specific minor conditions, and the designee (staff or IRB member) appointed to sign off on the condition when met. If the condition is met after the minutes for that meeting are approved, the approval is documented in the minutes of the first IRB meeting that takes place after the contingency is met.

Determinations made by the IRB
Determinations made by the IRB are recorded in the minutes and in PDOL/PDOL.net and IRB.net. For the expedited reviews, the determinations are recorded in PDOL/PDOL.net and IRB.net, and CORe with documentation of the protocol-specific findings justifying those determinations as appropriate, such as:
• Significant risk and non-significant risk device determinations, pursuant to:  
  o 21 CFR 812.2(b), 21 CFR 812.150(b)(9), and considering FDA Information Sheet
• Approval of waiver or alteration of informed consent, pursuant to:  
  o 45 CFR 46.116(c), 45 CFR 46.116(d), and FDA Guidance
• Waiver of informed consent documentation, pursuant to:  
  o 45 CFR 46.117(c) and 21 CFR 56.109(c)(1)
• Research involving adults with impaired decision-making
• Waiver of HIPAA Authorization, pursuant to 45 CFR 164.512(i)(2)(ii)
• Waiver of HIPAA Authorization for recruitment or screening, pursuant to 45 CFR 164.512(i)(2)(ii)
• Alteration of HIPAA Authorization, pursuant to 45 CFR 164.512(i)(2)(ii)
• Use of short form process for consent:  
  o 45 CFR 46.117(b)(2) or 21 CFR 50.27(b)(2)
• When research involves children, the following IRB decisions are documented:  
  o Appropriate children finding applicable to research:  
    o 45 CFR 46.404, 45 CFR 46.405, 45 CFR 46.406, 45 CFR 46.407, 45 CFR46.408 (OHRP)  
  o Whether the permission of one parent/guardian is sufficient or if permission from both parents/guardians is recommended (see guidance Parental Permission).
  o The participation of children who are wards of the state is approved under:  
    o 45 CFR 46.406, 45 CFR 46.407, only if 45 CFR 46.409(a) is satisfied, or  
    o 21 CFR 50.53, 21 CFR 50.54 only if 21 CFR 50.56(a) is satisfied
  o Appropriate involvement of pregnant women, fetuses, and neonates pursuant to:  
    o 45 CFR 46.204, 45 CFR 46.205, 45 CFR 46.206, and 45 CFR 46.207
• Determination of the level of risk
• Determinations of serious or continuing non-compliance
• Unanticipated Problems and Unanticipated Adverse Device Effect
• Determinations of Suspensions or Terminations
Expedited Review Categories

Other Issues

Other issues are documented in the minutes, including but not limited to:

- Other events and information that require prompt reporting to the IRB (according to the MD Anderson IRB Policy Reporting Protocol Deviations, Protocol Violations, and Unanticipated Problems and Events and Information that Require Prompt Reporting to the IRB)
- Approval of minutes of prior convened IRB meetings
- The approval of research contingent on specific minor conditions by the IRB Chair, IRB Associate Chair, IRB Vice-Chair, or designee, in the minutes of the first IRB meeting that takes place after the date of the approval
- Presentation of information from an outside consultant or expert as previously requested by the IRB
- Special situations such as use of a test article and humanitarian use devices
- The names of IRB members who abstain for reasons other than conflict of interest
- Other items as applicable

Disposition of the IRB Minutes

The IRB staff writes minutes and makes them available for IRB Chair review one week before the next IRB meeting. Minutes may not be altered by anyone including a higher authority once approved by the members at a subsequent IRB meeting.

The minutes of convened IRB meetings are considered confidential, and access to them is restricted and secured.
Chapter 9. Risks to Research Participants

Definitions

*Risk* in the context of human subject research refers to the combination of the probability and magnitude of some future harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research protocol. Both the probability and magnitude of possible harm may vary independently and result in risks that range from "high" to "low" depending on whether they are more (or less) likely to occur, and whether the potential harm is more (or less) serious.

*Minimal risk* means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. [45 CFR 46.102(i); FDA 21 CFR 56.102(i)]. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of routine physical examination.

*Other definitions of risk or greater than minimal risk*: Regulations, funding agency requirements or guidance documents applicable to specific situations or populations (e.g., prisoners, children) may refer to different definitions, including definitions of minimal risk (see Other Federal Agencies - Additional Requirements).

9.1 Steps to Minimizing Risk

These policies and procedures are based on: Common Rule 45 CFR 46.111(a) (1),(2) and FDA 21 CFR 56.111(a)(1),(2).

When reviewing the protocol application submitted by the principal investigator (PI) the IRB analyzes levels of risk, ensures risks are minimized, and ensures risks are reasonable relative to anticipated benefits, before approving the proposed research (see Chapter 14.11).

Identifying Potential Risks (PI Input)

The PI must describe in the Standard Protocol Form:

- Potential risks to participants, including a scientific estimate of their frequency, severity, and reversibility.
- The statistical incidence of complication and the mortality rate of the proposed procedure, if known.
- The planned procedures for protecting against or minimizing potential risks, including risks to confidentiality. Two plans are necessary:
• One to ensure necessary medical or professional intervention in the event of harm to participants
• One to ensure the safety of participants and the validity and integrity of research data. Data and safety monitoring must be commensurate with risks and the size and complexity of the protocols (see Chapter 9.2).

When proposing changes to the research, PIs must submit a protocol modification form describing the proposed changes and explaining their impact on the level of risk and potential benefits.

**Ensuring Risks Are Minimized (IRB Determination)**

The breadth of scientific disciplines represented by the IRB membership (see Chapter 6.3) allows for a critical assessment of research protocols. The IRB considers the overall level of risk to participants in evaluating the proposed research in accordance with the conditions outlined in 45 CFR 46.111(a)(1-7), 21 CFR 56.111(a)(1-7), and the ethical principles outlined in the *Belmont Report*. Furthermore, the IRB may consult with additional experts as needed (45 CFR 46.111(a)(1)(i), 21 CFR 56.111(a)(1)(i)).

Before approving a research protocol, the IRB must determine that risks are minimized as follows by:

- Ensuring that the proposed research has a sound research design
  - [45 CFR 46.111(a)(1)(i), 21 CFR 56.111(a)(1)(i)]
- The research does not expose subjects to unnecessary risks
  - [45 CFR 46.111(a)(1)(i), 21 CFR 56.111(a)(1)(i)] and
- Whenever appropriate, utilizing procedures that are already being performed on the subjects for diagnostic or treatment purposes

The IRB examines the research plan, including research design and methodology, to determine that there are no inherent flaws that would place research participants at unnecessary risk. This includes the risk that research lacking in statistical power may not lead to meaningful results. Appropriate safeguards can also minimize risk to participants, for example: having an adequate data monitoring plan, or protecting confidentiality by using coded data. If risks are not adequately minimized, the protocol will not be approved as written (see guidance *Evaluating Sound Protocol Design*).

The IRB also considers the professional qualifications and resources (including time, equipment, support services) of the research team to protect participants and minimize potential harm. The IRB may rely on the SRC review or information provided in the Department Chair Protocol Review and Prioritization Memo. Research personnel must have received appropriate training, and clinicians involved in the research must maintain appropriate professional credentials and licensing privileges (see Chapter 14.1 and 14.3).
Potential Risks v. Anticipated Benefits (PI Input)

During the IRB review process, if the protocol and informed consent document(s) are not sufficiently informative about potential risks and anticipated benefits to participant, the IRB may request that the PI provide additional information to include a description of the potential benefit(s) that may be gained by participants, and how the knowledge gained may benefit the participants, future participants or society. The IRB may ask the PI to explain how these potential benefits to the participant or society outweigh the risks inherent in the research.

Potential Risks v. Anticipated Benefits (IRB Determination)

The IRB determines whether the risks of the research are reasonable in relation to the anticipated benefits (if any) to research participants and the importance of the knowledge that may reasonably be expected to result (45 CFR 46.111[a][2], 21 CFR 56.111[a][2]),

The IRB bases its risk/benefit analysis on the information provided by the PI and by the expertise of its members and consultants who utilize the most current information about the risks and benefits of the interventions involved in the research.

The IRB considers only those risks that result from the research, and does not consider long-range effects (e.g., public policy implications) of applying the knowledge gained in the research. The IRB does not consider those risks and benefits that participants would receive even if not participating in the research. [45 CFR 46.111(a)(2) and 21 CFR 56.111(a)(2)]

The IRB has and follows written policies and procedures for reviewing the plans for data and safety monitoring, when applicable, and determines that the data and safety monitoring plan provides adequate protection for participants. (AAHRPP Element II.3.B)

9.2 Data Monitoring Plan

To approve research, the IRB must determine that, where appropriate, the research plan makes adequate provisions for data monitoring to ensure the safety of research participants. (45 CFR 46.111(a)(6), 21 CFR 56.111(a)(6)

Many protocols (e.g., if more than minimal risk) need a Data and Safety Monitoring (DSM) Plan:
- The DSM Plan must be commensurate with the level of risk, size and complexity of the protocol.
- The DSM Plan might need to include a DSMB or DSMC (a data safety monitoring board, or committee – the terms are generally used interchangeably): for example, a DSMB or DSMC may be required as part of the monitoring plan by NIH, FDA, other sponsors, or the IRB.

PIs are required to describe a Data Monitoring Plan, if applicable, in the Protocol Application. For additional information on institutional requirements for the inclusion of a DSM Plan or a DSMB/DSMC for specific protocols, please see Chapter 14.
The IRB does not consider those risks and benefits that participants would receive even if not participating in the research. [45 CFR 46.111(a)(2) and 21 CFR 56.111(a)(2)]

See:
- Guidance Data and Safety Monitoring - for detailed information on what a data monitoring plan might address, when a data monitoring plan is required, and when a data monitoring board or committee is required.
- Data Safety Monitoring Board (DSMB) in Phase I/II Cell and Gene Transfer Clinical Protocols
- Data Safety Monitoring Board in Phase III Cell and Gene Transfer Clinical Trials
- Data Safety Monitoring Plans, and Data Safety Monitoring Committees - Decision Chart
- Chapter 15.4 - discusses PI responsibilities
- Data Monitoring Committees - FDA March 2006 “Guidance for Clinical Trial Sponsors”
- Data Monitoring Plans and Data Safety Monitoring Committees – NIH and NCI policies:
  - NIH: NIH Policy for Data and Safety Monitoring
  - NIH: Further Guidance on a Data and Safety Monitoring for Phase I and Phase II Trials
  - NCI: Policy of the National Cancer Institute for Data and Safety Monitoring of Clinical Trials

Additional Requirements

Additional requirements might apply, depending on the source of support/funding (e.g., Department of Defense) (see Other Federal Agencies - Additional Requirements).

IRB Review of the Data Monitoring Plan

The IRB primary reviewer reviews the proposed Data and Safety Monitoring Plan, and the administration and composition of the monitoring entity, when applicable. If additional expertise is needed, the IRB will seek input from persons with appropriate knowledge.

Continuing Review; Timeframe for Reporting Data Monitoring Findings to the IRB

The IRB does not perform data monitoring, but ensures that appropriate monitoring is taking place, and reviews and acts on reports and recommendations, as necessary, from the monitoring entity.

The IRB must ensure that the conditions satisfied in order for initial IRB approval of the research are still satisfied at continuing review. These include, but are not limited to, determinations by the IRB regarding risks, potential benefits, informed consent, and safeguards for participants. Thus, the PI must include in the continuing review application the outcomes of data and safety monitoring including a summary of adverse events, any unanticipated problems, and any new information pertaining to the research - either from the research itself or from other sources, which have occurred since the previous IRB review. The amount of detail required depends on the type of research being conducted. In many cases, an appropriate summary would be a simple brief statement that there have been no unanticipated problems
and that adverse events have occurred at the expected frequency and level of severity as documented in the research protocol, the informed consent document, and any investigator brochure.

In addition, periodic (usually annual) reports from the monitoring entity (e.g., DSMB/DSMC) are submitted by the PI to the IRB at continuing review. (When a monitoring entity is used, the IRB conducting continuing review of the research may choose to rely on a current statement from the monitoring entity indicating that it has and will continue to review protocol-wide adverse events, interim findings, and any recent literature that may be relevant to the research.)

Whether the method of monitoring is by PI oversight or from the establishment of a DSMB or DSMC, the IRB can tailor a specific timeframe for future reporting of data monitoring findings to the IRB. The IRB can set the date of continuing review for the protocol as being less than the maximum of a year, if they determine that interim reporting of data monitoring information will serve to better protect participants. Alternatively, the IRB can request a report after a specific number of participants are enrolled or after a serious adverse event has been reported.

The IRB has and follows written policies and procedures for determining the risks to prospective participants who are vulnerable to coercion or undue influence and ensuring that additional protections are provided as required by applicable laws, regulations, codes, and guidance. (AAHRPP Element II.4.A)

9.3 Risks to Vulnerable Populations

The IRB is cognizant of the vulnerable nature of many participants. Food and Drug Administration (FDA) regulations and the Common Rule require IRBs to give special consideration to protecting the welfare of vulnerable participants.

In order to approve research involving vulnerable populations, the IRB must determine, where appropriate, that additional safeguards have been included to protect the rights and welfare of participants who are likely to be vulnerable to coercion or undue influence, such as:

- Children (45 CFR 46 Subpart D; 21 CFR 50 Subpart D),
- Prisoners (45 CFR 46 Subpart C),
- Pregnant women, human fetuses, or neonates (45 CFR 46 Subpart B),
- Persons with mental disabilities, or
- Economically or educationally disadvantaged persons

Additional Requirements

Additional requirements might apply, depending on the source of support/funding (e.g., Department of Defense) (see Other Federal Agencies - Additional Requirements).

The IRB includes among its members persons who are knowledgeable about and experienced in working with vulnerable participants. (45 CFR 46.107(a); 21 CFR 56.107(a)). When a research protocol involves a vulnerable population not otherwise covered by these policies, the IRB
takes steps to evaluate whether additional safeguards have been included in the research to protect the rights and welfare of participants.

See also Chapter 12.2 for consent procedures for vulnerable populations.

Considerations in Reviewing Research involving Vulnerable Participants

The IRB considers the following elements of the research plan when reviewing research involving vulnerable participants:

- **Strategic issues** that involve inclusion and exclusion criteria for selecting and recruiting participants; informed consent and willingness to volunteer; coercion and undue influence; and confidentiality of data.
- **Group characteristics**, such as economic, social, physical, and environmental conditions, to ensure that the research incorporates additional safeguards for vulnerable participants.
- **Participant selection to prevent over-selection or exclusion** of certain participants based on perceived limitations or complexities associated with those participants. For example, it is not appropriate to target prisoners as research participants merely because they are a readily available “captive” population.
- **Application of state or local laws** that bear on the decision-making abilities of potentially vulnerable populations. State statutes (as discussed in Chapter 12.1.2) address issues related to legally authorized representatives, and the age of majority for consent.
- **Procedures** for assessing and ensuring participants’ capacity, understanding, and informed consent or assent. When weighing the decision whether to approve or disapprove research involving vulnerable participants, the IRB verifies that such procedures are a part of the research plan. In certain instances, it may be possible for investigators to enhance understanding for potentially vulnerable participants. Examples include requiring someone not involved in the research to obtain the consent, the inclusion of a consent monitor, a participant advocate, interpreter for hearing-impaired participants, translation of informed consent forms into languages the participants understand, and reading the consent form to participants slowly and ensuring their understanding paragraph by paragraph.
- **Need for additional safeguards** to protect potentially vulnerable populations. For example, the IRB may require that the investigator submit each signed informed consent form to the IRB, that someone from the IRB oversee the consent process, or that a waiting period be established between initial contact and enrollment to allow time for family discussion and questions.

For information on the recruitment of vulnerable populations see:

- **Consent Process Observation**
- **Policy on Advertising and Recruiting for a Research Study**
- **Guidance for IRB Members and Investigators for Enrolling Pediatric Patients in Phase 1 Adult Studies**
- **Office of Human Subjects Protection website**
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- Chapter 14.13

Children

- **Children:** Under the regulations, children are persons who have not attained the legal age for consent to treatments or procedures involved in the research under the applicable jurisdiction in which the research will be conducted.

- The IRB follows the requirements of the DHHS regulations at 45 CFR 46, Subpart D and FDA regulations at 21 CFR Part 50, Subpart D in reviewing protocols involving children. The IRB makes the findings and determinations required by the DHHS and FDA regulations related to the risks before allowing research involving children to proceed.

- When the IRB makes a finding that 45 CFR 46.407 or 21 CFR 50.54 apply, the IRB must refer the protocol to the appropriate agency for review and approval. For protocols regulated by OHRP, the proposed activity is referred to the Secretary of HHS. For protocols regulated by the FDA, the proposed activity is referred to the FDA’s Office of Pediatric Therapeutics for public review and approval.

See guidances:

- **Additional Protections for Inclusion of Children in Research (OHRP)**
- **Additional Safeguards for Children in Clinical Investigations (FDA)**
- **Parental Permission**
- **Chapter 12.2.3** for consent requirements for research involving children participants.

Prisoners

**Prisoner:** Any individual involuntarily confined or detained in a penal institution. This includes individuals:

- sentenced to such an institution under a criminal or civil statute,
- detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution,
- detained pending arraignment, trial, or sentencing.

DHHS details special protections for research involving prisoners, who due to their incarceration may have a limited ability to make truly voluntary and un-coerced decisions about whether or not to participate as participants in research. [45 CFR 46, Subpart C]. The IRB will apply the standards of Subpart C to all prisoner research, whether or not DHHS-supported.

**DHHS-supported research:** The IRB must certify to the Secretary (of DHHS), via the Office for Human Research Protections (OHRP) that it has reviewed and approved the research under 45 CFR 46.305; additionally, the Secretary (through OHRP) must determine that the proposed research falls within permissible categories [45 CFR 46.306(a)(2)].

If biomedical or behavioral research is conducted or supported by DHHS, approval must be obtained from the Secretary of DHHS (through OHRP) before commencing research.
Non-DHHS-supported research: Certification to OHRP is not required; the IRB substitutes a comparable risk assessment measure in place of the review and approval by the Secretary of DHHS.

Refer to guidance Involvement of Prisoners in Research for:
- Special requirements regarding IRB composition and additional duties
- Categories of permissible research
- Other requirements pertaining to DHHS-supported research
- IRB required findings.

In order to consider research involving prisoners, the IRBs must:
- Ensure a majority of its members are not otherwise associated with the prison(s) involved in the research, and
- Include a prisoner or a prisoner advocate, who can adequately represent the interests of the prisoners, unless the research has already been reviewed by an IRB that included a prisoner advocate.

**NOTE:** The membership of the MD Anderson IRBs is not appropriately comprised to review research involving prisoners. Protocols that include prisoner populations will need to be reviewed by an appropriately comprised IRB, typically a for-profit independent IRB, and are required to be reviewed by the Vice President for Clinical Research Administration in consultation with the OHSP Director, Institutional Compliance Office and Legal Services prior to submission to the external IRB.

When a PI becomes aware that an enrolled research subject becomes a prisoner and the relevant research protocol was not reviewed and approved by the IRB (under 45 CFR 46, Subpart C) the PI should promptly notify the IRB of this event either by contacting the IRB Office directly, or by submitting an IRB Report Form. The PI should state that all research interactions and interventions with, and obtaining identifiable private information about, the now-incarcerated prisoner-participant will cease until the requirements of Subpart C have been satisfied with respect to the relevant protocol, unless the PI asserts that it is in the best interests of the participant to remain in the research protocol while incarcerated, in which case the IRB Chair may determine that the participant may continue to participate in the research until the requirements of Subpart C are satisfied. Upon receipt of notification that a previously enrolled research participant has become a prisoner, the IRB should promptly re-review the protocol in accordance with the requirements of Subpart C if the PI wishes to have the prisoner participant continue to participate in the research.

Research Involving Prisoners in Texas

If the research involves prisoners in a Texas facility, the IRB must comply with the additional limitations and requirements of the Texas Department of Criminal Justice; see [https://www.tdcj.state.tx.us/faq/external_research.html](https://www.tdcj.state.tx.us/faq/external_research.html).
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DHHS Conducted or Supported Epidemiologic Research Involving Prisoners as Subjects

Under certain conditions DHHS conducted or supported epidemiologic research involving prisoners may be approvable by the Secretary of DHHS, as outlined in the Federal Register Vol 68 No.119, June 20, 2003 and in the Office for Human Research Protections (OHRP) frequently asked questions available on the OHRP webpage.

Decisionally Impaired Participants

The IRB reviews the risk-benefit analysis including the possibilities of coercion and undue influence, and must determine whether such participants should be recruited and whether support mechanisms, such as surrogate consent, are appropriate. See Chapter 12.2.1 for more information on the consent process, and criteria for including decisionally impaired participants in research.

Pregnant Women, Human Fetuses, and Neonates

The Department of Health and Human Services (DHHS) details special protections for research involving pregnant women, human fetuses, and neonates (45 CFR 46, Subpart B).

Under these regulations, the IRB is required to document specific findings to minimize the potential for risk or harm to the fetus, and additional attention must be given to the conditions for obtaining informed consent, in accordance with the guidance Research Involving Pregnant Women, Fetuses, and Neonates.

In general, Subpart B requires that research involving pregnant women, human fetuses, and neonates should involve the least possible risk. Persons engaged in the research may have no part in the timing, method, or procedures used to terminate the pregnancy, or to determine the viability of the fetus. No inducements may be offered to terminate a pregnancy.

For additional information and requirements please reference the regulations below, or contact the IRB or the Institutional Compliance Office:

- 45 CFR § 46.204 - Research involving pregnant women or fetuses
- 45 CFR § 46.205 – Research Involving Neonates

Non-pregnant women of reproductive potential

Unilateral exclusion of non-pregnant women of reproductive potential from research is not permitted by the IRB. Exclusion requires compelling scientific justification. Where such justification exists, it may also be appropriate to exclude men of reproductive potential.

Other Potentially Vulnerable Participants

The context of the research is an important consideration for the IRB when reviewing research that involves other potentially vulnerable participants such as research involving homeless persons, members of particular minority groups, or the economically or educationally
disadvantaged. Research involving significant follow-up procedures or offering significant monetary compensation may unduly influence certain types of participants and the IRB takes such considerations into account. Nevertheless, research involving these participants is socially important for understanding and eventually improving adverse health and general well-being in these populations.

Employees and Students

Employees, lab personnel, students, and trainees at MD Anderson and its affiliates under the purview of the IRB are considered vulnerable participants, in particular because of the risk of coercion and undue influence by MD Anderson faculty or staff that may be in a supervisory position to the employee. The IRB has the same standards for approving research involving these groups as other vulnerable participants.

9.4 Suspension or Termination of IRB approval

Definitions

Suspension: Temporary withdrawal of IRB approval for some or all research procedures in a protocol or the permanent withdrawal of IRB approval of part of a protocol. Continuing review of the research is still required. A sponsor-imposed suspension alone does not constitute such a suspension, as it is not an action by the IRB to withdraw approval of a previously approved protocol. Similarly, an action by the Principal Investigator (PI) that halts or materially changes some or all of the PI’s protocol as previously approved by the IRB does not constitute such a suspension (but may need to be submitted to the IRB as a protocol modification).

Termination: Permanent withdrawal of IRB approval of a previously approved protocol. A final report is still required to be submitted to the IRB by the PI.

Suspension or Termination by the Convened IRB

The IRBs have the authority (45 CFR 46.113; 21 CFR 56.113) to suspend or terminate IRB approval of a previously approved protocol. Please see IRB Policy on IRB Committee Determinations for Reviewing Research Non-Compliance, Suspending or Terminating Research and IRB reporting procedures to Institutional and External Officials.

The IRB may act to suspend or terminate its approval of a protocol for any of the following reasons including but not limited to:

- Not conducting research in accordance with IRB requirements
- Unexpected serious harm to subjects.
The IRB shall:

- Notify the PI in writing of its decision to suspend or terminate its approval of a protocol along with a statement of the reasons for the IRB action and any terms and conditions of any suspension.
- Report the decision to suspend or terminate IRB approval of a previously approved protocol to the Vice President, Clinical Research Administration and others in accordance with the procedure set forth in Chapter 3.9.

The PI of the affected protocol shall be provided with an opportunity to respond in person or in writing to the IRB on a suspension or termination of IRB approval of the protocol.

If the IRB action in relation to the suspension or termination involves the withdrawal or modification of participation of current participants from the research, the IRB shall direct the PI to contact the participants to:

- Make such notification with an explanation, after its review and approval by the IRB.
- Describe any monitoring and follow-up for safety reasons that will be conducted.
- Provide contact information for the PI and the IRB where the participant may report any adverse events or unanticipated problems.

Suspension or Termination by an Authorized Individual

The Vice President for Clinical Research Administration, as the Institutional Official, is the only MD Anderson official authorized to suspend or terminate approval of a protocol that has been reviewed by the IRB. When the Institutional Official suspends an IRB-approved protocol, the following actions shall be taken immediately:

- Notify the PI: (i) to halt the portion of the IRB approved protocol that poses immediate, material risk to participant health and welfare, (ii) of the reasons for the suspension or termination, and (iii) of the opportunity to respond in person or in writing to the official and IRB on the suspension or termination
- Report the suspension or termination and its basis to the IRB.

The IRB shall:

- Immediately initiate the appropriate procedure to have the protocol reviewed at a convened IRB, and review and gather supporting documentation for the IRB to consider. The IRB staff may identify additional non-compliance during their review which will be communicated to the Institutional Official and the IRB Chair (e.g., the procedure for reviewing possible non-compliance or a possible unanticipated problem (see Chapter 3.9 and 3.10).

If the suspension of IRB approval of a protocol involves participant withdrawal from the research or modification of participation of current participants, the IRB shall direct the PI to contact the participants to:

- Make such notification with an explanation, after its review and approval by the IRB
- Describe any monitoring and follow-up for safety reasons that will be conducted
• Provide contact information for the PI and the IRB where the participant may report any adverse events or unanticipated problems.

Protection of Participants Who May Be Affected by the IRB Action

If the suspension or termination of IRB approval of a protocol will affect participants in such protocol (e.g., requires withdrawal of participants), the IRB shall utilize a process that takes into account the impact of the suspension or termination of IRB approval has on participants’ health and safety. This should occur before the suspension or termination, when it is feasible and related delay, if any, will not jeopardize participants’ health and safety. Examples include:

• Requiring the PI to submit proposed procedures for any withdrawal of participants
• Allowing participants to continue (e.g., treatment with an investigational drug) if the IRB determines that it is in their best interests
• Requiring submittal for review and approval of the IRB or its designee of all communications by the PI to participants about the IRB action
• Designating an investigator other than the PI to be responsible for carrying out the IRB decision
• Requiring the appointment of a substitute PI or transferring responsibility for participants to another investigator
• Requiring the PI to carry out follow-up or monitoring of participants appropriate to the circumstances (e.g., for any adverse impact on participants after suspension or termination)
• Requiring special reporting (e.g., adverse events or outcomes) concerning participants by the PI.
Chapter 10. Participant Recruitment and Selection

The IRB has and follows written policies and procedures to evaluate the equitable selection of participants. (AAHRPP Element II.3.C)

10.1 Equitable Selection

Guidance and information is made available to Principal Investigators (PIs) to assist and guide them in creating recruitment and participant selection methods that are fair and equitable. See:

- Recruitment
- Advertisements: Appropriate Language for Recruitment Material
- Chapter 14.4
- Determining Socioeconomic Status for a Research Participant

PIs are directed to enter detailed information on how participants will be identified and recruited in response to questions in the protocol submission form. PIs are required to identify the target populations (including age range, gender, and ethnic background), the inclusion and exclusion criteria and whether payments will be made for participation. In addition, PIs are required to justify the inclusion of targeted persons (e.g., healthy participants, employees, students or participants with certain medical conditions). In determining if the selection and recruitment of participants is equitable, the IRB takes into account the purpose of the research, the setting in which the research will be conducted, whether prospective participants will be vulnerable to coercion or undue influence, the selection (inclusion/exclusion) criteria, participant recruitment and enrollment procedures, and the influence of payments to participants. The IRB also evaluates whether the protocol imposes fair and equitable burdens and benefits - such that one group of persons does not disproportionately receive the benefits compared to another group assuming only the risks.

IRB staff and members review this information and confirm the recruitment and selection strategies are fair, equitable, and not misleading. If recruitment strategies fail to meet these requirements, the protocol will not be approved as written and the PI will be asked to modify the recruitment plan accordingly, as a condition of approval.

Vulnerable Subjects

Investigators must provide a rationale for involvement of vulnerable subjects, such as children, prisoners, pregnant women, economically and educationally disadvantaged, decisionally impaired, and homeless persons. The PI must substantiate his/her decision to involve a vulnerable population and further provide a rationale why a less vulnerable population would not serve the purpose of the research. When vulnerable populations will be targeted for enrollment, the IRB assesses the additional safeguards proposed by the PI to minimize the possible risks and the chance of harm to these populations. While pregnant women are considered vulnerable participants, women of reproductive age should not be arbitrarily
excluded from participation in research. If women are to be excluded, such exclusion must be fully justified by the PI based on scientific rationale and provided to the IRB.

Non-English Speaking Participants

Non-English speaking participants should not be systematically excluded because of language barriers. The IRB encourages the inclusion of non-English speaking participants and permits such persons to be enrolled via the short form consent process consistent with 45 CFR 46.117(b)(2) and 21 CFR 50.27(b)(2) (see Non-English Speaking Research Participant).

The IRB has and follows written policies and procedures to review proposed participant recruitment methods, advertising materials, and payment arrangements and determines whether such arrangements are fair, accurate, and appropriate. (AAHRPP Element II.3.C.1)

10.2 Review of Recruitment Methods, Advertising Materials and Payment

Recruitment Methods

PIs are required to provide details on all methods of recruitment proposed on a project, including how participants will be identified for recruitment. Guidance on recruitment is available, as well as sample phone screens when screening will be conducted over the phone to determine protocol eligibility. Some common recruitment methods include recruiting from one’s own patients, seeking referrals from colleagues (via word of mouth or referral letters sent to colleagues) and advertisements.

Advertisements

The IRB considers that advertisements begin the informed consent process and thus, consistent with the consent process, coercion and undue influence are prohibited during recruitment. If recruitment will be by advertisement, the mode of advertisement (flyers, radio, newspaper, or internet) and information contained in the advertisement must be approved by the IRB.

- **Audio and video tape:** The IRB may review and approve the wording prior to taping in order to preclude re-taping due to inappropriate wording. The IRB reviews the final version of the advertisement.

- **Printed advertisement:** The IRB reviews the final version.

See:

- Recruitment
- Advertisements: Appropriate Language for Recruitment Material
- IRB Policy on Advertising and Recruiting for a Research Study
- Recruiting Study Subjects (FDA)

Telephone Screening

For protocols involving telephone screening of participants in response to an advertisement, the IRB generally requires investigators to review all the required elements of informed consent orally with prospective participants. However, investigators may request a waiver of
documentation of consent limited to the screening portion (only) of the protocol if they demonstrate that the screening procedure meets regulatory criteria in 45 CFR 46.117(c)(2) or 21 CFR 56.109(c)(1).

Payment
PIs must disclose any proposed payments to participants in the protocol application form, including the method, type and timing of the payments. Payments to research participants may not be of such an amount as to result in coercion or undue influence on the research participant’s decision to participate. If a protocol has multiple paid visits, payment should be prorated throughout the duration of the protocol to provide partial payment to persons who withdraw before completing the protocol. See guidance Payment – Ethical Considerations, MD Anderson IRB Policy on Advertising and Recruiting for a Research Study, and Participant Remuneration Form Standard Operating Procedures.

Prohibited Recruitment and Payment Practices
The following activities are examined carefully and are generally not allowed:
- Payment from research participants
- Compensation for participation in the form of a coupon for a discount on the test article to be used after the product has been approved for marketing.
- Exculpatory language through which the participant or participant’s LAR is made to waive or appear to waive any of the participant’s legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Payment Arrangement among Sponsors/Organizations, Investigators and Others
Payment in exchange for referrals of potential participants (finder’s fees) and payments designed to accelerate recruitment tied to the rate or timing of enrollment (bonus payment) are not allowed.

Payment Practices – Additional Requirements
Other Federally Funded Research:
Additional requirements might apply, (such as payment and compensation limits, minimizing undue influence, etc.), depending on the source of support/funding (e.g., Department of Defense) (see Other Federal Agencies - Additional Requirements).

10.3 Social Media
All social media accounts, as well as social media campaigns, promoted posts and advertisements, created on behalf of MD Anderson and our programs, departments, research, events, and brand must be approved by Strategic Communications prior to moving forward. This is to ensure alignment with MD Anderson’s social media strategy, Social Media Policy (ADM1112) and best practices. Please review, the questions to consider when requesting a social media account before contacting Strategic Communications.
Chapter 11. Privacy and Confidentiality

MD Anderson has established the following written policies, together with the other policies referenced in this Chapter, to protect individuals’ privacy and the confidentiality of data.

In order to approve research, the IRB must be satisfied that, “when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of the data” [45 CFR 46.111(a)(7) and 21 CFR 56.111(a)(7)]. An invasion of privacy or breach of confidentiality may be a moral wrong or even present a risk of serious harm to participants (e.g., jeopardize their family relationships, community standing, employment, or lead to prosecution for criminal behavior). The IRB reviews each protocol, based on the information provided by the PI in the Protocol Application, and assesses the amount and type of private information involved, how the information will be collected, and plans for its use, storage and disclosure. As necessary, the IRB will ask for additional details during its review.

Definitions

Privacy means, in the context of a research protocol, respecting an individual’s right to be free from unauthorized or unreasonable intrusion, including control over the extent, timing and circumstances of obtaining personal information from or about them.

Confidentiality means respecting a potential or current participant’s right to be free from unauthorized release of information that the participant disclosed in a relationship of trust and with the expectation that it will not be divulged to others without permission in ways that are inconsistent with the understanding of the original disclosure. In the context of a research protocol, “confidentiality” refers to the understanding between the participant and investigator (e.g., as set forth in the consent and authorization documents) as to how participant information will be handled, managed, and disseminated (e.g., shared with others) as part of the research.

Private Information means individually identifiable information:

- About behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place
- Which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).

Sensitive Information is private information relating, but not limited, to:

- Sexual attitudes, preferences or practices
- Use or treatment for alcohol, drugs or other addictive products
- Illegal conduct
- Information which if released could reasonably cause stigmatization or discrimination, or result in damage to areas such as financial well-being, employability, or reputation.
• Certain health information, including psychological or mental health, communicable diseases or genetic information.

*Protected Health Information* (PHI) is defined in the [HIPAA privacy](https://www.hhs.gov/hipaa/index.html) regulations in [45 CFR 164.501](https://www.cfr.gov/title-45/45-cfr-164.501) and in the MD Anderson HIPAA policies.

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**The IRB has and follows written policies and procedures to evaluate the proposed arrangements for protecting the privacy interests of research participants, when appropriate, during their involvement in the research.** *(AAHRPP Element II.3.D)*

### 11.1 Protecting the Privacy of Participants

Privacy refers to persons and their interest in controlling the access of others to information about themselves.

To approve research, the IRB must determine that, where appropriate, there are adequate provisions to protect the privacy interests of potential or current participants, from the screening and recruitment through all phases of research. If the protocol does not include adequate provisions to protect the privacy interests of the participants, the IRB may not approve the protocol as written.

The PI must describe in the protocol submission the provisions for protecting the privacy of participants during screening, data collection and other interactions. The IRB assesses the information during the review process and at convened meetings. As necessary, the IRB will ask for additional details during its review.

Provisions for protecting the privacy interests of participants or participants should include:

- Ensuring that the conditions under which a procedure is performed or information is collected (e.g., physical locations, telephone contact, mail or email solicitations) afford protections against interactions with participants being witnessed, overheard or inadvertently intercepted or viewed. For example, a potential or current participant may feel uncomfortable:
  - Being seen entering a place that they feel might stigmatize them;
  - Having physical measurements recorded in a non-private setting;
  - Discussing private medical information in a setting with other than a health care provider or in other than a private clinical setting;
  - Answering sensitive questions by telephone while at work.
- Limiting the information being collected to only the minimum amount of data necessary to accomplish the research purposes.

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**The IRB has and follows written policies and procedures to evaluate proposed arrangements for maintaining the confidentiality of identifiable data, when appropriate, preliminary to the research, during the research, and after the conclusion of the research.** *(AAHRPP Element II.3.E)*
Researchers and Research Staff follow the requirements of the research protocol or plan and adhere to MD Anderson policies and procedures and to the requirements or determinations of the IRB. (AAHRPP Element III.2.C)

11.2 Protecting the Confidentiality of Participant Information

Confidentiality refers to maintenance of the Researcher’s agreement with the participant about how the participant’s identifiable private information will be handled, managed, and disseminated.

As a condition of protocol approval, the IRB determines that there are adequate provisions to protect confidentiality of information related to potential or current participants, throughout the research, including data analysis and retention. PIs are expected to design studies to maximize confidentiality to avoid unintentional and unauthorized release or other disclosures. The IRB follows waiver regulations when determining whether waiver of authorization (or alteration) is appropriate.

Additional Requirements

- Additional requirements might apply, depending on the source of support/funding (see Other Federal Agencies - Additional Requirements).

The PI must describe the provisions to protect the confidentiality of data in the Protocol Submission. The IRB assesses the information provided in the application during the review process and at convened meetings. The IRB may ask for additional details during its review, depending on the sensitivity of the information being used, maintained or disclosed. Generally, the greater the sensitivity of the information, the more stringent the security measures that are needed.

In reviewing confidentiality protections, the IRB considers the nature, probability, and magnitude of harms that would be likely to result from an unauthorized release of the collected information. It evaluates the proposed anonymizing techniques, (e.g., de-identification, coding), storage plans, access restrictions, data security methods (e.g., encryption) and other relevant factors in making its final determination concerning the appropriateness and adequacy of confidentiality protections. See the Protocol Application for the information requested by the IRB for this assessment.

For active protocols, any changes in confidentiality protection measures must be described in either a protocol modification or continuing review application. Such changes are reviewed according to the requirements described above for new protocols.

The IRB requires that investigators use best practices and adhere to MD Anderson security policies to protect the confidentiality of the information collected under a protocol, unless the participant explicitly consents otherwise, and is aware of any risks.
MD Anderson has guidelines for best practices for maintaining confidentiality. See the MD Anderson Privacy & Information Security Compliance including best practices for:

- Protecting PHI against public viewing;
- Storage and disposal of documents that contain PHI; [Patient Privacy - Safeguarding Paper PHI Policy (ADM1176)]
- Safeguarding computer workstations and databases that access PHI;
- Faxing and emailing PHI and [Patient Privacy_ De-Identification Of Protected Health Information (PHI) Policy (ADM1180)]

Techniques described in these policies may be generally applied to all information. The IRB may consult with Information Security or other MD Anderson security specialists if needed.

PIs must also follow MD Anderson security policies, as applicable to their respective division, which define requirements for securing information maintained in electronic form.

See:

- MD Anderson Information Security policies: Information Security Compliance Website

**Legally Required Release of Private Information**

The IRB identifies protocols that might collect information that could be subject to a legally mandated release of information, to the extent that this can be ascertained in advance. When such protocols are identified in advance, the IRB requires that the investigator notify the participants through language in the consent and HIPAA authorization document(s) of the possibility of legally mandated disclosure. Examples of reportable information include:

- Child abuse and neglect reporting, Texas Family Code Chapter 261;
- Elderly persons and persons with disabilities abuse and neglect reporting, Texas Human Resources Code Chapter 48;
- Reporting certain communicable diseases and notifiable conditions, Texas Health and Safety Code Chapters 81, 84, 87, 88 and 97;
- Reporting incidents involving medical devices, 21 USC 360i(b), 21 CFR Part 803.
- Release under a search warrant or a subpoena (e.g., civil or criminal litigation).

PIs may seek advice from the IRB or the relevant MD Anderson legal counsel, if they have any questions concerning compliance with these laws.

**Certificates of Confidentiality (CoC)**

Please see the document [Certificate of Confidentiality](#).

**Continuing Confidentiality Protections – Data Analysis, Dissemination and Retention**

PIs should consider taking additional precautions that were not feasible while the protocol was active, including:
• Removing some or all direct identifiers (e.g., name, medical record number) and coding the information;
• Limiting the individuals who have access to the participant identifiable information
• Employing secure archival methods or Information Security Office-approved long-term storage services.

11.3 HIPAA - Health Insurance Portability and Accountability Act Regulations
In accordance with HIPAA regulations [45 CFR Part 160 and 45 CFR Part 164], the IRB oversees the satisfaction of and compliance with some of those requirements (e.g. authorizations for research use/disclosure of PHI, preparatory to research use of PHI, waivers of authorization). This is in addition to any requirements under the Common Rule and FDA regulations. MD Anderson has established written policies and procedures to implement the HIPAA regulations.

• MD Anderson policies and procedures related to HIPAA and Privacy: Privacy & Information Security Compliance

The IRB, PIs, and other investigators accessing, using, or maintaining PHI have certain duties and responsibilities under those policies and HIPAA, particularly for research activities.

HIPAA Coordination
MD Anderson has designated a Privacy Officer. The Privacy Officer is responsible for the development and implementation of the HIPAA policies and procedures and overseeing compliance with HIPAA. The Privacy Officer employs a team of analysts and meets regularly with a Privacy Compliance Committee. The Privacy Officer and other Institutional Compliance Office attorneys and staff assist the IRBs with HIPAA legal questions as needed.

IRB staff meet periodically seek advice from the MD Anderson privacy attorneys to discuss IRB matters including privacy and confidentiality issues.

11.4 Confidentiality Breach - Unauthorized Release of Information
The IRB requires that PIs immediately inform it of any possible or actual unauthorized release of information. The IRB also may receive a complaint or allegation from a participant about such a release, since its contact information is contained in the consent document for that purpose. The IRB treats such a release or allegation of release as possible non-compliance. It follows the process set forth in Chapter 3, in order to review and respond to the situation.

The IRB will report any breach of confidentiality involving sites where MD Anderson investigators conduct research pursuant to any agreement with the external site.

Texas Code
The response must include any notification to the participant of any breach of system security relating to sensitive personal information as required by Section 521.053 of the Texas Business & Commerce Code.

**Potential Violation of HIPAA**

If a potential violation involves PHI, MD Anderson also treats it as a potential violation of HIPAA policies and the HIPAA privacy and security regulations. The IRB will communicate and coordinate its review and response with that required under the applicable MD Anderson HIPAA policies, including communicating with the Privacy Officer of MD Anderson. The Privacy Officer and Institutional Compliance Office handles the breach analysis and any required breach notifications, in accordance with MD Anderson’s [Patient Privacy _ Breach Notification Policy (ADM1033)](https://www.mdanderson.org/policies/provisional/hrrp/patient-privacy-breach-notification-policy.html).

See:

- Privacy & Information Security Compliance
- Preparatory to Research Uses of Protected Health Information Policy (ACA1230)
- Information Security Office Policy for the Use and Protection of Information Resources (ADM0335)
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Informed consent is a continuing process whereby the investigator and research participant have an on-going dialogue about all aspects of a research protocol that might inform a participant’s decision to take part in the protocol and their decision to continue their involvement as a participant. The purpose of the consent process is to assure knowledgeable decision-making and voluntary participation.

The consent process and documentation as a whole presents information in sufficient detail and facilitates the prospective participant’s or legally authorized representative’s understanding.

This process generally includes:

- Bringing the research protocol to the notice of potential participants;
- Presentation and explanation of the protocol activities to the prospective participant or his/her legally authorized representative (LAR);
- Documentation of the informed consent via a signed and dated written consent document;
- Ongoing discussions between the investigator and the participant regarding continued participation in the protocol.

The consent process must:

- Provide sufficient opportunity for the participant, or the participant’s legally authorized representative (LAR), to consider whether to participate;
- Minimize the possibility of coercion or undue influence;
- Be free of exculpatory language; and
- Be in language understandable to the participant or their representative.

The IRB also requires that the circumstances of the consent process be culturally and linguistically appropriate for the intended participants.

Refer also to Chapter 14.14 for more information on the consent document, and principal investigator responsibilities in the informed consent process.

The IRB has and follows written policies and procedures to evaluate the consent process and to require that the Researcher appropriately document the consent process. 
( AAHRPP Element II.3.F)
12.1 Requirements for Informed Consent

All relevant requirements in OHRP in 45 CFR 46.111 and 46.116, and in the FDA regulations in 21 CFR 50.20, 50.25, 50.27 and 56.111 that are applicable to the consent process and the consent document must be satisfied.

Researchers are required to use the most recently approved consent forms, assent forms, and HIPAA Authorization forms, which are available in iConsent or for printing directly from the electronic protocol system (when needed for non MD Anderson patients who do not have medical record numbers), PDOL viewer.

Under Texas law, there are specific requirements regarding the informed consent process, such as Texas Civil Practice and Remedies Code Chapter 74 and Title 25, Part 7, Chapter 601 of the Texas Administrative Code (identifying which treatments and procedures require full disclosure of specific risks and hazards), Texas Health and Safety Code Chapters 166 (regarding advance directives), 313 (regarding consent to treatment), 773 (regarding emergency medical services), and Texas Family Code Chapter 32 (regarding consent to treatment of a child by a non-parent or child).

The IRB has and follows written policies and procedures to evaluate the consent process and to require that the Researcher appropriately document the consent process. (AAHRPP Element II.3.F)

IRB Evaluation of Compliance with Informed Consent Requirements

The evaluation of compliance may be achieved by:

- IRB review of the informed consent process information and document(s) provided by the principal investigator including who will conduct the consent interview and who will provide consent or permission.
- Periodic consent form reviews comparing signed and dated consent forms with the IRB approved versions.
- Observation of the consent process, performed as requested by the convened IRB (see Chapter 12.7).
- The IRB will review the consent and determine that the required and appropriate additional elements of disclosure are included in the consent process.
- The IRB will review the consent and determine that the consent document begins with a concise (no longer than 1 page) and focused presentation of key information (for example, the study goals, potential benefits, length of treatment, study costs, alternative procedures, study risks, voluntary nature of study) that is most likely to assist a prospective participant or legally authorized representative in understanding the reasons why one might or might not want to participate in the research.
- The Executive IRB approves the informed consent templates, which contain the essential and additional consent elements (see Annotated MD Anderson ICD – Essential and Additional Elements).
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The IRB has and follows written policies and procedures to evaluate the consent process and to require that the Researcher appropriately document the consent process. (AAHRPP Element II.3.F)

12.1.1. Elements of Informed Consent
Legally effective informed consent includes the eight basic required elements and as applicable/appropriate the six additional elements specified in 45 CFR 46.116 and 21 CFR 50.25.

Please see, the Clinical Trials Registration and Reporting Requirements Policy (ACA3214) and Clinical Trials Registration and Reporting Requirements, Policy Table for information about a description of the process for posting the IRB-approved consent form for each clinical trial conducted or supported by a federal department or agency on a website specified by the US federal government.

Informed consent requirements for vulnerable and other special populations are addressed in Chapter 12.2.

The IRB has and follows written policies and procedures to evaluate the consent process and to require that the Researcher appropriately document the consent process. (AAHRPP Element II.3.F)

MD Anderson has and follows written policies and procedures that identify applicable laws in the localities where it conducts human research, takes them into account in the review and conduct of research, and resolves differences between federal or national law and local laws. (AAHRPP I.1.G)

12.1.2. Additional Consent Requirements
MD Anderson legal and regulatory counsel in MD Anderson’s Institutional Compliance Office and Legal Services department provide assistance to investigators and the IRB in resolving any conflicts among applicable laws.

- Texas Law
- HIPAA and PHI
- HIV Testing or Research on AIDS
- Genetic Testing
- Data and Tissue Repositories
- Xenotransplantation
- International research
- Human Embryonic Stem Cell and Induced Pluripotent Stem research
- Other Federal Agencies – Additional Requirements

Health Insurance Portability and Accountability Act (HIPAA)
If the protocol involves protected health information (PHI) as defined by HIPAA (refer to the Patient Privacy Uses and Disclosures of Protected Health Information Policy [ADM0401]), then HIPAA authorization is included in the consent process. HIPAA authorization is an authorization to use or disclose PHI. MD Anderson uses a combined informed consent and authorization document; templates of such document are available for researchers to use for preparing specific consent and authorization documents with assistance from the OHSP scientific editing staff. MD Anderson legal and regulatory counsel in the MD Anderson Institutional Compliance Office are available to advise and help both the IRB and researchers with HIPAA-related questions and matters.

Consent templates incorporating HIPAA authorization are provided on the Office of Human Subjects Protection website (see Informed Consent Templates [Clinical], [PA], and [Psychosocial]).

**HIV testing and disclosure** (Texas Health and Safety Code Chapter 81) (OHRP)
Individually identifiable research records generated by AIDS-related research are confidential and may only be disclosed with the prior written consent of the participant.

**HIV Testing and Disclosure**
Individually identifiable research records generated as part of AIDS-related research are confidential and may only be disclosed with the prior written consent of the participant except in situations where such consent is not required under applicable Texas law as confirmed by MD Anderson’s Legal Service department.

**Genetic Testing**
If a protocol includes genetic testing, the IRB requires that the informed consent information disclose the risks specific to this type of testing. Genetic testing includes research that studies the characteristics, genes, and gene versions that are transmitted by parents to offspring. This may include many types of information, such as personal appearance and biochemistry, gene sequences, genetic landmarks, individual or family medical histories, reactions to medication, and responses to treatment. The IRB includes detailed provisions and issues in its informed consent template provisions that should be considered by the principal investigator when the research includes genetic testing. The template is also used by IRB staff and members as a guide for their review of such a consent document.

**Data and Tissue Repositories**
The NIH guidance on Data and Tissue Repositories is of interest to investigators who collect data or tissues of participants for repositories, and IRB staff and members who review such protocols.
When such repositories collect individually identifiable health information of participants, the HIPAA privacy regulations in 45 CFR Parts 160 and 164 must also be satisfied. This may require either a written HIPAA authorization from the participants or a waiver of authorization by the IRB. These requirements are discussed in Chapter 11.

**Xenotransplantation**

*Xenotransplantation*: Any procedure that involves the transplantation, implantation, or infusion into a human recipient of either (A) live cells, tissues, or organs from a nonhuman animal source or (B) human body fluids, cells, tissues or organs that have had ex vivo contact with live nonhuman animal cells, tissues, or organs.

In reviewing protocols and informed consent involving xenotransplantation, the IRB acts in accordance with the Guideline on Infectious Diseases Issues in Xenotransplantation issued by the federal Public Health Service (PHS) on January 19, 2001, or current version in effect at the time of IRB review. The PHS Guidelines require that various other administrative panels (e.g., Biosafety Committee) review such protocols, in addition to the IRB. The principal investigator should consult the PHS Guideline prior to drafting the consent document, since they contain detailed guidance about the content of the informed consent information provided to potential xenotransplantation product recipients. For example, they must be informed of the importance of complying with long-term or life-long surveillance necessitating routine physical evaluations and the archiving of tissue or body fluid specimens.

**International Research**

When conducting research in certain communities or social contexts, whether in the U.S. or abroad, it may be inappropriate to document consent by using the standard written and signed consent document. Other consent procedures may be more culturally or socially sensitive and may afford better protection to participants (see Chapter 1.4.1).

Investigators may ask the IRB to consider a waiver or alteration of some of the mandatory elements of consent [45 CFR 46.116(d)], or a waiver of documentation of consent [45 CFR 46.117(c); 21 CFR 56.109(c)] (see Chapter 12.5).

**Consult Legal Counsel If Necessary:** Principal investigators should contact the legal and regulatory counsel in the Legal Services department and Institutional Compliance Office to assist in determining who under local law may serve as a legally authorized representative, if children or adults who are unable to consent may be enrolled as participants.

**Stem Cell Research**
At MD Anderson, the conduct of research involving human stem cells is governed by federal, and State of Texas law, and must be reviewed by the IRB and HEIPSCRO (Institutional Review Board and Human Embryonic & Induced Pluripotent Stem Cell Research Oversight Committee).

Requirements - Other Federal Agencies

Additional requirements might apply, depending on the source of support/funding (e.g., Department of Defense) (see Other Federal Agencies - Additional Requirements).

12.1.3. Consent Templates and Glossary of Lay Terms

The Office of Human Subjects Protection website provides consent form templates, that include the required elements of informed consent. Additionally, the MD Anderson Adverse Events (AE) Database provides language, written in lay terminology, for other medications and procedures (e.g., related to oncology drugs, MRI, tissue banking), in which certain additional information may need to be provided to participants. For research involving children, an Assent Template is also provided (see Informed Consent Templates [Clinical], [PA], and [Psychosocial]).

To assist principal investigators in preparing consent documents comprehensible to lay persons (i.e., at approximately 8th grade level) a glossary of lay terms is also available on the NCCN Informed Consent Language (ICL) Database.

12.1.4. Short Form Consent Process

Federal regulations permit the use of a short form consent process (45 CFR 46.117(b)(2)) with the prior approval of the IRB. The IRB requires the use of a full consent form translated into the participant’s language after 2 participants have been consented using the short form or verbal translation preparative sheet (VTPS) in the same language (not English) and there are 5 accrual slots remaining. The participant population at MD Anderson is international and diverse thereby allowing non-English speaking populations to be enrolled in research.

For use of the short form of consent documentation, the IRB determines:

- The Verbal Translation Preparative Sheet (VTPS) (see Using the Multiple Language Verbal Translation Preparative Forms and Process) informs the potential participant of the types of information they should receive during the verbal translation of the Informed Consent Document.
- There will be a witness to the oral presentation. The witness may be the interpreter (including the hospital interpreter), staff (not associated with the protocol), a family member, or other person. The witness will be fluent in the participant’s language and English.
- The participant or the participant’s legally authorized representative will sign and date the VTPS presented in the participant’s language
- The witness will sign and date both the VTPS and informed consent document
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- The person actually obtaining consent will sign and date a copy of informed consent document.
- A copy of the signed and dated VTPS will be given to the participant or the participant’s legally authorized representative.
- A copy of the informed consent document will be given to the participant or the participant’s legally authorized representative.

Please see Institutional Policies CLN0470 and CLN0547:
- Language Assistance Policy (CLN0470)
- Informed Consent Policy (CLN0547)

On the Office of Human Subjects Protection website there is information on the requirements for use of a VTPS (see Consenting Non-English Speaking Participants).

The IRB has and follows written policies and procedures requiring appropriate protections for prospective participants who cannot give consent or whose decision-making capacity is in question. (AAHRPP Element II.4.B)

(Also addresses portions of AAHRPP Element II.4.A)

12.2 Consent Procedures for Vulnerable and Other Special Populations Including Consent by a Legally Authorized Representative

When considering approval of research, the IRB considers issues such as the selection of participants, privacy and confidentiality, coercion and undue influence, and risk-benefit analysis. Decisions are guided by the ethical principles underlying human research as set forth in the Belmont Report.

Special consideration is given to protecting the welfare of vulnerable participants, such as children, prisoners, pregnant women, fetuses, and mentally disabled persons, handicapped persons, or economically or educationally disadvantaged persons (45 CFR 46.111(b) and 21 CFR 56.111(b)). There are specific regulatory provisions for research involving pregnant women, fetuses, and neonates (45 CFR 46, Subpart B), prisoners (45 CFR 46, Subpart C), and children (45 CFR 46, Subpart D and 21 CFR 50 Subpart D).

Also see Chapter 9.3 concerning determination of the risks to vulnerable populations as defined in applicable federal regulations, and specifically for determining the required risk categories in protocols involving children and prisoners.

Additional Requirements

Depending on the type of research project, or the source of support/funding for the protocol or institution at which the protocol will be conducted (e.g., Department of
Education), other additional requirements might apply (see Other Federal Agencies - Additional Requirements).

The IRB has and follows written policies and procedures requiring appropriate protections for prospective participants who cannot give consent or whose decision-making capacity is in question. (AAHRPP Element II.4.B)

(Also addresses portions of AAHRPP Element II.4.A)

12.2.1 Adults with Impaired Decision-Making Capacity – “Decisionally impaired”

Decisionally impaired individuals are those with diminished capacity for judgment and reasoning due to a psychiatric, organic, developmental, or other disorder that affects cognitive or emotional functions. Other individuals may be considered decisionally impaired or have limited decision-making ability because they are under the influence of or dependent on drugs or alcohol, suffering from degenerative diseases affecting the brain, are terminally ill, or have severely disabling physical handicaps.

The IRB must determine whether such participants should be recruited or whether support mechanisms, such as legally authorized representative consent, are appropriate.

IRB considerations include:

- Can the person or their legally authorized representative understand the information?
- Can the person or their legally authorized representative retain enough of the information to think the question through?
- Is the person legally able to give consent?
- If not, should the person be involved in the discussion anyway?
- What are the alternatives to participation for the person? Does the person believe that those alternatives are real?
- What are the pressures on the person to consent or refuse? If legally authorized representative permission is necessary, what are the pressures on the legally authorized representative?
- Is the selection of participants equitable, particularly given the special considerations raised by research involving vulnerable populations?

Obtaining Consent from a Legally Authorized Representative

The IRB, consistent with state and federal human subjects regulations, requires that consent for research be obtained from the participant’s legally authorized representative, if the subject lacks the capacity to consent (e.g., OHRP 45 CFR 46.116, FDA 21 CFR 50.20, Texas Health and Safety Code Chapters 166 and 313, and Texas Family Code Chapter 32).

(Also addresses portions of AAHRPP Element II.4.A)
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Criteria for Inclusion in Research
The IRB considers and evaluates the following criteria before approving research involving adult participants with impaired decision-making capacity:

- Adequate provisions are made for obtaining consent from the participant or the participant’s legally authorized representative.
- Whether assent of the participants is a requirement, and, if so, whether the plan for assent is adequate.
- The protocol must have an adequate plan for the assessment of the capacity to consent.

The IRB may consider additional safeguards to protect participants, such as:

- Requiring the involvement of participant advocates
- Requiring independent monitoring
- Requiring waiting periods
- Appointing a monitor to supervise the informed consent process.

Such decisions may be based on the amount of risk involved in the research and the likelihood that participants will derive health benefits from their participation.

Assessment and Determination of decision-making capacity
If it is believed that the prospective participant does not have decision-making capacity to consent for him or herself, such capacity must be determined by a physician (generally an investigator on the protocol); this process would not be applicable to non-clinical, community-based research. A determination of lack of decision-making capacity shall be made after an appropriate medical evaluation that concludes there is little or no likelihood that the participant will regain decision-making capacity in a reasonable period of time, or as established by legal determination under Texas law with assistance from MD Anderson’s Legal Services department. This definition of lack of decision-making capacity is not limited to the legal definition but also may be a clinical judgment that a person lacks the capacity to understand the circumstances of participating in research and to make an autonomous decision to take part.

Decision-making capacity should be evaluated on an individual basis to avoid incorrect assumptions as to an individual’s ability to make decisions. Criteria for determining competence might vary according to the degree of risk or discomfort presented by the research procedures and the extent to which therapeutic gain can be anticipated.

Some approaches to this assessment include:

- The protocol investigators may ask a physician/psychologist outside the research team to evaluate the potential participant's decisional capacity.

The IRB may consider additional safeguards to protect participants, such as:

- Requiring the involvement of participant advocates
• Requiring independent monitoring
• Requiring waiting periods
• Appointing a monitor to supervise the informed consent process.

Such decisions may be based on the amount of risk involved in the research and the likelihood that participants will derive health benefits from their participation.

**Obtaining Consent from a Legally Authorized Representative**

The IRB, consistent with state and federal human subjects regulations, requires that consent for research be obtained from the participant’s legally authorized representative (LAR), if the subject lacks the capacity to consent (e.g., OHRP 45 CFR 46.116, FDA 21 CFR 50.20). Chapter 313 of the Texas Health and Safety Code addresses consent to medical treatment by the legally authorized representative, and does not address consent for research. MD Anderson follows Texas law provisions for determining LAR for consent to treatment and for determining LAR for consent to participate in research.

**Participants in Psychiatric Units or Mental Health Facilities: Special Rules**

LARs for an inpatient on a psychiatric unit or in a mental health facility or a patient on a psychiatric hold may not be able to consent for research under different Texas laws, particularly if the research participant has been adjudicated to lack the capacity to consent and a conservator appointed. An investigator who proposes to involve such participants with the possible need for LARs should discuss the situation with the IRB staff or legal and regulatory counsel in MD Anderson’s Legal Services department and Institutional Compliance Office.

**Criteria for enrollment**

- Individuals who lack decision-making capacity may be enrolled in protocols with consent provided by the LAR, if: The proposed research entails:
  - No greater than minimal risk to the subject as determined by the IRB; or
  - If the research presents some probability of harm, there must be at least a greater probability of direct benefit to the subject;
  - Greater than minimal risk and no prospect of direct benefit to individual subjects, but is likely to yield generalizable knowledge about the subject’s disorder or condition that is of vital importance for the understanding or amelioration of the subject’s disorder or condition.
- The disorder (e.g., Alzheimer’s) leading to the individual’s lack of decision-making capacity is being studied, whether or not the lack of decision-making itself is being evaluated (e.g., an individual who lacks decision-making capacity as the result of a stroke can participate in a protocol of cardiovascular effects of a stroke), but only if the protocol cannot be performed with only persons who have decision-making capability...
• The subject of the protocol is not directly related to the individual’s lack of decision-making capacity, but the investigator can make a compelling argument for including individuals who lack decision-making capacity in the protocol (e.g., transmission of methicillin-resistant Staphylococcus aureus (MRSA) infections in a nursing home where both individuals with, and those without, decision-making capacity are affected).

The IRB has and follows written policies and procedures requiring appropriate protections for prospective participants who cannot give consent or whose decision-making capacity is in question. (AAHRPP Element II.4.B)

12.2.2 Pregnant Women, Fetuses and Neonates

In accordance with OHRP, the IRB requires that additional protections be provided to pregnant women, fetuses and neonates involved in research. General considerations related to research involving pregnant women, fetuses and neonates are set out in Chapter 9.3. The special informed consent requirements are specified in 45 CFR 46, Subpart B (OHRP) and are summarized in the guidance Research Involving Pregnant Women, Fetuses, and Neonates.

Pregnant Children

If the pregnant person is under the age of 18 and is not emancipated, the IRB generally requires, consistent with OHRP, that parental permission and child assent be obtained. If the research is therapeutic, and the principal investigator believes that the child’s participation in the research falls into one of the categories under Texas law where an unemancipated minor is permitted to consent to her own medical care, the principal investigator should confirm this with IRB staff or the legal and regulatory counsel in MD Anderson’s Legal Services department and Institutional Compliance Office.

Nonviable Neonates

The IRB will not permit elements of the informed consent process to be altered or waived in research involving nonviable neonates, even if the general requirements for waiver are satisfied.

When it has been determined that the neonate is viable, the neonate is considered a child and the consent requirements laid out below apply.

The IRB has and follows written policies and procedures requiring appropriate protections for prospective participants who cannot give consent or whose decision-making capacity is in question. (AAHRPP Element II.4.B)

12.2.3 Children and Consenting Minors

The IRB imposes additional protections on research involving children, in accordance with 45 CFR 46, Subpart D and 21 CFR 50, Subpart D.
By regulatory definition, “children” are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. In Texas, a person under 18 years old is considered a minor, and may not legally give consent, although there are certain exceptions for emancipated minors.

Since minors cannot legally give consent, informed consent must be obtained from parents (“parental permission”), or the legally appointed guardian. The IRB requires the investigator to obtain the permission of a child's parent(s) or guardian before enrolling the child in a protocol.

See guidance Parental Permission.

Assent

When, in the judgment of the IRB, the children are capable of providing assent the IRB may determine that assent is required, that adequate provisions are made for soliciting the assent of the children, and whether and how assent must be documented. Generally, children aged 7 and above may be asked to give their assent to participation.

When Minors, Including Emancipated Minors, may Consent without Parental Permission

There are certain situations in which the IRBs permit minors to consent to participation in research without parental permission. The PI will need to consult with the IRB, Institutional Compliance, and/or Legal Services prior to enrolling a minor in a research protocol without parental permission, to ensure that the applicable legal requirements are met. The criteria under which a waiver of parental permission may be granted are discussed in the Checklist - Vulnerable Populations - Children.

See guidances:
- Checklist - Vulnerable Populations - Children
- Parental Permission
- Chapter 12.4 for information on documentation of informed consent, and assent.

The IRB has and follows written policies and procedures to evaluate the consent process and to require that the Researcher appropriately document the consent process. (AAHRPP Element II.3.F)

The IRB has and follows written policies and procedures requiring appropriate protections for prospective participants who cannot give consent or whose decision-making capacity is in question. (AAHRPP Element II.4.B)

12.2.4. Illiterate Participants
The IRB allows individuals who speak and understand English, but who cannot read the consent materials due to illiteracy, to enroll in a protocol by “making their mark” (e.g., signing or marking an “X”) on the consent document, after going through the informed consent process. This also applies to individuals who speak a language that does not have a written form.

This process would apply to a participant who is competent and understands and comprehends spoken English, but is physically unable to talk or write, but can indicate approval or disapproval by other means.

If a participant, or their LAR, is illiterate:

- Information in the consent materials will be presented orally by the individual carrying out the informed consent process.
- Sufficient time should be allowed for questions to be asked and answered, both by the participant, and by the person obtaining consent to ensure the participant comprehends the consent information.
- A witness, individual not associated with the protocol, must be present during the entire informed consent discussions, and must sign and date the informed consent document.
- The person obtaining consent will document in the research record and medical record (if applicable), the method used for communication with the prospective participant and the specific means by which the prospective subject communicated agreement to participant i.e. “made a mark on the informed consent document”
- Additionally, FDA guidance on Illiterate English Speaking Subjects contains recommendations for documenting the consent process when a participant is competent and understands and comprehends spoken English, but is physically unable to talk or write, but can indicate approval or disapproval by other means.

See Language Assistance Policy (CLN0470)

Participants (or their LARs) must be given a copy of the signed consent document(s), and any other written information provided to participants.

The IRB has and follows written policies and procedures requiring appropriate protections for prospective participants who cannot give consent or whose decision-making capacity is in question. (AAHRPP Element II.4.B)

### 12.2.5. Non-English Speaking Participants

MD Anderson is located in a culturally diverse region of Houston, Texas, and treats patients from all over the world. Investigators are encouraged to recruit and include all segments of the community in research, including individuals whose primary language is not English.
Participants who do not speak English should be presented with a consent document written in a language understandable to them, and which embody all the elements necessary for legally effective informed consent.

The MD Anderson IRBs strongly encourage the use of a full consent form translated into the participant’s language whenever possible. When all of the participants in a protocol (i.e., the target population) are anticipated to be non-English speaking, a full translated consent is required. Refer to the IRB Policy Consenting Non-English Speaking Participants for information on translating consent forms. If a non-English speaking participant is initially consented through an approved short form process using the VTPS, to the extent that the protocol involves high risk, first-in-humans, or ongoing interventions or interactions over an extended period of time, the IRB will require that the informed consent document is translated into the specific language after 2 participants are consented in that language using the VTPS process (see VTPS Form - Spanish or Request the VTPS in Other Languages).

When a full-length form embodying all elements of consent is required by the IRB to document consent, the IRB requires that appropriately translated consent documents be submitted to the IRB for review and approval prior to their use in enrolling participants. The IRB may utilize expedited review procedures in approving such documents if the English language consent document has already been approved.

Investigators may use language translators or interpreter services to obtain consent in a language understandable to the participant or the participant's legally authorized representative.

**Short Form Consent Process**

Federal regulations permit the use of a short form consent process (45 CFR 46.117(b)(2) and 21 CFR 50.27(b)(2)) with the prior approval of the IRB; for more information see Chapter 12.1.4 above, and the Office of Human Subject Protection website.

The IRB has and follows written policies and procedures requiring appropriate protections for prospective participants who cannot give consent or whose decision-making capacity is in question. *(AAHRPP Element II.4.B)*

**12.2.6. Prisoners**

The IRB considers prisoners to be a vulnerable population because both their incarceration and the constraints imposed on them during their incarceration may render them unable to make a truly informed and voluntary decision regarding whether to participate in research. The IRB imposes additional protections pertaining to biomedical and behavioral research involving prisoners, limits the types of research that can be approved, and requires special consent information as specified in OHRP in 45 CFR 46 (Subpart C). Additionally, the Texas Department of Criminal Justice
requirements apply. Guidance Involvement of Prisoners in Research is provided (see Chapter 9.3) for an explanation of these additional safeguards. If the Principal Investigator is not familiar with these legal requirements, the principal investigator who proposes to involve prisoners in research should contact IRB staff or legal and regulatory counsel in MD Anderson’s Institutional Compliance Office or Legal Services department prior to submission of the protocol and consent document to the IRB for review. The MD Anderson IRB will not be the IRB of record for research involving the prisoner population.

**DHHS Conducted or Supported Epidemiologic Research Involving Prisoners as Subjects**

Under certain conditions DHHS conducted or supported epidemiologic research involving prisoners may be approvable by the Secretary of DHHS, as outlined in the Federal Register Vol 68 No.119, June 20, 2003.

> The IRB has and follows written policies and procedures to evaluate the consent process and to require that the Researcher appropriately document the consent process. *(AAHRPP Element II.3.F)*

**12.3 IRB Review of the Consent Process, including Consent Documents**

Principal Investigators should refer to Chapter 14.14 for information regarding the development of an informed consent process and method of documentation appropriate to the type of research and the protocol population.

Principal investigators must submit for IRB review any consent document(s) and explanation of the circumstances under which informed consent will be sought for new protocols, at continuing review, and whenever a modification to the consent process or documents is requested.

The Informed Consent Checklist for Investigators solicits the information necessary for the IRB to evaluate whether the informed consent process will be appropriately conducted given the protocol-specific circumstances (e.g., level of risk, inclusion of special participant populations) and adequately protects participants, considering issues such as whether:

- Participants have sufficient time to discuss concerns and decide whether to participate in the research;
- The possibility of coercion and undue influence is minimized;
- Communications to the participant or their LAR are in a language understandable to them; and
- Consent process communications do not include any exculpatory language through which the participant or their LAR is made to waive, or appear to waive, any of the participant’s legal rights, or which releases or appears to release the investigator, sponsor, institution, or agents from liability for negligence.
The same evaluation criteria apply to review and approval of the consent process and consent document(s) when reviewed by the expedited process, as by convened board review.

The IRB staff review the consent document(s) and consent process information (see Informed Consent Checklist for Investigators). For continuing review or modifications, any new information that could impact participants’ risks (e.g., adverse events) or procedure changes are also examined to ensure the consent document is appropriately updated. Re-consent may be required.

Examples of when re-consent might be required include when there is new information (e.g., risks, procedures, etc.) that could impact participants’ willingness to participate, or any other time the IRB determines it is necessary. Consent process requirements are discussed in Chapter 12.1 above (see IRB Guidance on Re-Consenting Participants on a Research Protocol, Considerations for Re-Consent of Participants Tool, and Abbreviated Informed Reconsent Document).

The IRB considers the relationship between the person(s) who will solicit, obtain consent, and explain the consent document and the potential participant. The IRB requires that the circumstances of the consent process be culturally and linguistically appropriate for the intended participants, and protects participants by minimizing the possibility of coercion and undue influence and allowing adequate time for them to discuss and decide whether to participate in the research.

The IRB also reviews any direct advertising (e.g., newspaper, TV or radio ads, posters, flyers, letters or postcards, emails, postings on bulletin boards/internet/web), since it is considered by the FDA “to be the start of the informed consent and subject selection process.” In order to approve advertisements, the IRB must determine that the direct advertising is not unduly coercive and does not promise a certainty of cure or favorable outcome or other benefits beyond what is outlined in the consent and the protocol (see Chapter 10). See guidance Advertisements, Appropriate Language for Recruitment Material and Policy on Advertising and Recruiting for a Research Study.

Consideration at an IRB Convened Meeting

The IRB determines that all basic, and all additional elements appropriate to the research, are included in the consent process. All the relevant requirements in OHRP in 45 CFR 46.109(b) and 46.116, and in the FDA regulations in 21 CFR 56.109(b), 50.20 and 50.25, that are applicable to the consent process and the consent document, must be satisfied for IRB approval.

The IRB may require modifications to the consent document as a condition for approval. If the modifications are minor and can be dictated verbatim at the meeting, the protocol may be approved contingent upon the modifications being made. The Board will
Chapter 12 – Informed Consent and Assent
MD Anderson HRPP Policies and Procedures Manual

determine if a member or IRB staff can confirm that the modifications have been implemented as specified before the contingency can be removed. If modifications are greater than minor or cannot be dictated verbatim at the convened meeting, the protocol is deferred, and the consent document is referred back to the principal investigator for the drafting of the modifications and submission at a future convened meeting. If the principal investigator disagrees with the verbatim modifications specified by the IRB, the protocol is brought back to the convened board for review at a meeting. The convened board will review the principal investigator’s rationale and response regarding why the board’s request regarding the consent document will not be followed.

The approval date and the activation date for the consent document will be added to the consent document(s) (see Chapter 14.15).

Additional Requirements
See Other Federal Agencies - Additional Requirements.

The IRB has and follows written policies and procedures to evaluate the consent process and to require that the Researcher appropriately document the consent process. (AAHRPP Element II.3.F)

12.4 Documentation of Informed Consent – Signature/iConsent Requirements

Documentation of informed consent refers to a participant, or their legally authorized representative (LAR), signing and legally dating an IRB-approved, dated consent document, which includes the eight basic elements of informed consent and the six additional elements of informed consent, when appropriate (45 CFR 46.116; 21 CFR 50.25(a),(b)).

When a person agrees to be a participant in a research protocol, signing the consent document indicates that they have participated in the consent process, and understand the information provided to them.

Documentation requirements for informed consent are specified in OHRP in 45 CFR 46.117(a),(b) and FDA 21 CFR 50.27(a),(b).

In order to approve research, the IRB must determine that informed consent will be appropriately documented, unless the IRB waives documentation under OHRP or FDA regulations (see Chapter 12.5.2). If a participant lacks the capacity to consent, then consent for research must be obtained from their LAR (see Chapter 12.2).

Consent is documented through use of a consent document that is electronically or manually signed and dated by the participant or the participant’s legally authorized representative that embodies all of the required elements of informed consent (see
Only the IRB approved informed consent document may be used, and unless the requirement is waived by the IRB, the document must be signed by the participant (or the participant’s LAR), and a copy must be given to the person signing the form. FDA regulations require that the signature be dated. Please see, the Electronic Signature Letter to FDA and iConsent Data Integrity Review for documentation of compliance.

MD Anderson’s policies stipulate that the signed consent document must be scanned into the participant’s medical record manually or filed into the record electronically using the electronic iConsent system.

Short Form Consent Process (Use of Verbal Translation Preparative Sheet) – Additional Signature Requirements

Subject to prior approval of the IRB, consent may be documented through use of a short form written consent document with the requirements and process specified in 45 CFR 46.117(b)(2) and the FDA regulations in 21 CFR 50.27(b)(2). The short form consent process is generally applicable to situations involving non-English participants. If the participant agrees to take part in the protocol, the following signatures are required:

On the short form consent document (translated):
- Participant or the participant’s legally authorized representative [LAR]
- Witness (the interpreter may act as the witness)

On the informed consent document (English):
- Person obtaining consent
- Witness (the interpreter may act as the witness)

For information on using the short form consent process see Chapter 12.1.4 above and the Office of Human Subjects Protection Website.

Children Participants, Documentation of Informed Consent, and Assent

Since children (minors) cannot legally give consent, informed consent must be obtained from parents (“parental permission”), or the legally appointed guardian. For information on the requirements for documentation of consent for children participants, see policy, Assent of Minors to Research and guidance, Parental Permission.

When, in the judgment of the IRB, the children are capable of providing assent, the IRB may determine whether and how assent must be documented. See the Informed Consent Templates – Clinical Template and Chapter 12.2.3.
Chapter 12 – Informed Consent and Assent

12.5 Waiver or Alteration of Informed Consent Requirements

- Waiver or alteration of the consent process
- Waiver of documentation of informed consent – (“waiver of signature”)
- Contacting Relatives of Index Patients

12.5.1 Waiver or Alteration of the Consent Process

Under OHRP 45 CFR 46.116(c) (d), and (e), IRBs have authority to alter or waive the requirement to obtain informed consent. FDA guidance also allows for this process for certain FDA-regulated minimal risk clinical investigations. FDA does not allow for waivers of parental permission for studies that fall under 45 CFR 46.408(c).

FDA regulations provide for exceptions to the informed consent requirements for emergency use of a test article (see Chapter 5.9), and waivers granted for planned emergency research (see Chapter 12.6).

For non-FDA regulated human subjects research, the IRB may approve an investigator’s request to waive or alter the requirement to obtain informed consent if the investigator demonstrates with specificity that the waiver or alteration criteria are met. To approve such a request, the IRB must find and document the following:

- The research involves no more than minimal risk to the subjects;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- The research could not practicably be carried out without the waiver or alteration; and
- Whenever appropriate, subjects will be provided with additional pertinent information after participation.

For FDA-regulated research, in accordance with guidance issued by the FDA in July 2017, and until the FDA issues regulations to permit a waiver or alteration of informed consent under appropriate human subject protection safeguards consistent with section 3024 of the Cures Act, the IRB may approve a request to waive or alter the requirement to obtain informed consent if it finds that:

- The clinical investigation involves no more than minimal risk (as defined in 21 CFR 50.3(k) or 56.102(j)) to the subjects;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- The clinical investigation could not practicably be carried out without the waiver or
• alteration; and
• Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Under 45 CFR 46.116(c) the IRB may waive or alter the consent process when:
• The research or a demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to protocol, evaluate, or otherwise examine:
  o public benefit or service programs;
  o procedures for obtaining benefits or services under those programs;
  o possible changes in or alternatives to those programs or procedures; or
  o possible changes in methods or levels of payment for benefits or services under those programs
  and
• the research could not practicably be carried out without the waiver or alteration.

To request a waiver or alteration of the informed consent process the investigator must demonstrate that each of the criteria under Section 45 CFR 46.116 (c) or (d) (OHRP) or per FDA guidance is met for the given protocol as noted in the Protocol Application in PDOL.

To approve a waiver or alteration of the informed consent process the IRB must find and document that all regulatory criteria under 45 CFR 46.116 (c) or (d) (OHRP) or per FDA guidance are met.

**Special Considerations for Research Involving Deception**

In research involving deception, the investigator may, with protocol-specific justification, request an alteration of the consent process. The IRB may approve the research, including the request to alter the requirement for informed consent if the investigator demonstrates that deception or incomplete disclosure is necessary and addresses concerns relating to participant protection; e.g., debriefing.

**Research Involving Children: Waiver of Parental Permission/Guardian Consent**

The IRB will often consider a request for a waiver or partial waiver of parental permission for minimal risk research to be conducted in a classroom.

The IRB may waive parental permission by determining that the criteria for waivers or alterations are met. However, research is ordinarily not suitable for a waiver of parental permission if it involves any of the following issues:
• Parental political affiliations or beliefs
• Mental or psychological problems
• Sexual behavior or attitudes
• Illegal, antisocial, or self-incriminating behavior
• Appraisals of other individuals with whom the minor has a familial relationship
• Relationships legally recognized as privileged (lawyers, doctors, clergy), and
• Religious affiliations or beliefs.

If the IRB waives the requirement for parental permission, it may require an alternative mechanism to protect the child participants (e.g., appoint a qualified child advocate).

Additional Requirements - Other Federal Agencies
Additional requirements might apply, depending on the source of support/funding (e.g., Department of Defense and Department of Education (such as compliance with Family Educational Rights and Privacy Act [FERPA]) (see Other Federal Agencies - Additional Requirements).

12.5.2 Waiver of Documentation of Consent – (“waiver of signature”)
As allowed by OHRP (45 CFR 46.117 (c)) and FDA regulations (21 CFR 56.109(c)), the IRB may waive the requirement to obtain written documentation of informed consent. This provision can be used only for the waiver of documentation of consent, not for waiver or alteration of the consent process itself. A waiver of documentation of consent does not mean that requirements of the consent process are removed.

Even if a waiver of documentation is granted by the IRB, permitting the investigator to forego obtaining the participant’s signature on a written consent document, the investigator still must provide the participant with all of the information described in Chapter 12.1 required to constitute a complete and appropriate consent process, through an information sheet, or through an oral script in a language understandable to the participants (see Using the Consent Statement for Questionnaires). In all cases in which the requirement for documentation of consent is waived, the IRB may require the principal investigator to provide participants with the written consent document with an option to sign the consent document, or with a written statement regarding the research.

To approve a waiver of documentation, the IRB must find that the protocol-specific justification for waiving documentation satisfies regulatory criteria. Specifically, the IRB must determine the regulatory basis for the waiver as one of the following (note that a) does not apply for FDA-regulated research):
• Under OHRP (45 CFR 46.117(c)(1) the IRB must find and document either:
  o the only record linking the participants and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality. Each participant will be asked whether he/she wants documentation linking the participant with the research, and the participant’s wishes will govern; or
  o the research presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context;
For research subject to OHRP and FDA regulations, the IRB must find and document that the research involves no more than minimal risk to participants and involves no procedures for which written consent is normally required outside of the research context. (45 CFR 46.117(c)(2), 21 CFR 56.109(c)(1)).

Guidance CHECKLIST: Waiver or Alteration of Consent Process and CHECKLIST: Waiver of Written Documentation of Consent is available to IRB members and on the Office of Human Subjects Protection website.

Waiver or Alteration of HIPAA Authorization

In order to waive or alter an authorization, the investigator must provide sufficient information on which the IRB may make the following three findings specified by the Privacy Rule (45 CFR 164.512(i)(2)(ii):

- The use or disclosure of protected health information (PHI) involves no more than minimal risk to the privacy of individuals based on:
  - An adequate plan to protect the identifiers from improper use and disclosure;
  - An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers, or such retention is otherwise required by law; and
  - Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by the Privacy Rule;
- The research could not be practically conducted without the waiver or alteration; and
- The research could not be practically conducted without access to and use of the protected health information.

See MD Anderson HIPAA Policy on the Privacy & Information Security Compliance Website.

12.5.3 Contacting Relatives or Other Potential Research Participants of Index Patients

Certain types of research conducted at MD Anderson may present the opportunity to recruit additional study subjects based on information provided by the index case. Since the research participant is not considered a covered entity under the HIPAA privacy regulation, there is no regulation barring the participant from disclosing the names and contact information of his or her relatives or other individuals that might be interested in participating in the research.

The IRB provides the following information for investigators preparing protocols, which have the potential to recruit additional participants based on information provided by the index case:
• The informed consent document each participant signs must clearly state that any names and contact information of relatives or other potential research participants provided to the investigator will be used to contact those individuals to determine their eligibility and desire to participate. This should be an optional procedure so that individuals may still participate in the research protocol even if they choose not to provide the names of other individuals to contact unless the research protocol stipulates otherwise.

• The investigator should directly ask the index case if they think the individuals whose names they are providing would mind being contacted to discuss the study. The investigator should contact only those individuals the index case believes would be receptive to being contacted.

• In addition to the informed consent that the participants sign, the protocol should include waivers of informed consent and authorization to allow the investigator to contact potential participants using information provided by the index case. The waivers are needed since the potential participants are not our patients and therefore cannot be screened without a waiver under the “preparatory to research” exemption of HIPAA.

• Depending on the nature of the research, if the contacted individual decides to participate in the study, they should sign the protocol specific informed consent for that study.

The IRB has and follows written policies and procedures for making exceptions to consent requirements for planned emergency research and reviews such exceptions according to applicable laws, regulations, codes, and guidance. (AAHRPP Element II.4.C)

12.6 Exceptions to Informed Consent in Emergency Situations

Note: “Planned emergency research” is not synonymous with “emergency use of a test article”, which is addressed in Chapter 5.9.

Planned emergency research refers to research planned for emergency settings, including the planned use of a test article.

Planned emergency research involves an extensive approval process, including FDA approval, prospective IRB review, and approval and consultation with representatives of the communities where the research will be conducted and from where participants will be drawn. Investigators must submit a protocol application including a description of the informed consent process or a request to waive informed consent; often in emergency settings it is not possible to obtain informed consent from a potential participant when there is insufficient time and a legally authorized representative (LAR) is not available.

The IRB may waive the requirement for informed consent in accordance with an exception under 21 CFR 50.24 (FDA) or 45 CFR 46.101(i) or 45 CFR 46.116(f) (OHRP), depending on whether or not the research is subject to FDA regulation, given that all
required IRB determinations under these provisions can be made. Under these regulations, the IRB may permit planned research in an emergency setting without the informed consent of the participants or their legally authorized representatives in a limited class of emergent situations where the participant is in need of an emergency experimental intervention, but cannot give informed consent due to a life-threatening medical condition and there is not sufficient time to obtain consent from the participant’s legally authorized representative.

In addition, advance notice of such planned emergency research protocols will be provided to the Office for Human Research Protections pursuant to 45 CFR 46.101(i).

See also:
- Informed Consent Requirements in Emergency Research (OHRP)
- Exception from Informed Consent for Studies Conducted in Emergency Settings (FDA)

**Additional Requirements - Other Federal Agencies**

Additional requirements might apply, depending on the source of support/funding (e.g., Department of Defense, Department of Education (such as who may grant waivers of the consent process and human research protections policy requirements) (see Other Federal Agencies - Additional Requirements).

_MD Anderson has and follows written policies and procedures that allow the Institutional Review Board to function independently of other organizational entities in protecting research participants. (AAHRPP Element I.1.C)_

### 12.7 Observation of the Consent Process

See the Charges by the Institutional Official to:
- Charge to the Executive Institutional Review Board on Human Subjects in Medical and Nonmedical Research
- Charge to the Institutional Review Board on Human Subjects in Nonmedical Research
- Charge to the Institutional Review Boards on Human Subjects In Medical Research

As part of the IRB oversight options, the IRB may require that a staff member or an outside third party observe the consenting of research participants to determine:
- Whether the informed consent process has been appropriately completed and documented;
- Whether the participant has had sufficient time to consider protocol participation, that no coercion has been used by the consenting staff; and
- That the information presented to the participant reflects the content of the consent form and is conveyed in understandable language.

The IRB may require that one or more informed consent process situations be observed for selected protocols. IRB considerations used to choose such protocols include:
• High risk studies
• Studies that involve particularly complicated procedures or interventions
• Studies involving potentially vulnerable populations (e.g., ICU patients, children)
• Studies involving protocol staff with minimal experience in administering consent to potential protocol participants, or
• Situations when the IRB has concerns that the consent process is not proceeding well.

See:
• IRB Policy on Obtaining Informed Consent for Participation and Authorization for Uses and Disclosures of Protected Health Information for Clinical or Health Services Research Protocols
• Non-English Speaking Research Participant
• Using the Multiple Language Verbal Translation Preparative Forms and Process
• Consent Process Observation
• Determining What Qualifies as a Protocol Specific Procedure
Chapter 13. Collaboration Among IRBs in Multi-Site Research

All MD Anderson research that involves human research participants, may only be carried out with IRB approval and oversight. Such IRB approval and oversight may be provided by one of the IRB’s administratively supported by MD Anderson or by an IRB authorized to provide oversight under an IRB authorization agreement with MD Anderson, including for studies that are subject to the single IRB requirement.

When MD Anderson is conducting research at an external site (e.g., nursing home, school) and is not the coordinating site or lead investigator is not an MD Anderson workforce member, and that site is engaged in research, the MD Anderson IRB associated with the protocol will require contact information for the coordinating/lead site, whether the site has an IRB, and, confirmation from the site’s IRB that they have permission to conduct the research.

MD Anderson Serving as Participating Institution

When MD Anderson is a participating institution (sending data or tissue samples out of MD Anderson) the PI must submit data in a timely manner to the coordinating institution, report unanticipated problems (UPs) and other reportable events in a timely manner to the coordinating institution and the MD Anderson IRB, and ensure that the PI’s study team has the current approved version of the protocol and consent form. These, and other requirements will be specifically outlined in an IRB authorization agreement, or other agreement which would cover specific reporting requirements.

Relying on a Single IRB (sIRB)

MD Anderson’s IRB may agree to rely on a single IRB (sIRB) for multisite studies to provide initial and ongoing regulatory reviews. The reliance terms are outlined in an IRB Authorization Agreement (IAA) (e.g., MD Anderson has signed on to SMART IRB), which supports IRB reliance across the nation (see Use of the Single IRB Mechanism for Federally Funded Research).
Projects). The sIRB is responsible for reviews required by federal regulations at 45 CFR 46, and 21 CFR 50 and 56 (initial review, continuing review, modifications, reportable events). When MD Anderson IRB relies on a sIRB, MD Anderson's local IRB still retains responsibility to ensure investigator compliance with the protocol, the sIRB's determinations, applicable federal and state regulations, and MD Anderson policy. MD Anderson's IRB bears responsibility for the local conduct of these studies, e.g., managing noncompliance and UPs, ensuring training, and study monitoring. In addition, local ancillary requirements, managing reliance agreements, and handling study specific issues that arise are MD Anderson's responsibility (see IRB Authorization Agreement Tip Sheet).

The PI is required to submit the protocol, informed consent document from the IRB of record that includes the MD Anderson local context language including HIPAA language, other protocol documents to the scientific review committee and the IRB. In addition, a PDOL PI Generic Memo will need to be submitted that includes a request for the MD Anderson IRB to rely on the single IRB and the rationale for the request. Protocols submitted using the standard protocol form will need to undergo review by the Scientific Review Committee unless the PI submits a request and rationale to support bypassing the scientific review. The request to bypass the scientific review process can be completed by making the selection in PDOL on the protocol page. Below is the selection that the PI can pick in order to bypass the scientific review process:

- No patients will be enrolled at MD Anderson – Data Analysis Only
- Expanded Access Study
- Humanitarian Use Device
- Focus Group Project – IRB approval times for focus group projects may be extended due to the need for an initial PBHSRC review
- Study conducted per 2001 TCH/Baylor agreement (patients receiving radiation treatment only at MD Anderson)
- Patients receiving standard of care procedure at MD Anderson as part of enrollment on a non-MD Anderson study at an external site
- Other (PI must provide additional information)

External IRB

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.

- Utilizing an IRB Agreement or Authorization
- Responsibilities Matrix for Utilizing a Single or External IRB Mechanism and an IRB Authorization Agreement
- Utilizing a Single or External IRB Mechanism SOP
- External IRB Submissions_SOP
- External IRB Submissions with an Institutional Conflict of Interest_SOP
- NIH Policy on Single IRB Review for NIH Funded Research SOP
The IRB Role in the National Cancer Institute Central IRB (NCI CIRB) Initiative

The CIRB Initiative is sponsored by the NCI in consultation with the Department of Health and Human Services Office for Human Research Protections (OHRP). The OHSP staff function as a liaison between the CIRB and the investigators, and as a resource to investigators when needed.

MD Anderson participates in the independent CIRB model. The OHSP Director completes the Annual Institutional Worksheet, which apprises the CIRBs of local context, includes required informed consent template language, applicable local and State regulations, and MD Anderson policies. PIs of studies that will be carried out under CIRB oversight are required to submit the protocol and the Study Specific Worksheet in the PDOL system (see CIRB Amendments Workflow and CIRB New Submission Workflow). Prior to the protocol being activated, these documents and information will be reviewed by the following ancillary reviewers to ensure that institutional requirements of the following departments or institutional templates/processes are met:

- Investigational Pharmacy
- OHSP Editorial Services
- Informed Consent Templates (Clinical Template)
- Clinical Research Finance (see OCRF website)

Each year, investigators are also required to submit an Annual Investigator Worksheet directly to the CIRB for each investigator for each study in which they wish to enroll participants. The Annual Investigator Worksheet should also be submitted in PDOL once approved by CIRB.

The CIRB is responsible for continuing review, review of subsequent modifications, non-compliance, and UPs. As described in the Annual Institutional Worksheet, the IRB has a policy for reporting UPs and protocol deviations/violations for review. In order to appropriately monitor our local patient population, investigators will be required to comply with this local IRB policy. In addition to complying with the NCI CIRB reporting guidelines for serious adverse events, investigators will also comply with the local IRB policy for reporting serious internal adverse events.

PI’s are required to report any serious or continuing noncompliance or UPs with the research to OHSP. Serious adverse events do not need to be submitted to MD Anderson, and should be submitted to the CIRB in accordance with the CIRB reporting policies.

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.

The IRB has and follows policies and procedures for managing multisite research by defining the responsibilities of participating sites that are relevant to the protection of research participants, such as reporting of unanticipated problems or interim results. *(AAHRPP Element II.2.H)*

### 13.2 Information Management in Multi-Site Research

#### MD Anderson Serving as Coordinating Institution

When MD Anderson is serving as the coordinating institution, the PI must describe the plans for communicating information relevant to the protection of participants among the participating sites and institutions as part of the protocol submission, including communications of adverse outcomes, UPs, protocol modifications, and interim results.

When completing the protocol, PIs must indicate if MD Anderson is serving as the coordinating institution. The PI must list all other sites involved with the proposed research, the contact person at each site and contact information, such as phone number and email address. The PI must indicate if each participating site has an IRB and if that IRB has reviewed and approved the research.

When MD Anderson is the coordinating institution receiving data or tissue samples from other sites the PI must submit the following documentation to the MD Anderson IRB before receiving any data or tissue samples from a site:

- Standard Operating Procedures for the Coordinating Institution that include procedures for assuring IRB approval at participating sites and appropriate language in the participating site’s consent forms that allows MD Anderson to have access to the information or does not prohibit MD Anderson from having access.

By submitting the protocol, the PI documents his/her acceptance of the responsibility of ensuring that all participating sites have obtained IRB approval prior to initiation of the research at that site. The agreement should include a description of the scope of responsibilities for the Coordinating Institution.

If a participating site does not have an IRB, that site may request that the MD Anderson IRB serve as the IRB of Record. A written agreement must be reached between the participating site and the MD Anderson IRB. This written agreement must be reviewed, approved and signed by the Institutional Official.

For a clinical trials for which MD Anderson serves as a coordinating center, central laboratory or central data safety & monitoring board, the consent forms used at all sites must indicate that data or samples are being sent to MD Anderson. Data or tissue samples, even though they are anonymous, may not be received from an outside institution whose consent form prohibits data or tissue from being sent outside the institution.
Documentation of regular communication (e.g., teleconferences) with the participating sites to update and inform all participating sites about progress of the study must be maintained by the MD Anderson PI.

**Reporting to the IRBs in Multi-Site Research**

As the lead investigator at the coordinating institution, the PI is responsible for receiving data and reports from the outside sites in a timely manner and distributing them to the MD Anderson IRB as required (see Chapter 3.10). MD Anderson IRBs give the same considerations to such reports in multi-site research as they do to internal reports.

**Identifying Material Changes in Multi-Site Protocols**

For multi-site studies where MD Anderson is the IRB of record, the PI must report any material changes in the protocol that take place at any of the participating research sites. The IRB may require independent verification to ensure that no material changes have occurred in multi-site research or cooperative study protocols since the previous IRB review.

**Additional Requirements**

*Other Federal Agencies*: Additional requirements might apply, (such as a formal agreement to specify the roles and responsibilities of each party), depending on the source of support/funding (e.g., Department of Defense) (see Other Federal Agencies - Additional Requirements).
Chapter 14. Principal Investigator Responsibilities

MD Anderson policies, procedures, and education programs help Principal Investigators (PIs) and all MD Anderson investigators carry out research studies in an ethical manner. In addition to following applicable federal, state, and local regulations, investigators follow ethical principles and standards appropriate for their discipline. In designing and conducting clinical studies, PIs follow Good Clinical Practice (GCP) guidelines defined by the Food and Drug Administration, and have the protection of participants’ rights and welfare as their primary concern.

The protection of human participants in research is the shared responsibility of PIs, sponsors, and the IRBs; the PIs are ultimately responsible for the safety and welfare of participants.

When conducting research with human participants, the PI agrees to, as part of the protocol submission:

- Design studies that are scientifically sound and that will yield valid results and conduct the protocol according to the protocol approved by the IRB
- Be appropriately qualified to conduct the research and trained in Human Research Protection ethical principles, regulations and policies and procedures, and ensure all research personnel are adequately trained and supervised
- Compliance with federal, state, and local laws and M.D Anderson policies, including disclosure of any potential conflict of interest
- Adhering to the institutional Code of Conduct: MD Anderson Do the Right Thing;
- Report promptly any new information, modification, or unanticipated problems
- Ensure that the rights of participants are protected, including privacy and confidentiality of data
- Ensure that, when de-identified materials are obtained for research purposes, no attempt will be made to re-identify them without IRB approval
- Apply relevant professional standards.

The PI is also responsible for the timely and proper administration of the research project. Beyond the scientific and clinical conduct of the protocol, responsibilities include:

- Fiscal management of the project
- Training and supervision of postdoctoral candidates, students, and residents
- Compliance with the sponsor’s terms and conditions (e.g., non-disclosure of sponsor confidential information)
- Submission of all technical, progress, financial, and invention reports on a timely basis
- Submission of modification and continuing review applications in a timely manner
- Obtaining approval for changes prior to implementation.

Compliance with the IRB
Chapter 14 - Principal Investigator Responsibilities
MD Anderson Human Subjects Research Manual

- Federal regulations require that any research protocol involving human subjects be reviewed and approved by an IRB. IRB approval must be obtained before any recruitment or screening can take place.
- It is the PI’s responsibility to submit a written protocol to the IRB for review. At submission, the obligations of the PI with respect to oversight of their research protocols and research staff during recruitment, selection of protocol participants, and conduct of the protocol according to the protocol as approved by the IRB are stated in the protocol submission, and must be agreed to by the PI for the submission to be accepted. The PI is responsible for ongoing adherence to the determinations and requirements of the IRB for the duration of the research. The documents required for protocol submission are listed in Chapter 8.
- The PI is responsible for submitting any modifications or planned deviations to the IRB prior to implementation (see PI Override Form).
- A detailed discussion of the roles and responsibilities of IRBs is presented in Chapter 6.

Researchers determine that the resources necessary to protect participants are present before conducting each research study. (AAHRPP Element III.1.D)

14.1 Human Research Protection Resources

PIs are required to indicate in the protocol submission, Department Chair Prioritization Memo, whether they will have access to adequate resources to carry out the research. Resources, including space, personnel, services and equipment required for conducting the proposed research properly and safely, must remain available as needed throughout the research. The PI will maintain information about the qualifications and number of protocol staff, personnel training, available facilities, and the time available to conduct and complete the research, and must demonstrate sufficient access to a population allowing recruitment of the required number of participants.

PIs should continually monitor the resources allocated for their research and notify the IRB if any change in the availability of resources may adversely impact the rights and welfare of participants.

In addition to IRB approval of the protocol, human participant research (including recruitment and enrollment) that is sponsored cannot begin until a contract has been finalized, or a grant award activated. See Standard Operating Procedure for Activating Research protocols (Clinical, PBHSR, and protocol applications).

For clinical research that is not required to undergo scientific review, the protocol is submitted directly to the IRB. Within the protocol submission, the PI is required to provide a rationale why scientific review is not needed. This requirement does not apply to minimal risk laboratory research or prospective/retrospective chart reviews. Below are the selections that the PI can choose to bypass the scientific review process:
• No patients will be enrolled at MD Anderson— Data Analysis Only
• Expanded Access Protocol
• Humanitarian Use Device
• Focus Group Project – IRB approval times for focus group projects may be extended due to the need for an initial PBHSRC review
• Protocol conducted per 2001 TCH/Baylor agreement (patients receiving radiation treatment only at MD Anderson)
• Patients receiving standard of care procedure at MD Anderson as part of enrollment on a non-MD Anderson protocol at an external site
• Other

See, Guidance for IRB Members and Investigators for Enrolling Pediatric Patients in Phase 1 Adult Studies.

Researchers and Research Staff identify and disclose financial interests according to organizational policies and regulatory requirements and, with MD Anderson, manage, minimize, or eliminate financial conflicts of interest. (AAHRPP Element III.1.B)

14.2 Identification and Management of Conflict of Interest

PIs and research staff are expected to follow MD Anderson policies addressing the disclosure of conflicts of interest as described in Chapter 3 and the policies referenced therein.

Disclosures of potential conflicts of interest are reviewed and resolved by the Conflict of Interest Committee. The IRB has the final authority to decide whether the management of identified potential conflict of interest, if any, is sufficient before it approves involved research (see Chapter 3 and Chapter 6).

Researchers and Research Staff are qualified by training and experience for their research roles, including knowledge of applicable laws, regulations, codes, and guidance; relevant professional standards; and the Organization’s policies and procedures regarding the protection of research participants. (AAHRPP Element III.2.A)

14.3 Qualification of Principal Investigators and Research Staff

Training in the Protection of Human Subjects

MD Anderson requires that PIs and other personnel involved in the design or conduct of a project, including projects deemed to be exempt research under 45 CFR 46.101, confirm completion of training in the protection of human research participants. Individuals involved in the design or conduct of a project may include, but are not limited to: investigators, nurses, research or data coordinators, persons administering informed consent or surveys, post-docs, and students.
Collaborating individuals operating under the MD Anderson FWA and third party (subcontract) research personnel or consultants must also comply with this education requirement. MD Anderson utilizes the interactive online tutorial as its training program. Required HSPT training for investigations includes, but is not limited to, modules on the history and ethical principles of human subject research, basic IRB regulations and review process, informed consent, and research with vulnerable participants.

Good Clinical Practice (GCP) training is available, as applicable. Training is also available through the Office of Protocol Support and Management and the Office of Human Subjects Protection Brown Bag sessions, webinars, and other resources provided by MD Anderson.

Completion of the required training is a condition for IRB approval of protocols and release of funds, regardless of the project’s source of funding. During the review the IRB evaluates whether these requirements are met for each protocol event (new protocol, modification and continuing review).

See also:
- Chapter 1 Ethical and Legal Principles Governing Human Subject Research
- Chapter 3 Policies and Procedures Available to Principal Investigators (PIs) and Research Staff
- Chapter 4 Knowledge of Human Research Protection Requirements, for an outline of education provided for individuals responsible for human research, and description of the required training
- Chapter 5 Sponsor-Investigator Research: Additional training is provided for investigators who have additional responsibilities as the research sponsor
- Chapter 15 Sponsored research agreement includes provisions regarding Protection for Research Participants

14.4 Knowledge of Applicable Federal, State and Local Laws

The Office of Clinical Research Administration disseminates and makes available to the MD Anderson research community via the Office of Clinical Research Administration website and education programs, the following resources to promote knowledge about applicable Federal, State and organization policies for human subjects research:

- Human Research Protection Program policies
- Guidance on topics affecting the conduct of research, such as informed consent, vulnerable populations, conflict of interest, reporting requirements, etc.
- Template consent forms that include federal, state and local requirements
- Electronic system for protocol submission - with application questions intended to address required considerations
- Electronic system for patient registration and research data capture
- Information and instructions on submitting protocols to the IRB
- References and links to federal, state and organizational requirements
- Contact information for IRB staff for assistance
Investigators can also reference the following websites for additional information on retention and access to research data, rights and responsibilities in the conduct of research, PI responsibilities, and other topics related to human subjects research.

See:
- Office of Human Subjects Protection website
- Office of Protocol Support & Management website
- Office of Protocol Review & Reporting website
- IND Office
- Office of Research Administration
- Office of Sponsored Programs
- Institutional Compliance Office Research Compliance Plan
- Do The Right Thing Policy
- Institutional Policies

When MD Anderson investigators conduct research in states other than Texas, they are expected to be knowledgeable of and adhere to the laws of the state in which research is being conducted, as well as those of Texas. Investigators are advised to seek guidance from the IRB staff or Legal Counsel if they have questions as to the applicable laws.

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**Researchers and Research Staff know which of the activities they conduct are overseen by the Human Research Protection Program, and they seek guidance when appropriate. (AAHRPP Element III.1.A)**

### 14.5 Knowledge of the Definition of Human Subject Research

Prior to submitting a protocol for IRB review investigators are instructed to consider whether their project meets the statutory definition of human subject research or clinical investigation. Step-by-step guidance is available to the investigators on the Human Subjects Research website: Does My Project Need IRB Review? This provides guidance based on the Department of Health and Human Services Office of Human Research Protections and FDA-specific requirements.

IRB staff is also available to assist investigators in determining if a project needs to be submitted for IRB review. If the proposed activity clearly does not involve "research" or “clinical investigation” and "human subjects", it does not require submission to the IRB. If there is any doubt as to whether an activity is human subject research, the investigator should contact the Office of Human Subjects Protection, or submit a Protocol Application for the IRB to make an official determination of Human Subject Research. See Chapter 3 for additional information on the definition of human subject research.
14.6 Delegation of Research Responsibilities

PIs may delegate certain research responsibilities. However, PIs must maintain oversight and retain ultimate responsibility for the conduct of their research and of those to whom they delegate responsibility. The conduct of a protocol usually requires the involvement and contribution of other individuals under the direction of the PI, based on their qualifications and capabilities. In delegating protocol-specific tasks and responsibilities to other members of the research team, the PI must ensure that those assuming a duty are well trained, competent and meet institutional, federal and state licensing requirements, as applicable.

See Supervisory Responsibilities of Investigators and Delegation of Authority Form.

14.7 Student Projects

Students may only participate in a research project where an MD Anderson faculty member or employee is serving as the student’s Mentor. When serving as a Mentor, the MD Anderson faculty or employee is responsible for providing supervision and guidance to the student by:

- Serving as the PI for the protocol
- Overseeing the design and conduct of the protocol
- Ensuring that the student assuming research duties is well-trained and competent
- Ensuring that the student has taken the required institutional human subjects and privacy training courses
- Protection of the rights and welfare of participants, including obtaining informed consent and maintaining privacy and confidentiality of data
- Reviewing the Protocol Application in PDOL (minimal risk research) prior to submission to the IRB
- Providing guidance in the protection of research subjects
- Assuring proper application and reporting to the IRB
- Working with the student to identify modifications warranted by unanticipated problems or circumstances involving risks to participants or others.

14.8 Special Considerations for the Oversight of Research Protocols in FDA-Regulated Drug or Device Studies

FDA regulations and guidance specify the responsibilities of sponsors (and their investigators) using FDA test articles. [21 CFR 31 Subpart D; 21 CFR 812 Subparts C, E]. The FDA requirements are summarized in guidance Special Considerations for the Oversight of Research Protocols in FDA-regulated Drug or Device Studies.

For FDA-regulated drug studies, please see the IRB Policy on Return of Unused Study Medications to Pharmacy.
Researchers and Research Staff follow reporting requirements during a research study in accordance with applicable laws, regulations, codes, and guidance; MD Anderson policies and procedures; and the IRB’s requirements. *(AAHRPP Element III.2.D)*

### 14.9 Data Safety Monitoring Plan (DSMP)

MD Anderson develops clinical cancer trials funded by the NCI. As a comprehensive cancer center, MD Anderson is committed to following the regulations and requirements set forth by the NCI, especially as they relate to the DSM process. An effectively formulated and executed institutional plan should improve both participant protection and protocol conduct and should greatly reduce the need to set up new policies *ad hoc* on a trial-by-trial basis.

When appropriate, the research plan must make adequate provision for monitoring data to ensure the safety of subjects. *(45 CFR 46.111(a)(6); 21 CFR 56.111(a)(6)) (see also Chapter 9).*

The responsibility for human participant protection in human subject research is shared among the IRB, PI, protocol sponsors and oversight boards or committees. The safety of participants must be considered in protocol design.

*Studies that are more than low risk* to participants must include a data safety monitoring plan (DSMP) to evaluate whether the character, incidence, and severity of expected harms match those expected, and to evaluate the causality of unexpected harms. A description of the DSMP is required in the Protocol Application submitted to the IRB. In order to approve research, the IRB determines that when appropriate, there will be adequate monitoring of data to protect the safety and well-being of participants.

Monitoring may be conducted by the PI, or a Monitoring Entity (ME). In all studies, the PI has ultimate responsibility for identifying potential risks and identifying adverse events occurring in the protocol population and reporting the events to the sponsor and to the IRB as required in Chapter 3 *(see also Chapter 14.12).*

For high risk studies, e.g., Phase I/II Cell and Gene Transfer Clinical Studies, there may be further discussion at a convened meeting to consider whether a Data Safety and Monitoring Board should be required, or if a robust Data Safety Monitoring Plan would be adequate, as described in Data Safety Monitoring Board in Phase I/II Cell and Gene Transfer Clinical Trials.

Researchers employ sound study design in accordance with the standards of the discipline. *(From AAHRPP Element III.1.C)*

### 14.10 Sound Protocol Design

The significance of the research depends upon the validity of the results. It is unethical to put subjects at risk or to inconvenience them through participation in a protocol that may produce little or no reliable information. Regardless of the source of funding, it is the PI’s responsibility to judge the research design to be sound enough to meet its objectives before submitting the
protocol for IRB review. The Protocol Application provides questions addressing the various considerations for sound protocol design. When designing studies, the PI should consult the guidance Evaluating Sound Study Design and include all pertinent information in the Protocol Application. The Protocol Application also includes a description of the provisions for monitoring the data and reporting to the IRB and other entities.

In developing, or in evaluating the adequacy of, a research design involving investigational drugs or biological products, the PI should refer to the FDA Guidance Documents representing the Agency’s current thinking on good clinical practice (GCP) and the conduct of clinical studies, and including selected guidelines of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (“ICH”), as published in the Federal Register on May 9, 1997.

The PI should also be familiar with the various types of control groups, their relative advantages and disadvantages, and the ethical issues associated with each control type, as outlined in the FDA guidance Choice of Control Group and Related Issues, published May 2001. Although directly applicable to FDA-regulated studies involving investigational drugs or biological products, many of the principles can be applied to clinical studies in general.

Additional Requirements

See Other Federal Agencies - Additional Requirements for other requirements depending on the source of support/funding (e.g., Department of Defense).

Researchers design studies in a manner that minimizes risks to participants. (From AAHRPP Element III.1.C)

14.11 Detection of Harm, Minimization of Risks and Mitigation of Potential Injuries through Protocol Design and During the Course of the Research

Risks may affect physical, psychological, social, legal or economic well-being, including loss of privacy or breach of confidentiality. The PI must minimize risks at all times by using procedures that are consistent with sound research design and that do not expose participants to unnecessary risks, and whenever appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes.

When submitting a protocol submission to the IRB, the PI must:

- Describe the potential risks.
- Include, where possible, a scientific estimate of their frequency, severity, and reversibility. If statistical incidence of complication and the mortality rate of proposed procedures are known, this data should be included.
- Explain how risks will be minimized.
- Justify the level of risk.
- Describe adequate provisions for monitoring the data during the conduct of the research to minimize risk to participants (see Chapter 9).
For proposed changes to the research, including any change to mitigate potential harm to participants, the PI must submit a protocol modification to the IRB describing any resulting changes in the level of risk to participants, and explaining the risk level and potential benefits. The PI is required to provide a scientific rationale justifying the necessity for the modification.

At Continuing Review, the PI is expected to indicate whether there have been any changes to the protocol that would significantly impact the design, safety or risk to participants.

All studies considered more than low risk must include a data and safety monitoring plan which describes how the PI will oversee the participants’ safety and welfare and how unanticipated problems involving risks to participants or others, and adverse events will be characterized and reported.

See also:
- Evaluating Sound Study Design
- Data and Safety Monitoring By-laws
- Other Federal Agencies - Additional Requirements
- Chapter 9.1 (measuring and minimizing risks to participants)
- Chapter 14.10 above (sound study design)
- Chapter 14.12 (Principal Investigator responsibilities in assessing and reporting events)

See also:
- Chapter 3.10 Events and Information that Require Prompt Reporting to the IRB

Researchers and Research Staff follow reporting requirements during a research study in accordance with applicable laws, regulations, codes, and guidance; MD Anderson policies and procedures; and the IRB’s requirements. (AAHRPP Element III.2.D)

14.12 Reporting to the IRB - Unanticipated Problems Involving Risks to Participants or Others (UPs), and Other Reportable Information

PI Responsibilities

PIs are responsible for reporting unanticipated problems involving risks to participants or others (UPs) and other reportable information to the IRB. For industry-sponsored projects, PIs are responsible for maintaining contact with the sponsor, and receiving reports from the sponsor, and if applicable, the monitoring entity (e.g., DSMB, DMC) and reporting suspected UPs and other reportable information to the IRB. For projects that do not have a Sponsor, the PI is solely responsible for reporting UPs and other reportable information to the IRB.
The PDOL PI Generic Memo may also be used to report to the IRB events or information other than those required by regulation.

**Assessment by Principal Investigator**

The PI is responsible for the initial assessment of whether an event is a UP or other reportable information.

PIs must assess each adverse event, whether received from a sponsor, monitoring entity or occurring on a sponsor-investigator project, and promptly report to the IRB, UPs and other reportable information according to the guidance Events and Information that Require Prompt Reporting to the IRB (see flowchart Process for Handling Reports).

In all cases, UPs that are deaths or life-threatening experiences (at MD Anderson or when MD Anderson is the coordinating institution in a multi-site protocol), must be reported within 5 working days from when the PI learns of the event.

**Reporting Assessed Events and Information**

For events required to be reported to the IRB, PIs should complete an Internal/External SAE form or a Potential Unanticipated Problem form and attach the form to a generic memo and submit via the electronic database system (PDOL). The memo should be addressed to IRB_Help@mdanderson.org. Adverse events that are deemed not to be UPs or other reportable information should be included in a narrative summary for the IRB at Continuing Review.

**Reporting Timeframes**

<table>
<thead>
<tr>
<th>Type of event or information</th>
<th>Protocol has a monitoring entity in addition to, or other than, the PI</th>
<th>PI is the only monitoring entity for the protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>UP that is a death or life-threatening experience, (at MD Anderson or when MD Anderson is the coordinating institution in a multi-site protocol)</td>
<td>Report to IRB within 5 working days from when the PI learns of event.</td>
<td></td>
</tr>
<tr>
<td>Other UP * (not death or life-threatening experience)</td>
<td>Report to IRB within 5 working days</td>
<td>Report to IRB within 5 working days</td>
</tr>
</tbody>
</table>
Reportable information (items 2-6 in guidance Events and Information that Require Prompt Reporting to the IRB)

- from when PI receives assessment from monitoring entity
- from when PI learns of event or new information

The IRB will review and assess the events and information reported, and address them as described in Chapter 3.12.

**Serious Adverse Events**

- Internal SAE Form
- Internal SAE Addendum Form
- Departmental External SAE Form

**When Modifying the Protocol is Indicated**

An event or new information might prompt a protocol modification – either initiated by the PI, or specified by the IRB after reviewing a report. When an event or new information requires a modification to a previously approved protocol (e.g., new side-effect in the consent form or suspension of enrollment) a modification must be submitted for IRB review, and must be approved by the IRB prior to implementation of the proposed changes. The only exception to pre-approval is for modifications necessary to eliminate apparent immediate hazard to the research participants; in this case, the PI must submit the modification to the IRB immediately following its implementation.

**Gene Transfer Protocols**

The above information on reporting UPs and other reportable information also applies to gene transfer protocols. In addition, for these protocols, all injuries and serious adverse events occurring at MD Anderson or at other participating institutions must be reported to the Biosafety Panel as outlined in the NIH Guidelines and the Incident Reporting template.

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The IRB has and follows written policies and procedures to evaluate the equitable selection of participants. (**AAHRPP Element II.3.C**)

The IRB has and follows written policies and procedures to review proposed participant recruitment methods, advertising materials, and payment arrangements and determines whether such arrangements are fair, accurate, and appropriate. (**AAHRPP Element II.3.C.1**)

Researchers and Research Staff recruit participants in a fair and equitable manner. (**AAHRPP Element III.1.E**)
14.13 Recruitment

PIs are referred to the MD Anderson recruitment policies and procedures set forth in Chapter 10.1.

The PI must provide all necessary information on the protocol submission to allow meaningful review by the IRB of the recruitment process (see Chapter 10.2).

The PI is instructed to follow the guidance on recruitment, telephone screening (which includes phone script samples), and advertisements (see Advertisements Appropriate Language for Recruitment Material).

In selecting a population from which to draw participants for a particular research protocol, the PI must consider whether the choice of population results in an equitable distribution of the burdens and benefits of research. The PI must provide appropriate justification in the protocol application when recruiting participants among vulnerable populations such as prisoners, pregnant women, economically and educationally disadvantaged, decisionally impaired, and homeless persons. (45 CFR 46.111(a)(3); 21 CFR 56.111(a)(3))

- Chapter 10.1 (equitable selection)

Researchers maintain appropriate oversight of each research study, as well as Research Staff and trainees, and appropriately delegate research responsibilities and functions. (AAHRPP Element III.2.B)

Researchers and Research Staff follow the requirements of the research protocol or plan and adhere to the policies and procedures of the Organization and to the requirements or determinations of the IRB. (AAHRPP Element III.2.C)

Oversight of Research Staff during Recruitment

The PI is responsible for ensuring recruitment activities, whether undertaken by research staff or the PI, are in accordance with methods set forth in the protocol submission and approved by the IRB. The PI must ensure that informed consent is obtained from each research participant before that individual participates in the research protocol. The PI may delegate the task of obtaining informed consent to another individual knowledgeable about the research, while retaining ultimate responsibility over the conduct of the protocol in accordance with the IRB Policy on Obtaining Informed Consent for Participation and Authorization for Uses and Disclosures of Protected Health Information for Clinical or Health Services Research Protocols. The PI may delegate authority to individuals who are licensed as physicians in the state of Texas to obtain legally effective informed consent of the participant for any protocol that involves administration of drugs, radiotherapy, and use of surgery, invasive procedures, or investigational devices.

The PI may delegate authority to obtain informed consent to an individual who is not a physician in limited circumstances, and only when protocols have no more than minimal risk
and do not involve administration of drugs, radiotherapy, use of surgery, invasive procedures or investigational devices. This individual, referred to as an authorized designee, is not required to be listed as a collaborator on the protocol, but may assume other protocol roles (e.g., sub-investigator).

The PI should assure that the delegated individual is qualified by education, training and experience and has an understanding of the scientific content of the protocol. Any such delegation should be described in a delegation log and/or the in the body of the protocol.

The PI is expected to maintain a delegation log that details who has authority to obtain informed consent (e.g., the person including name, title and dates of delegation). The log should also describe the delegated tasks, identify the training that individuals have received that qualifies them to perform delegated tasks, and identify the dates of involvement in the protocol. A separate log should be maintained for each protocol that the investigator conducts.

This delegation log does not need to be submitted to the IRB for approval. However, the IRB may require that the delegation log be submitted for approval or that the delegation be specifically described in the protocol.

The PI is responsible for providing adequate supervision of those to whom tasks are delegated and is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the protocol.

Recruitment of MD Anderson Employees

While employees are not vulnerable subpopulations per se, they may perceive that they are under some pressure from their superiors to agree to participate. PIs must provide a rationale when the research procedures include direct recruitment of employees of MD Anderson. When employees are involved, the protocol plan must include the following:

- How employees will be protected from coercion and undue influence, and
- What alternatives exist to participation
- How the PI will ensure the confidentiality of any private and sensitive information
- How employees will be protected from any negative impact of their research participation on the employees’ employability, insurability and/or any licensure requirements.

Including Children as Participants

Children should be included in research, along with adults, unless there is a compelling rationale for their exclusion. Research that limits enrollment to children is generally not appropriate unless:

- The condition or disease is limited to children, or
- The research seeks to obtain information on a test article or procedure that previously had been studied only in adults.
The IRB has and follows written policies and procedures to review proposed participant recruitment methods, advertising materials, and payment arrangements and determines whether such arrangements are fair, accurate, and appropriate. (AAHRPP Element II.3.C.1)

Appropriate Payment

Payments to research participants may not be of such an amount as to result in coercion or undue influence on the participant’s decision to participate.

Payments may not be provided to participants on a schedule that results in coercion or undue influence on the participant’s decision to continue participation. For example, payment may not be withheld as a condition of the participant completing the research. If the participant withdraws early, payment must be prorated to reflect the time and inconvenience of the participant’s participation up to that point.

See Participant Remuneration Standard Operating Procedures.

See Informed Consent Policy (CLN0547)

See Policy on Remuneration in Research Studies

See Reimbursement SOP

• How to Determine Which Remuneration Form to Use
  o Patient Disclosure Acknowledgement for Reimbursement Form,Bank of America
  o Patient Disclosure Acknowledgement for Reimbursement Form_(Abbreviated_not Bank of America)

Researchers determine that the resources necessary to protect participants are present before conducting each research study. (AAHRPP Element III.1.D)

Researchers employ consent processes and methods of documentation appropriate to the type of research and the study population, emphasizing the importance of comprehension and voluntary participation to foster informed decision-making by participants. (AAHRPP Element III.1.F)

14.14 Consent Process

Also see Chapter 12 on informed consent and assent.

Informed Consent is a Continuing Process

Informed consent is a continuing process whereby the investigator and research participant have an on-going dialogue about all aspects of a research protocol that might inform a participant’s decision to take part in the protocol, and their decision to continue their involvement as a participant. Although consent is given it may be withdrawn at any point. The informed consent process should be regarded as continuing throughout the duration of the
The purpose of the consent process is to assure knowledgeable decision-making and voluntary participation.

This process generally includes:
- Bringing the research protocol to the notice of potential participants.
- Presentation and explanation by the investigator (or delegate) of the protocol and protocol activities to the participant or their legally authorized representative (LAR).
- Documentation of informed consent via a signed and dated written consent document.
- Ongoing discussions between the investigator and the participant regarding continued participation in the protocol.

The PI is expected to be familiar with:
- The informed consent policies in Chapter 12, including the criteria for a legally effective informed consent process, and any additional federal, state (Texas), and institutional requirements.
- Additional requirements might apply depending on the source of support/funding (e.g., Department of Defense) (see Other Federal Agencies - Additional Requirements).
- The consent process information and consent form templates (see Clinical Template) provided on the Office of Human Subjects Protection website (see OHSP Website) pages. The basic and possible additional consent requirements, and those specific to certain types of research activity (such as genetic testing, data and tissue repositories, and xenotransplantation), are addressed in Chapter 12.1.2.

Consent requirements for research involving vulnerable and other special populations - including consent from a legally authorized representative (LAR) – are described in Chapter 12.2. This addresses adults with impaired decision-making capacity, prisoners, children, pregnant women, fetuses and neonates, and MD Anderson employees and students.

The Consent Document

The Office of Human Subjects Protection website (OHSP Website – HSRM) provides consent form templates, which address the required elements of informed consent, as well as providing language for other situations, (such as MRI, tissue banking), in which certain additional information may need to be disclosed to participants. For research involving children, an Assent Template is also provided (see Informed Consent Templates - Clinical).

To assist PIs in preparing consent documents comprehensible to lay persons (i.e., at approximately 8th grade level) a glossary of lay terms is available on the MD Anderson Office of Human Subjects Protection website. This glossary of terms is also available online on the NCCN webpage under the name NCCN Informed Consent Language Database. This database was created by MD Anderson in collaboration with Dana Farber Cancer Institute. There is also a database of medications and procedures called the Adverse Event (AE) Database. This database is linked in to the online protocol system and lists, in lay terminology, all of the potential side effects of the medications and procedures in the database. This database was created at the...
request of the IRB so that the consent forms for multiple protocols, looking at the same drug or drug combinations, contain consistent terminology and information when it comes to the potential side effects of these therapies or interventions. The MD Anderson IRB must review and approve any changes made to the AEs listed for particular medications or procedures in the database.

The IRB encourages and recommends the use of a full consent form, translated into the participant’s language whenever possible. In certain situations, the use of a ‘short form consent process’ may be permitted by the IRB, incorporating the use of a short form consent document translated into the participant’s language. Templates of short form consent documents have been translated into over 35 different foreign languages based on the various nationalities of our patient populations. The short form contains the basic required elements of informed consent and are provided on the Office of Human Subjects Protection website. When a participant who speaks a non-English language needs to sign a short form but the form has not yet been translated into that language, the IRB office initiates the process of having the short form translated into that language.

In the event that the PI proposes to use a consent document based on one already developed by the sponsor or a cooperative multi-site research group, the PI is responsible for reviewing the existing document to determine if it fairly and adequately describes the research aims, procedures, risks, and benefits. The explanation of risks in the consent document should be based upon information presented in such documents as the protocol, the investigator’s brochure, any previous research reports, and, where applicable, the labeling for the drug or device.

If the research involves extensive screening procedures, the PI may wish to develop a separate pre-screening consent document that explains the screening procedures in detail and provides a brief summary of the underlying research. In such circumstances, screening could begin after the individual signed the screening consent form but before the signing of the main consent document, which would be signed only if the individual satisfied the screening criteria and was actually enrolled in the protocol.

See Chapter 12.1.4 for detailed information on consent documents, the long form, and the use of the short form consent process.

14.15 Providing Consent Process Information to the IRB

In the protocol submission, the PI must:

- Describe the consent process in enough detail to allow for meaningful review by the IRB,
- Include the proposed written informed consent document(s) that address(es) each of the elements of informed consent in the context of the research (unless the IRB waives the documentation requirement – see below), and
- Include any written material to be given to prospective participants to explain the nature of the research.
The PI is responsible for making all modifications to the proposed consent document as requested by the IRB. Any other change to the consent document must be submitted to the IRB for prior review and approval.

**Requesting Waivers or Alteration of Consent Requirements**

Under specific circumstances, the PI may request that the IRB grant a:

- Waiver or alteration of the consent process – i.e., the requirements for obtaining informed consent, or
- Waiver of documentation – i.e., the requirement to obtain a signature on a written consent document.

The requirements for these two options differ. Refer to Chapter 12.1.2 for explanation.

**Obtaining Informed Consent**

The PI is responsible for obtaining and documenting the informed consent of individuals who participate in research, unless the requirement to obtain and document informed consent is altered or waived by the IRB.

No research procedures, including screening procedures to determine if an individual is eligible to enroll in the research, may begin until after the participant has signed the consent form, unless the IRB has approved a waiver or alteration of consent. Retroactive consent – i.e., consent obtained or documented after the participant has undergone one or more research procedures is not permitted by federal human subjects protection and FDA regulations, and is not legally effective informed consent.

The PI must use the consent document currently approved by the IRB. The IRB approval date must appear on the consent document. MD Anderson requires use of an electronic consenting platform (iConsent) that automatically files the signed and dated consent into the participant’s medical record for participants who have an MD Anderson medical record. When the consent is pulled up, the IRB approval date is listed on the bottom of every page. In instances when a paper consent is used, for example with community based research, it is printed from the Consent Form Printer Database and also includes the IRB approval date.

No participants should be involved in research prior to the IRB approval date, and no participants should be involved in research using a consent document in which the IRB-approval has expired.

The PI or their delegate should plan to discuss research with potential participants at a time when they are not under duress, and to allow sufficient time and opportunity to ask questions and to consider whether or not to participate in the research before agreeing to participate.

In discussing research with potential participants, the PI or their delegate:
• May not describe items or procedures under investigation as if they are known to be safe and effective as a treatment for the potential participant's disease or condition, or as if they present a known advantage,
• May not understate the risks of the research, as there may be no countervailing benefits to participants.

The PI or their delegate is responsible for giving the participant a copy of the signed informed consent document, and for maintaining the original form. This is true regardless of whether the participant is consented using iConsent or paper. In both instances, a signed copy of the consent is given to the participant and a signed copy is filed either electronically or physically scanned into the medical record.

**Obtaining Informed Consent in the Clinical Research Context - Special Considerations**

The distinction between treatment and research is especially important if the PI is also the potential participant’s attending physician, a situation that increases the risk of confusion. Thus, it must be clearly stated to the participant that they will be involved in research and that if randomization is involved, that this is also described.

The purpose of medical or behavioral treatment is to provide interventions designed solely to enhance the well-being of the patient or client. By contrast, research is designed primarily to develop generalized knowledge rather than to benefit each participant in the research.

Research involves activities to test a hypothesis and draw conclusions, and any therapeutic benefit to the participants is secondary to the objectives of the research.

Research involving randomization of participants, whether to proven or experimental procedures, raises further issues. In these circumstances, the PI should ensure that each participant understands that the assignment will not be based upon the attending physician's clinical judgment as to which treatment may prove more beneficial to that participant, and may involve additional testing that would not be performed as clinical care.

**Consent Situations Requiring Prompt Reporting to the IRB**

Situations where informed consent is not properly obtained or not documented, and no corresponding waiver or alteration of the consent process has been granted by the IRB, may constitute noncompliance. Such circumstances may require reporting to the IRB. These include, but are not limited to:
• Involving an individual in research without first obtaining their informed consent and a signed informed consent document (unless the IRB has explicitly waived these requirements).
• Involving an individual in research using a consent form other than the current IRB-approved form.
• Situations where the PI believes informed consent documents have been lost, misplaced, or destroyed.

See also:
• Chapters 3, 12, and 14 for information on reporting to the IRB
• Events and Information that Require Prompt Reporting to the IRB

Researchers and Research Staff have a process to address participants’ concerns, complaints, or requests for information. *(AAHRPP Element III.1.G)*

**14.16 Response to Participants’ Requests for Information and Complaints**

**Requests for information**

The PI and members of the research staff are required to respond promptly and adequately to all requests for information received from participants, prospective participants and their family members or designated representatives. In addition to providing information and answering questions that arise as part of the informed consent process, the PI must inform the participant that he/she is available to answer any questions that arise about the research in the future. The consent form must list the full name and contact information for the PI, and other research protocol staff as appropriate. The consent form must also inform participants how to reach the IRB if they have any questions about their rights as research subjects (see MD Anderson consent form template for contact information language).

**Complaints**

The PI is expected to investigate and respond promptly to complaints, and to follow the proper procedure for addressing and reporting complaints to the IRB. A complaint is a formal or informal, written or oral, expression of dissatisfaction by the participant or the participant’s representative. Complaints that are not resolved promptly by the PI or member of the research staff must be reported to the IRB as follows:

Complete and submit a PDOL Generic Memo that will be submitted to the IRB with the following:
• A brief description of the complaint and the circumstances in which the complaint was made and any action taken to date in addressing the complaint. Complaints are handled in accordance with the policies described in Chapter 3.16 and Chapter 11.4.

If the complaint is not directly related to the conduct or design of the research, the IRB may refer the complaint to the appropriate MD Anderson institutional official or committee (e.g., as provided for in the MD Anderson institutional policy on the handling of grievances). In circumstances in which the complaint is referred, the IRB should provide the participant with the name and contact information for the referral.
For complaints directly received by the IRB, the IRB will obtain the following information from the participant or participant’s representative:

- Participant’s name
- Participant’s MRN, if applicable
- Protocol number
- Participant contact information
- Brief description of complaint/issue

The IRB staff who received the call will email the PI and the additional contact(s) for the protocol and provide the above information provided by the participant. The IRB Chair, OHSP Director, IRB Manager, and Quality Assurance Specialist will be copied on the email. The IRB staff will request that the PI provide a resolution to the participant and a follow-up to the email. The IRB Chair will make a determination if any additional actions are needed based on the PI’s response to resolving the participant’s concerns. Specific details regarding this process can be found in the IRB Standard Operating Procedure for Handling Revocation of Consent or Other Participant Complaints.

For participant concerns directly related to the conduct of the research on the protocol, there is an escalation process that will be followed per the IRB Standard Operating Procedure for Handling Revocation of Consent or Other Participant Complaints.

Investigators should list all complaints received about the research in the past year, whether or not they were previously reported to the IRB, in continuing review submissions to the IRB.

Privacy issues
If the complaint involves MD Anderson privacy practices, all documentation relating to the complaint must be retained for at least six years from the date of creation and the institutional privacy officer is notified.

If such a complaint cannot be handled promptly, the MD Anderson Privacy Officer must be notified. Please contact the Institutional Compliance Office at 713-745-6636.

Final Report
At the conclusion of the protocol, PIs involved in research which enrolled participants must submit a final report when a request to terminate the protocol is submitted to the IRB. Please see IRB Policy on Human Subjects Research Termination, Termination of IRB Oversight and Activities that are not subject to IRB Oversight. PI’s should submit the IRB Policy on IRB Committee Determinations for Reviewing Research Non-Compliance, Suspending or Terminating Research and IRB reporting procedures to Institutional and External Officials when requesting termination.

Confidentiality of Records and Personal Data
PIs working with human subjects must safeguard the privacy of participants and protect the confidentiality of personal information:

- Safeguard mechanisms must be established, maintained, and documented throughout the research process.
- Sustained attention must be paid to maintaining confidentiality of research data in the design, implementation, conduct, and reporting of research.
- Full information about the privacy and confidentiality of data must be provided to prospective participants through the informed consent process.
- Unintentional breaches must be avoided by taking additional precautions in communication, administration and storage of information.

Privacy and confidentiality are addressed in Chapter 11.

**Privacy Rule (HIPAA)**

When conducting research that involves the use and disclosure of protected health information (PHI), the PI must abide by the applicable HIPAA policy of MD Anderson, and must be able to account for disclosures of PHI when an individual requests such accounting.

See:

- Chapter 11
- MD Anderson Policies and Procedures Related to HIPAA and PHI
Chapter 15. HRPP Coverage of Sponsored Research

Definitions for Chapters 15, 16, and 17

**Sponsored Research**: Research supported by external entities through the provision of funding or other transfers of value, such as investigational drugs, devices or biologics, as documented by a contract that sets forth a specified statement of work (e.g., the research proposal). (See MD Anderson’s Institutional Policies and Procedures)

15.1 Agreement Includes Protection for Research Participants

MD Anderson uses MD Anderson’s Checklist for Sponsored Research Agreement when negotiating agreements with the sponsors of sponsored research projects. This checklist helps MD Anderson in confirming that the contract contains the appropriate provisions to protect research participants.

*MD Anderson has a written agreement with the Sponsor that addresses medical care for research participants with a research-related injury, when appropriate. (AAHRPP Element I.8.A)*

15.2 Provision Addressing Medical Care for Participants

**MD Anderson**

In any sponsored research agreement, medical care for participants is addressed by:

- Including a provision that addresses whether the sponsor would be responsible for the cost of medical treatment for injuries arising from the research (see paragraph 11.b. in MD Anderson’s Checklist for Sponsored Research Agreement).
- Matching the substance of any such provision in the consent form with the sponsored research agreement language
- Including a statement in the consent form that If participants suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care, that they may contact the Chair of MD Anderson’s IRB at 713-792-2933 with questions about study-related injuries and that by signing the consent form, they are not giving up any of their legal rights.

See:

- Chapters 12, 13, and 18.
Chapter 16. Communication from Sponsors Affecting IRB Oversight

In studies where Sponsors conduct research site monitoring visits or conduct monitoring activities remotely, MD Anderson has a written agreement with the Sponsor that the Sponsor promptly reports to MD Anderson findings that could affect the safety of participants or influence the conduct of the study. *(AAHRPP Element I.8.B)*

When the Sponsor has the responsibility to conduct data and safety monitoring, MD Anderson has a written agreement with the Sponsor that addresses provisions for monitoring the data to ensure the safety of participants and for providing data and safety monitoring reports to MD Anderson. *(AAHRPP Element I.8.C)*

16.1 Data and Safety Monitoring (DSM) in Sponsor Agreements

In any sponsored research agreement, MD Anderson includes contract provisions that obligates the sponsor to promptly notify MD Anderson of any aspects of the protocol, including any information discovered during the site monitoring visits, or of the protocol results that may adversely affect the safety, well-being, or medical care of the research participants, or that may affect the willingness of the research participants to continue participation of the protocol, influence the conduct of the protocol, or may alter the IRB’s approval to continue the protocol *(see paragraph 11.c. of MD Anderson’s Checklist for Sponsored Research Agreement)*.

In studies where the sponsor has the responsibility to conduct data and safety monitoring, MD Anderson will require the sponsor to provide the data and safety monitoring plans to the Principal Investigator (PI) and the IRB. The sponsor will also provide routine and urgent reports from data and safety monitoring to the Principal Investigator who will provide them to the IRB.

For sponsored research, MD Anderson agreements specify that, as appropriate:
- Provisions are made for monitoring study data which could affect participants’ safety, and
- Urgent reports (those meeting the criteria in guidance Events and Information that Require Prompt Reporting to the IRB) are submitted according to the guidelines specified in the HRPP Guidance Policy “Events and Information that Require Prompt Reporting to the IRB”. The time frame for providing routine and urgent data and safety monitoring reports to the organization will be indicated, consistent with what is stated in the data and safety monitoring plan approved by the IRB *(see Checklist for Sponsored Research Agreement, section 11c. AAHRPP Provisions for AAHRPP certification compliance)*.

Per the IRB Continuing Review of Research Policy, data safety monitoring reports are required to be reported to the PI so that routine monitoring reports will be submitted as part of Continuing Review applications submitted to the IRB.
Chapter 17. Knowledge Benefit and Participants’ Interests

Before initiating research, the Institution has a written agreement with the Sponsor about plans for disseminating findings from the research and the roles that Researchers and Sponsors will play in the publication or disclosure of results. (AAHRPP Element I.8.D)

17.1 Publication of Research Results

MD Anderson’s mission is to eliminate cancer in Texas, the nation, and the world through outstanding programs that integrate patient care, research and prevention, and through education for undergraduate and graduate students, trainees, professionals, employees and the public. For research programs, MD Anderson furthers its mission by ensuring that the sponsored research agreement MD Anderson enter into for any research protocol gives MD Anderson the right to publish and/or disseminate the results of the research.

MD Anderson requires that its sponsored research agreements give MD Anderson the right to publish or present the results and data of its research (see paragraph 14 of MD Anderson’s Checklist for Sponsored Research Agreement). Additionally, MD Anderson will only give sponsors the right to review and comment on any draft manuscripts regarding the research results and not the right to approve the manuscripts (see paragraph 14.e. of MD Anderson’s Checklist for Sponsored Research Agreement).

Additionally in any sponsored research agreement, if the sponsors insist on including research data or results in the definition of sponsor’s confidential information or if the sponsor wants to own the data and results of the research, MD Anderson requires that the contract provisions still allow MD Anderson the ability to publish and use the research data and results (See paragraphs 14.g., h. and 15.a.iii. of MD Anderson’s Checklist for Sponsored Research Agreement).

When participant safety could be directly affected by study results after the study has ended, MD Anderson has a written agreement with the Sponsor that the Researcher or MD Anderson will be notified of the results in order to consider informing participants. (AAHRPP Element I.8.E)

17.2 Communicating Protocol Results to Participants

When the IRB learns of events that could affect participant welfare after a protocol has closed (e.g., a drug studied at MD Anderson is withdrawn by the FDA), the IRB seeks information, deliberates, and considers whether (and how) to contact participants who might be affected. Even when the protocol is not yet closed, but participants have completed participation, the IRB informs former participants when information is learned that could affect their welfare.
When MD Anderson negotiates any sponsored research agreement, MD Anderson uses reasonable efforts to obligate the sponsor for the term of the agreement and two years thereafter, to promptly notify MD Anderson of any aspects of the protocol, including any information discovered during the site monitoring visits, or of the protocol results that may adversely affect the safety, well-being, or medical care of the research participants, or that may affect the willingness of the research participants to continue participation of the protocol, influence the conduct of the protocol, or may alter the IRB’s approval to continue the protocol. MD Anderson also includes contract provisions allowing MD Anderson to promptly notify the IRB of any such events and to send research participants a written communication about the results where the safety or medical care of the research participants may be affected by the research results (see paragraph 11.c. of MD Anderson’s Checklist for Sponsored Research Agreement).
Chapter 18. Addressing Concerns of Research Participants

MD Anderson has and follows written policies and procedures that establish a safe, confidential, and reliable channel for current, prospective, or past research participants or their designated representatives that permits them to discuss problems, concerns, and questions; obtain information; or offer input with an informed individual who is unaffiliated with the specific research protocol or plan. (AAHRPP Element I.4.A.)

Researchers and Research Staff have a process to address participants’ concerns, complaints, or requests for information. (AAHRPP Element III.1.G.)

Consent Form Requirements

The IRB requires that all consent forms include information on how to contact the principal investigator conducting the research protocol. Participants are instructed to call the investigators if they have any questions about the research, about their rights as a research participant, or if they believe they have suffered a research-related injury. Each consent form must also include telephone numbers for the IRB (a local number and a toll free number). The IRB contact information affords current or past research participants or their designated representatives a means to contact an informed individual who is independent of the research team. The IRB also serves as a conduit for receiving information from any party who is not satisfied with the manner in which a protocol is (or was) being conducted, or if any party has any concerns, complaints or general questions about research or the rights of research participants.

Informed Consent Templates (Clinical Template), available on the Office of Human Subjects Protection website, include instructional text and verbatim language for the inclusion of the investigator’s contact information and IRB telephone numbers under the consent form heading “Contact Information.”

Recruitment Material Requirements

The IRB requires specific contact information to be included in participant recruitment materials – flyers, newspaper ads, newsletters, and web postings. Guidance Advertisements: Appropriate Language for Recruitment Material provides appropriate language to include in recruitment material.

All recruitment materials must include the appropriate contact information for the investigator(s) conducting the protocol. The IRB reviews all recruitment materials, and the addition of IRB contact information is required when appropriate.

Telephone (Screening) Scripts

The IRB requires investigator and IRB contact information be included in telephone scripts. Telephone scripts are often used to screen prospective participants. Like the consent forms,
telephone scripts must include telephone numbers for IRB (a local number and a toll free number), as well as telephone numbers for the investigators. This contact information provides prospective participants with channels of communication to the investigators and the IRB for questions, concerns, input, information or complaints.

Responding to Contacts from Participants or Others

Prospective Participants

Calls from prospective participants interested in medical or nonmedical research are generally forwarded to the appropriate clinical or behavioral department for follow up with the interested caller. Calls are forwarded to askMDAnderson at 1-877-MDA-6789.

All other contacts are referred to an IRB Senior Staff member.

Participant Concerns

Concerns of research participants are followed up by IRB Senior Staff who call the individual to gather more information. As appropriate, concerns may be forwarded to the OHSP Director, the IRB Manager, or an IRB Chair. Minor concerns are generally resolved by a phone call.

More complex concerns are followed up by the OHSP Director or the IRB Manager in consultation with the IRB Chair. Concerns may be referred to, and addressed in consultation with other departments within MD Anderson such as the Institutional Compliance Office, Risk Management, Legal Services, Clinical Ethics, and Patient Advocacy. The Institutional Official and the IRB Chair are informed and involved in resolution of participant concerns throughout the process.

Institutional Compliance Hotline

The Institutional Compliance office has a compliance hotline for research participants to ask questions, offer input, raise concerns or complaints about research, a research related injury, or any question about the rights of research participants (see Institutional Compliance Program - Compliance Hotline: 1-800-789-4448).

Research where an Institutional Conflict of Interest Has Been Identified

When there is an Institutional Conflict of Interest (ICOI), information about the ICOI is included in the participant ICD template. Information on how the ICOI will be managed, including employment of an external IRB, and external ethicist and notification of the UT system is also included in the ICD. Contact information for each of these groups is also included in the ICD that the participant signs.

Reference Materials

IRB Standard Operating Procedure for Handling Revocation of Consent or Other Participant Complaints
Chapter 19. Education and Outreach

MD Anderson employs several mechanisms for communication and education to increase public awareness and educate potential research participants.

MD Anderson conducts activities designed to enhance understanding of human research by participants, prospective participants, or their communities, when appropriate. These activities are evaluated on a regular basis for improvement. (AAHRPP Element I.4.B.)

19.1 On-line Resources and Educational Materials

Clinical Trials at MD Anderson website

The Clinical Trials at MD Anderson website contains:

- The Patients and Family page which provides information and resources about participating in research for participants, prospective participants, and community members, including:
  - Frequently asked questions (FAQs)
  - Link to a listing of current clinical protocols taking place at MD Anderson
  - Definitions of research terms (e.g. clinical protocols, including the various phases and informed consent)
  - General information on the rights of research participants and questions to ask before agreeing to participate in research
  - Links to OHRP brochures: Becoming a Research Volunteer: It's Your Decision (in English and Spanish)
  - Links to entities and organizations where research information can be obtained (e.g. National Cancer Institute, FDA and OHRP)
  - Contact information for inquiries about current research at MD Anderson

MD Anderson Cancer Center Community Services

MD Anderson Cancer publishes a newsletter and maintains a research-related website that promotes public awareness and participant education. See the MD Anderson Cancer Center website Community Services. It also offers prospective participants information on available research opportunities and other research related topics.

Other MD Anderson Resources

- Other departments at MD Anderson provide web-based information on current research opportunities (e.g. Behavioral Tree, MD Anderson Prevention Research Center).
- The MD Anderson Learning Center is a free public consumer health information library that provides scientifically based medical information to help people make informed decisions about their health and their health care. The Health Library is a community service of MD Anderson Cancer Center.
Chapter 19 - Education and Outreach

MD Anderson Human Subjects Research Manual

• The MD Anderson UT Graduate School Clinical & Research Training, consists of Graduate Medical Education, Clinical Education for Non-Physicians, Postdoctoral training.
  o Graduate Medical Education: MD Anderson’s comprehensive educational programs in a state-of-the-art setting provide outstanding opportunities for physicians, medical professionals and students.
  o Clinical Educations for Non-Physicians: Clinical Education for Non-Physicians encompasses graduate level training for fellows and residents of professional disciplines such as pharmacy, radiation oncology/physics, physician assistant, psychology and ethics. These clinical training programs provide exceptional learning experiences with the commitment to the investigation and treatment of cancer, preparing health care professionals to be leaders in their chosen specialty.
  o Postdoctoral Training: The postdoctoral experience (current Postdocs and prospective Postdocs) at MD Anderson trains highly-skilled scientists and investigators through intensive research engagement and professional development initiatives in one of the world’s leading cancer institutions.

**MD Anderson conducts activities designed to enhance understanding of human research by participants, prospective participants, or their communities, when appropriate. These activities are evaluated on a regular basis for improvement.** *(AAHRPP Element I.4.B.)*

19.2 Participant Research Inquiries

Participant inquiries about clinical studies received by the Clinical Research Registration Team (CR REG), OHSP staff through IRB Help, askMDAnderson, and other MD Anderson Cancer Center areas referred to the appropriate department.

The Clinical Trials at MD Anderson summarizes resources for obtaining information and contacting appropriate individuals/offices, including the Clinical Trials at MD Anderson resource page for Patients and Family.

19.3 Outreach

• Center for Community-Engaged Translational Research (CCETR): a research resource of the Duncan Family institute that helps investigators implement their research in community settings and supports the recruitment and retention of minorities and women to clinical protocols. CCETR supports research projects that translate new or current research findings into community settings.
• MD Anderson: The Learning Center is a patient education library that provides current and reliable information on cancer prevention, treatment, coping and general health as well as about services available at MD Anderson.
• MD Anderson Patient Education Office offers group classes supporting all areas of health, including the mind, body and spirit. Classes are free and open to patients, family members and caregivers. Class schedules are available below the class descriptions.
• MD Anderson UT Heath Graduate School and School of Health Professions:
MD Anderson UT Health Graduate School: The graduate school is a unique partnership between two institutions: The University of Texas MD Anderson Cancer Center and The University of Texas Health Science Center at Houston (UT Health). This partnership in graduate education has existed for more than 50 years.

School of Health Professions: The University of Texas MD Anderson Cancer Center School of Health Professions, in concert with the mission and visions of MD Anderson Cancer Center, is committed to the education of healthcare professionals, through formal academic programs that award institutional certificates and degrees in health sciences.

Office of Clinical Research Administration Clinical Practicum: The fall and spring of each year, a select group of students sign up for the clinical practicum. The practicum provides an overview of clinical research as it relates to human subjects research and how to conduct a clinical protocol. They students are either post-doctoral graduate students and/or junior faculty (MD/PhD) who are hoping to gain a better understanding of the protocol submission and review process at MD Anderson Cancer Center.

MD Anderson conducts activities designed to enhance understanding of human research by participants, prospective participants, or their communities, when appropriate. These activities are evaluated on a regular basis for improvement. (AAHRPP Element I.4.B.)

The Organization promotes the involvement of community members, when appropriate, in the design and implementation of research and the dissemination of results. (AAHRPP Element I.4.C.)

19.4 Community Participation in Research

For certain types of studies it might be appropriate to involve individuals from the community in which the research will take place, in the design and conduct of the research. MD Anderson supports and facilitates such community participation through a number of initiatives which address community-based issues, and by supporting researchers with programs that address issues of importance to the community in which we operate. These efforts may involve close collaboration with constituent communities and interest-groups.

Information for the community at large and potential research participants is available on numerous websites supported by the, and informational literature is distributed locally to community organizations, clinics, and other locations.

As appropriate to their protocol, researchers are encouraged to contact resources at MD Anderson for information on engaging and involving the community in research.

MD Anderson resources
MD Anderson resources include:

- The Center for Community-Engaged Translational Research (CCETR): a research resource of the Duncan Family institute, that helps investigators implement their research in community settings and supports the recruitment and retention of minorities and women to clinical protocols. We help translate MD Anderson's scientific discoveries into real-world interventions and programs through a range of applications, project implementation and dissemination. To reach this objective, CCETR supports research projects that translate new or current research findings into community settings. CCETR’s work spans innovative research areas, including physical activity and cancer prevention, lung cancer screening, treatment decision making, smoking cessation, obesity and community health. CCETR is collaborating on projects that help patients make informed decisions about cancer screening and treatment, contributes to building a research agenda around obesity in African American families, improves community designs to support healthful lifestyles and increases minority patient access to clinical protocols.

- CCETR Services include:
  - Identifying and connecting investigators with reliable and experienced community research partners.
  - Facilitating introductions to and discussion of collaboration opportunities with community research partners
  - Minority and women recruitment assistance
  - Technical assistance with grant development, implementation and dissemination (e.g., consulting with investigators on the development of specific aims, assisting with evaluations and dissemination planning, reviewing protocol instruments for cultural appropriateness)
  - Training on topics related to cancer disparities, cultural competency, population demographics and community-engaged research.

Community based participatory research is not limited to MD Anderson, but may involve collaboration between the MD Anderson and other sites or institutions - for example, the effort to translate basic biomedical research and discoveries, by having community outreach activities such as high school career day, job shadowing, campus tours, and speaking to community groups about cancer prevention involving staff and faculty of both locations.

Additionally, the CCETR works with a number of community partner organizations such as free clinics, churches, community services, health and cancer coalitions, and survivorship organizations. CCETR is also focused on improving outcomes important to patients and has studies funded by Patient-Centered Outcomes Research Institute (PCORI) funds – PCORI studies help patients and those who care for them make better-informed healthcare choices.

For more information on the goals, and current and planned programs and activities of the CCETR, see the CCETR website.
• **MD Anderson Department of Epigenetics and Molecular Carcinogenesis**: Faculty members give age-appropriate presentations to local K-12 schools about cancer and other scientific topics and there are also educational programs for high school and college students.

• **myCancerConnection Cancer Survivorship Conference** an annual event sponsored by myCancerConnection. myCancerConnection offers one-on-one support by connecting patients to a cancer support community of patients, survivors and caregivers who have been there. Requests are matched by disease, mode of treatment and experience. Support is open to patients, caregivers and cancer survivors who were treated anywhere, and connections have been made around the globe.

• **MD Anderson’s Clinical Cancer Prevention Department & Lyda Hill Cancer Prevention Center**:  
  o The Department of Clinical Cancer Prevention goals are to support and enable the Cancer Prevention Center to deliver cancer prevention, screening and surveillance services, to conduct state-of-the-art cancer research and to translate these research findings to the general population as the new standard of care; and to disseminate cancer prevention advances throughout MD Anderson, the community, the nation and the world.  
  o The Cancer Prevention Center offers a range of services to help you learn how to reduce your cancer risk or to detect cancer early - when it’s most treatable. Cancer screening exams are based on age, gender and disease risk. The center also offers risk assessment, risk reduction and diagnostic evaluation services.

• **Departments of Epidemiology**: The mission is to conduct collaborative research with clinical and basic science departments, and to support the need for quantitative sciences in the fields of genomics, proteomics, radiotherapy, molecular and cell biology, computer-assisted diagnoses, and image analysis.

• The **Bioinformatics and Computational Biology**: The mission of Bioinformatics and Computational Biology is to conduct collaborative research with clinical and basic science departments, and to support the need for quantitative sciences in the fields of genomics, proteomics, radiotherapy, molecular and cell biology, computer-assisted diagnoses, and image analysis.

• **MD Anderson Cancer Prevention & Population Sciences**: The ultimate goal of the Cancer Prevention and Population Sciences division is to keep people in a state of health and wellness, preventing them from crossing the threshold to disease and requiring treatment. Research underlies all the Division does. It is translated into advances in clinical care; into the education of future cancer prevention researchers and clinicians; and out into the community.  
  o The division is home to one of the largest and most developed cancer prevention programs in the nation. It is comprised of:  
    ➢ five departments: Behavioral Science, Clinical Cancer Prevention, Epidemiology, Health Disparities Research, and Health Services Research,
- multiple centers: Behavioral Research & Treatment Center, Center for Energy Balance and Cancer Prevention & Survivorship, Cancer Prevention Center, Center for Translational and Public Health Genomics,
- two institutes: Duncan Family Institute for Cancer Prevention and Risk Assessment and McCombs Institute for the Early Detection and Treatment of Cancer.

- **MD Anderson Postdoctoral Association**: The MD Anderson Postdoctoral Association is comprised of and led by postdoctoral fellows with the goals of improving, enhancing and enriching the postdoctoral experience at MD Anderson. The Postdoctoral Association Executive Committee (PDAEC) plans events that promote community among postdocs at MD Anderson and fosters interactions between postdocs of other Houston-area institutions. The PDAEC is comprised of three teams: Governance, Community Engagement and Career Advancement.
  - The **Governance Team** facilitates communication between the postdoctoral community and The Office of Postdoctoral Affairs and Development (OPAD) to develop and implement Postdoctoral Association Executive Committee policies that are beneficial to postdocs of the Postdoctoral Association.
  - The **Community Engagement Team** engages and brings a sense of community to the postdocs at MD Anderson through hosting, raising awareness, and increasing participation of events. The Team also enhances the interaction between postdocs and mentors by acknowledging and highlighting mentors’ accomplishments.
  - The **Career Advancement Team** provides resources that guide postdoctoral fellows through all of the stages of their training towards their professional career goals and through the course of their career development. They host the Annual Postdoctoral and Career and Science Symposium.

- The **Office of Health Policy** oversees several programs and initiatives at MD Anderson in the areas of community education, outreach, medical care and/or partnerships. The group also coordinates activities with external policy-related organizations.

- **Work in the Office of Health Policy includes**:
  - The **Uncompensated Care Program**, which manages and tracks unreimbursed costs for uninsured and underinsured patients served by MD Anderson.
  - Professional education services, including hosting our bi-annual Survivorship Conference for Health Care Professionals, supporting our Professional Education website and managing both the Faculty Speakers Bureau and Cancer Prevention and Survivorship Rotation.
  - Community programs and collaborations, such as Project VALET, which offers mammograms to uninsured women, and the FIT program, which provides free colon cancer screenings to low-income, uninsured, Medicaid or Medicaid-eligible adults age 50 to 75. Many of these efforts are supported by the Medicaid 1115 Waiver, which gives states the ability to design and improve their healthcare efforts.
  - Overseeing the Texas Cancer Information website, which connects people in the state to cancer information and services.
Considerations for IRB Review

In addition to applying all relevant federal, state and local regulations and MD Anderson policies, when reviewing such research, the IRB may consider the following, as pertinent to the type of research proposed:

- The appropriate community, and community representatives have been identified
- The research plan involves collaboration and communication between researchers and community in research design, conduct, and dissemination of results as appropriate
- It is recognized that the design and conduct of each phase of the research may be a somewhat iterative process, as researchers and community members gain knowledge and familiarity with the process
- Additional expertise will be called upon as needed to provide input on cultural or local context, or other special circumstances
- In addition to traditional research publication routes, results will be disseminated in ways that are accessible and intelligible to the community involved in the research
- Possible impacts of the research on the community beyond the life of the current project are addressed.
For a complete history of the revisions to the manual or for any questions, please contact IRB Help.