INVESTIGATOR'S MANUAL

INSTITUTIONAL REVIEW BOARD

POLICIES AND PROCEDURES

SIGNATURE SECTION AND REVISION HISTORY

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DEFINITIONS

Adverse Event means any unfavorable medical occurrence in a human subject including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.

Assent is an affirmative agreement by an individual not competent to give legally valid informed consent, to participate in research.

Conflict of Interest refers to situations in which financial or other personal considerations (non-financial) may compromise, or have the appearance of compromising a researcher's professional judgment in conducting or reporting research.

Data and Safety Monitoring: is the process for reviewing accumulated outcome data from ongoing clinical research in order to ensure the continuing safety of current subjects and prospective subjects, as well as the continuing validity and scientific merit of the research. It typically involves a data and safety monitoring plan and may also include the development of a Data and Safety Monitoring Board (DSMB) or Data Safety Committee (DSC).

Data and Safety Monitoring Board (DSMB) or Data Safety Committee (DSC) (collectively referred to as DSMB/C in this document): is a formal committee—usually independent of the investigators or sponsor—that is established specifically to monitor data throughout the study to determine its scientific and ethical validity, and to assure the safety of subjects.

Disability A substantial disruption of a person's ability to conduct normal life functions.

Equity Interest refers to any interest in the profits of or interest in any commercial or non-profit enterprise, including common stock and other equity securities, and any right to acquire any of the foregoing such as an option, warrant or other security convertible into an equity security.

Exempt Research Activity Any research activity that falls within one or more categories set forth in 45 CFR 46.101 (b), or 21 CFR 56.104 which are stated in this chapter. The PI can submit a request for exempt status however confirmation of exempt status must be granted by the IRB Chairman or designee.

External Adverse Events Adverse events experienced by participants enrolled in studies at sites that are not under LAU IRB jurisdiction. These are typically safety reports submitted by sponsors to investigators participating in multi-center trials, for example, events reported through Medwatch Form FDA 3500A or CIOMS Suspect Adverse Reaction Report.

Expedited Review A review conducted by the IRB Chair or a designated voting member or group of voting members, rather than at a convened IRB meeting. Protocols eligible for expedited review must meet the requirements set forth in 45 CFR 46.110, i.e. protocols present no greater than minimal risk ***and*** fall within the listed categories which are stated in this chapter and as confirmed by the IRB staff. Investigators may also request expedited review for minor changes in approved and ongoing research.

Expected and Unexpected Adverse Events *Refer to section 5.1.3*

Human Subjects is defined as living individuals about whom an investigator (whether professional, faculty, staff, or student) conducting research obtains (i) data through intervention or interaction with the individual, or (ii) identifiable private information."

Illiterate Subject is an individual that has insufficient reading and writing skills for ordinary practical needs.

Informed Consent is defined as a process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form

Internal Adverse Events are adverse events occurring to a particular participant at the site, under the LAU IRB jurisdiction

Investigational Product a product of an active ingredient or a placebo being tested or used as a reference in a clinical research project / clinical trial

IND Safety Reports – Investigational New Drug Safety Reports - Also known as MedWatch Form 3500A under FDA or CIOMS (WHO), these written reports used by the sponsor to notify the FDA and all participating investigators of any serious and unexpected AE that is associated with the research; or any finding from tests in laboratory animals that suggests a significant risk for human subjects including reports of mutagenicity, teratogenicity, or carcinogenicity.

Major Protocol Violation: Any violation that may impact subject safety, affect the integrity of study data and/or affect subjects' willingness to participate in the study.

Minority Group is a term referring to a group of people differentiated from the social majority

Minor Protocol Violation: Any violation that does not impact subject safety, compromise the integrity of study data and/or affect subject's willingness to participate in the study.

Principal Investigator A person responsible for the overall conduct of a research project at a site.

Protocol Amendment A written description of a change(s) to or formal clarification of a research project.

Protocol Exception: Any temporary protocol deviation (e.g., one-time enrollment of a single subject who does not meet eligibility criteria) that is approved by the IRB prior to its initiation.

Protocol Deviation: Any alteration/modification to the IRB approved protocol. The protocol includes all research related documents, such as consent form and advertisement.

Protocol Violation: Any protocol deviation that is not approved by the IRB prior to its initiation or implementation.

Randomization the process of assigning trial participants to treatment or control groups using elements of chance to determine assignments in order to reduce bias (ICH)

Randomization Code the code used during randomization that documents the assigned arm or group

Recruitment process used by investigators to enroll appropriate participants into a clinical research project based on inclusion and exclusion criteria

Reimbursement: includes re-payment to research participants to cover expenses they incur while participating in a clinical research study e.g. reimbursement for taxi fare or parking and may be made only if a receipt is provided by the subject. Reimbursement payments must be included in the study budge

Related/ Unrelated Adverse Events *Refer to section 5.1.3*

Remuneration: Payment for participation in research.

Research personnel is anyone who is assigned by the Principal Investigator and delegated one or more research related tasks

Serious (SAE)/ Non-Serious Adverse Event *Refer to section 5.1.3*

Source Documents original documents, data and records (such as hospital records, clinic and office charts, laboratory notes, evaluations, etc) where data is first recorded

Study coordinator is someone who usually works closely with the PI on overall administrative aspects of the study design, development and execution, as delegated. Some of these activities may also be delegated by the PI to a **Research Nurse who may either occupy dual study coordinator/research nurse responsibilities or share some similar responsibilities with the study coordinator.**

Unanticipated Problem *Refer to section 5.1.2*

Vulnerable Population individuals whose willingness to volunteer in a research project / clinical trial may be unduly influenced by the expectations, whether justifiable or not, of benefits associated with participation, or of benefits associated in case of refusal to participate. Examples of members of a group with a hierarchical structure, patients with incurable diseases, in nursing homes, children and minority groups, refugees, and those incapable of giving consent

PURPOSE AND SCOPE

This document defines the Human Research Protection Program (HRPP) oversight at the Lebanese American University (LAU) and the LAU Medical Center - Rizk Hospital (LAUMC-RH). It describes its mission and objectives, and details the required Policies and Procedures for the conduct of research.

APPLICABILITY

The IRB Policies and Procedures applies to all members of the LAU and LAUMC-RH community who engage in research involving human participants, use of human tissue or personal health information. All individuals involved in research must be knowledgeable about the bylaws, policies and the requirements detailed in the IRB Policies and Procedures for the conduct of research.

The information presented in this document is intended for use by members of the LAU and LAUMC-RH research community including but not limited to healthcare professionals, investigators, faculty members, nurses, residents, students, staff, administrators, and board members.

All research projects (including associated amendments) involving human participants conducted at LAU and/or the LAU Medical Center - Rizk Hospital (LAUMC-RH) or by its Faculty/Staff and students at outside premises must be submitted to the LAU Institutional Review Board Office for review and approval prior to data collection or study initiation.

MISSION AND OBJECTIVES

The mission of the HRPP is to guide investigators and research personnel in conducting their research while protecting the rights, safety and welfare of human subjects participating in research conducted at LAU and/or LAUMC-RH or by its faculty, staff and/or students at outside premises.

Consistent with its mission, the objectives of the HRPP are to assist the university in developing its regulatory structure and oversight in order to:

i) Increase knowledge and understanding of the guiding ethical principles that should be followed in the conduct of research involving human subjects and,
ii) Promote an environment, in which research involving human subjects is conducted by qualified personnel and according to the highest ethical and scientific standards.

INSTITUTIONAL REVIEW BOARD

The Institutional Review Board is a board established by the university and is responsible for the review, approval and oversight of research involving human participants. Its responsibility is mandated by the Board of Trustees at the university as per the Faculty Bylaws and Policy for Institutional Review Board.

AUTHORITY AND RESPONSIBILITY

The Dean for Graduate Studies and Research is the Institutional Official charged with the final authority and responsibility for the IRB Policies and Procedures manual.

The primary administrative responsibility for the day-to-day operation of the oversight of research under the HRPP lies with the Office for Institutional Review Board (IRB).

COMPLIANCE WITH THE ETHICAL REQUIREMENTS FOR RESEARCH

The LAU IRB office is responsible for communicating to the LAU and LAUMC-RH leadership and community, through the Dean for Graduate Studies and Research, the following:

- Commitment to protect human participants / subjects participating in research
- Compliance with the ethical principles and regulatory requirements set forth in this document
- Adherence with the requirements set forth by the LAU IRB for the submission processes of research projects as detailed in the related processes and IRB Policies and Procedures, and any other related documents

EDUCATION AND AWARENESS

The LAU IRB office mandates that all those involved in a research project must be listed on the IRB application and must complete the training mandated by the IRB on the Protection of Human Participants in Research, under the National Institute of Health: https://phrp.nihtraining.com/users/login.php

The IRB office is also responsible to provide educational session and training to its faculty, physicians, staff, residents and students on the following:

- History of the regulations and the regulatory framework
- Role and responsibilities of the IRB
- IRB Submission requirements and timelines for review
- Responsibilities of the investigators, student investigators and research personnel
- Informed consent requirements and protection of human participants in research

Educational and awareness sessions are also provided at, but not limited to the following:

- New faculty meetings and orientations
- Individual School orientations
- Grand rounds
- Medical Student Educational program
- Part of the LAU curriculum
- Quality Improvement - as requested by the IRB

ASSESSING QUALITY, EFFICACY AND EFFECTIVENESS OF THE HRPP

The LAU IRB Office conducts audits, surveys and monitoring activities to assess compliance with the organizational policies and procedures and applicable laws and regulations. The LAU IRB office evaluates as well the quality, efficacy and effectiveness of the Human Research Protection Program as it applies to the conduct of research and the protection of human participants.

The LAU IRB Office takes specific procedures in place in the event of findings of non-compliance pertaining to the conduct of research.

ETHICAL PRINCIPLES AND REGULATORY REQUIREMENTS

This document and all IRB policies are governed by ethical principles described in the following regulatory documents:

- **The Nuremberg Code**

  The Nuremberg Code is a set of principles for human experimentation that emerged during the 1947 Nuremberg Trials in response to the Nazi human experimentation carried out during the Second World War. The principles constituted in the Code—include informed consent, properly formulated scientific experimentation and beneficence towards participants—were further elaborated on in the subsequent Declaration of Helsinki.

- **World Medical Association Declaration of Helsinki**: *Ethical Principles for Medical Research Involving Human Subjects;*

  The Declaration of Helsinki is a set of ethical principles for clinical research that is widely regarded as the cornerstone document of human research ethics. It was developed in 1964 by the World Medical Association to provide guidance to physicians and other participants in human subject research. The Declaration elaborated the ten principles first stated in the Nuremberg Code, and tied them to the Declaration of Geneva (1948)—a statement of physician's ethical duties. Several revisions have been adopted since then.

- **The Belmont Report**: Ethical principles and Guidelines for the Protection of Human Subjects of Research

  The primary ethical principles applied to research covered by the HRPP are those set forth in The Belmont Report published in 1979 by the U.S. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.

  The Belmont Report identifies the three basic ethical principles that should guide the conduct of human subject research and it presents their respective applications, as explained below.

  - ***Respect for Persons*—**This principle states that first, the autonomy of individuals should be respected and second, that persons with diminished autonomy (e.g., minors, persons with cognitive impairment) are entitled to additional protections through: Informed consent, protection of subject privacy and confidentiality and special protections for vulnerable populations

  - ***Beneficence*—**This principle requires that the investigator not only protect individuals from harm, but make reasonable efforts to secure their well-being by maximizing benefits and minimizing risks to subjects through: Risk/benefit analysis and Scientific merit

  - ***Justice*—**This principle emphasizes an equitable distribution of the benefits and burdens of research. It is a violation of the principle of justice to select a class of subjects (e.g. patients from a specific ethnic or income group) simply because of easy availability rather than for reasons directly related to the premise of the study

IRB CHAPTER 1 – IRB / RESEARCH PROJECT SUBMISSION REQUIREMENTS

The purpose of this chapter is to describe the requirements for submitting research projects to be reviewed by the LAU Institutional Review Board. (Please also visit the LAU IRB website at http://gsr.lau.edu.lb/irb/). Research projects include all projects but not limited to interventional studies, projects that require the collection of data from medical records or documents with identifiable private information, conducting surveys, interviews, circulating questionnaires, etc. The submission to the IRB should take place before any study related procedure, as described in this chapter.

PROCEDURE 1.1 – THE IRB APPLICATION SUBMISSION PROCESS

1.1.1 Research Project Submission Form

For all research projects to be submitted to the LAU IRB, the PI is required to complete the **"Research Proposal Submission Form"** and submit along with the IRB required documents (refer to section 1.1.2). This is a mandatory cover form for all research conducted by LAU faculty, staff and students. Principal investigators must also ensure securing the necessary signatures on the form.

Any non-LAU researcher or student seeking to conduct research at LAU or LAUMCRH or involving faculty, staff or students, must have an LAU member to serve as SPONSOR of the research project.

1.1.2 Preparing the Initial IRB Application and supporting documents

Investigators are required to prepare the documents to be submitted to the LAU IRB depending on the submission review criteria detailed in section 1.2 of this document. **The investigator must submit one hard copy and one electronic copy of all required documents.** Each application has a list of documents at the beginning of the application to identify what documents must be submitted.

Please refer to the detailed submission processes IRB.PRO1 (for submission requirement process) and IRB.PRO2 (for Classroom projects)

The following is a list of Initial applications. One application should be submitted from the following list depending on the type of submission for review:

- **Initial Protocol Application**, **Biomedical Research** – *for all research projects that require Full or Expedited review, please see review criteria in Section 1.2 detailed below*
- **Initial Protocol Application**, **Social Behavioral Research** – *for all research projects that require Full or Expedited review, please see review criteria in Section 1.2 detailed below*
- **Protocol Exempt Application** – *for all research projects that fall under an Exempt review, please see review criteria in Section 1.2 detailed below*
- **Classroom Project Application** – *for all student research projects as part of a classroom project, the faculty instructor must complete an application and lists all student projects*

LAUMC-RH Research Signature Page *– the PI must complete and secure the relevant signatures and submit along any of the above applications, if the research project is to be conducted at LAUMC-RH*

Below is a complete list of documents to be submitted along with the relevant IRB Initial application, as applicable:

- Completed and signed "Research Proposal Submission Form" –for submission by an LAU faculty, student or staff
- Completed relevant LAU IRB Application
- LAUMCRH Signature page, for all research projects to be conducted at LAUMCRH
- A detailed protocol or research project *(please refer to section 1.1.4)*
- Grant Application / study contract and/or Clinical Trial Agreement (CTA) including detailed budget information
- Informed consent form(s) including any short forms and translations; *assent form for research involving children*
- Recruitment materials (cover letters, brochures, email notices /referrals, advertisements including translations
- Research Instruments e.g. diaries, surveys, questionnaires, Quality of Life handouts, telephone scripts, etc
- Educational materials including information sheets, study guides
- Investigator's Brochure, Product Monograph, Package Insert, or Device Manual
- Product - New Drug Application or Investigational Device Application
- Indemnification documentation / Insurance, if applicable (for drug and device studies)
- Study material including case report form and data collection tools
- Human Subject Protection training certificate for all study personnel, valid within 3 years from the date on the certificate (*Protecting Human Subject Research Participants*)
- Curricular Vitae for the Principal Investigator and any Co-investigator involved in subject contact
- Investigator Financial Disclosure Form completed and signed for all PI and other investigators, only for funded/sponsored studies

1.1.3 IRB required application following IRB initial review and approval

During the course of the research project and following initial IRB review and approval, the PI should notify the LAU IRB of any changes that might occur during the course of the study.

Below is a list of applications required, as applicable:

- **Continuing Review Application** – *for all research projects that have been approved under Full or Expedited review and requires renewal to continue past expiry date noted in the Approval letter*
- **Protocol Amendment application** – *for all research projects where the PI intends to amend the protocol, informed consent, any change to the research project procedures as detailed in Section 1.2*
- **Request for Protocol Closure Form** – *for all research projects that have completed, closed, suspended or terminated as detailed in Section 1.2*

1.1.4 The Research Project Document – Research Protocol

PI carries a great degree of responsibility for the conduct of research. In general, a well-written protocol includes the following information – ***See supporting documents - Research Protocol Template, for easy reference:***

- Study rationale and objectives (including background information)
- Eligibility criteria (study population / inclusion and exclusion criteria)
- Study design and methodology - procedures to follow

- Potential Risks and Benefits
- Measures to safeguard participants from known and possible risks /hazards
- Endpoints that will be used to evaluate responses and data collected
- Assessments that will be conducted to gather data and how data will be handled and managed
- Adverse event management and reporting, as applicable
- Types of statistical and clinical analyses that will be performed to evaluate the significance of the results

1.1.5 Acknowledgement receipt – Office of the IRB

The administrator (s) at the LAU IRB office will confirm receipt of each submission within 1-2 working days. They will notify the PI or coordinator of any missing documents. Only complete submissions will be assigned a reviewer.

1.1.6 Coordination with other offices for Sponsored and Funded Research

The LAU IRB office coordinates with relevant offices within LAU and LAUMC-RH responsible for overseeing sponsored and funded research agreements and grants and notifies relevant offices when LAU IRB approval has been granted. ***Please refer to the detailed submission processes IRB.PRO1 (for the relevant steps)***

PROCEDURE 1.2 – TYPES OF REVIEW

Each submission undergoes either full or expedited review as summarized in the following table and detailed below:

Full Review	***Expedited Review***
○ **Initial Applications** ○ **Protocol Amendment (major changes)** ○ **Continuing Review**	○ **Initial Applications (including Exempt)** ○ **Protocol Amendment (minor changes)** ○ **Continuing Review** ○ **Exemption Determination**

1.2.1 Request for Full review

A research project submission is subject to full review unless it is classified as minimal risk and fulfills criteria under expedited review or fits exempt criteria *(refer to Supporting Documents)* as determined by the IRB.

- **Initial Protocol Application**

The PI must submit **one original hard copy and one electronic copy** of the applicable *Initial Protocol Application* and all required documents, as outlined in the form. The PI selects the appropriate application depending on the research project, whether it is Biomedical or Social Behavioral. The LAU IRB follows a Primary and Secondary review system before taking the submission to a convened meeting. Following full review, the IRB makes a decision at a convened IRB meeting.

- **Amendment to a previously approved research project**

An amendment to a protocol is sometimes necessary in order to improve the scientific merit of the study, ensure the safety of human participants, or capture an administrative change in the research protocol. A major amendment undergoes a full board review while a minor amendment receives an expedited review. However, in both scenarios the IRB must review and approve the changes.

Any amendment to an approved research protocol is required or planned when it includes but not limited to the following:

- A change to the informed consent documents,
- Study personnel,
- Research design, recruitment procedures, study tools etc.
- Advertisement for participant recruitment,
- Funding status

In the above cases, the investigator must submit to the LAU IRB one original hard copy and one electronic copy of the completed ***Protocol Amendment Application*** together with a revised copy of the pertinent original documents (e.g. protocol, consent form, questionnaire, or advertisement) with the changes identified or tracked in the documents. The PI must provide a rationale for the proposed modifications and or changes. ***No protocol amendments /changes may be initiated without prior IRB approval.***

- **Continuing Review**

Through continuing review, the IRB gains an overview on the progress of an on-going study and its adherence to the LAU Laws and Policies and Procedures regarding human subjects' participation in research and their protection. During a continuing review, the IRB will re-assess the risk-benefit ratio of each study.

Therefore, all research projects that involve an intervention and/or interaction with human participants are reviewed ***once per year***, unless otherwise specified in the original approval letter.

The PI must submit one original hard copy and one electronic copy of the following documents as applicable, but not limited to the following, *a minimum of 30 days before date of expiry of an approved research study*. A complete checklist is present at the beginning of the application.

- Continuing Review Application
- A copy of the latest approved consent form,
- Other required attachments or documents to support the application
- Detailed written progress report
- Any new information that has emerged, either from the research itself or from other sources that could alter the IRB's previous determinations, particularly with respect to risk to subjects.

Note: *If the continuing review does not occur within the timeframe set by the IRB, the research will be automatically suspended. It is important to note that for suspended research, enrollment of new human subjects cannot occur; continuation of research interventions and interactions in already enrolled human subjects should only continue when the IRB or the IRB Chair finds it in the best interest of the individual human subject to do so.*

1.2.2 Request for Expedited Review

- **Initial Protocol Application**

The PI must submit **one original hard copy and one electronic copy** of the applicable *Initial Application* and all required documents, as outlined in the form. The PI selects the appropriate application depending on the research project, whether it is Biomedical or Social Behavioral. The primary and secondary reviewers evaluate the submission on behalf of the IRB to determine whether the protocol is eligible for expedited review based on the criteria (as detailed in the Appendix section) or if it requires full board review at the next convened IRB meeting. If the research project fits expedited review, the research project is reviewed and a letter of Approval, issued by the IRB, will be sent to the PI to initiate the study following review and approval.

- **Continuing Review**

The PI must submit one original hard copy and one electronic copy of the completed ***Continuing Review Application*** and all required documents, as outlined in the form. The continuing review of IRB-approved research may be conducted using expedited procedures in the following instances:

- If the project was previously reviewed and approved using the expedited procedure and conditions have not changed such that the research would no longer be eligible for expedited review (e.g. protocol change, or experience shows the research to be of greater than minimal risk).
- If conditions have changed to make the research eligible for expedited review under the relevant criteria and the overview confirms the research to be of no greater than minimal risk.
- If the research is now: (a) permanently closed to the enrollment of new subjects, (b) all subjects have completed all research-related interventions, and (c) the research remains active only for long-term follow-up of subjects.
- If no subjects have been enrolled (at the local site) since the initial approval and no additional risks have been identified.
- If the study interventions and data collection are now all over and the *only* remaining research activities are limited to data analysis.
- If the research is not conducted under an investigational new drug application or an investigational device exemption, **and** the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk, and that no additional risks have been identified since IRB review at a convened meeting.

Note: *If the continuing review does not occur within the timeframe set by the IRB, the research will be automatically suspended. It is important to note that for suspended research, enrollment of new Human Subjects cannot occur; continuation of research interventions and interactions in already enrolled Human Subjects should only continue when the IRB or the IRB Chair finds it in the best interest of the individual Human Subject to do so.*

1.2.3 Request for Exempt Review

The PI must submit **one original hard copy and one electronic copy** of the completed ***Protocol Exemption Application*** and the required documents for review, as outlined in the form. If the application is complete and meets the exemption eligibility criteria (as detailed in the Appendix section), it will be either reviewed by the IRB chairman or designee for confirmation of the exempt status otherwise the application is returned to the PI requiring further information or clarifications. In addition, the IRB is notified at convened meetings and the exemption documented in IRB records. A letter of Exemption issued by the IRB will be sent to the PI to initiate the study.

1.2.4 Completion, Suspension, and Termination

Investigators must notify the IRB once the study status has changed by completing the ***Request for Protocol Closure Form***. The following lists the different possibilities of study status:

- **Completion**—of a study means that all research participants have completed the study and research-related activity has been stopped, including participant follow-up, data collection, data analysis and/or final reports or publications. The investigator is responsible to notify the IRB once a study has been completed. Any follow up to the study must be re-submitted to the IRB for review and approval.

- **Suspension or Closure**—is an action to pause a study while still operational, either for a definite or indefinite period of time. The action may be requested by the investigator, the sponsor (if any) or the IRB (based on the results of a continuing review or on-site visit primarily related to participant safety). The research project may not proceed unless the suspension is removed. Once suspended, the IRB must review any new information regarding the study in order to remove the suspension and allow the study to continue.

- **Termination**—of a study is to end a research project prior to its previously expected completion date (early termination), or to end a study that was never initiated, or to end ***expired research*** where the investigator does not respond to the IRB's correspondence related to research project renewal within the determined timeframe. Once terminated, all study activities must cease.

PROCEDURE 1.3 – IRB DELIBERATIONS AND DECISION

1.3.1 IRB Discussions

The IRB review and decision for research projects that fall under Expedited review process (for research projects that fit Exempt or Expedited categories) are discussed with the IRB Chair and approval is granted accordingly.

The IRB discussions regarding research projects that require full board review occurs only during a convened meeting (at a full review). After initial presentation/review from the primary and secondary reviewers, the IRB members consider whether the research project is well-designed and possesses complete information regarding the design and scientific rationale underlying the proposed research.

The IRB considers the ethical, scientific and feasibility aspects of the proposed research when assessing research project submissions. It uses the following criteria when assessing research projects as summarized below:

- ***Scientific Validity***: The IRB reviews the use of procedures which are consistent with sound research design, based on justification of the research and which do not unnecessarily expose subjects to risk.

- ***Levels of Risk and Favorable Risk/Benefit Ratio***: The IRB identifies whether the level of risks or discomfort, are reasonable with respect to anticipated benefits, if any and risk is identified as physical, psychological or social / economical. Practically, all research involves some risk even though it might be very minimal, such as slight discomfort in answering certain personal questions, some embarrassment over one's performance on a certain task etc. the IRB will assess the extent to which researchers have identified those potential risks and to what extent have they identified to minimize them. Furthermore, the IRB conducts a ***risk/benefit analysis***, which involves a careful evaluation of predictable risks and burdens in comparison with foreseeable benefits to the subject or to society, in order to assess the ethical validity of a research project prior to its initiation. In order for a research project to be considered ethically sound, risks must be minimized and potential benefits must be enhanced in order to yield a ***favorable risk/benefit ratio***. Some common risks include deception, inducement to participate or coercion, disclosure of personal information including audio and video taping.

- ***Equitable Selection of Subjects***: To determine the proper recruitment of the appropriate participant population, the IRB evaluates the purpose of the research, the eligibility criteria, the expected outcome of the research, the inclusion of vulnerable populations and the special considerations provided to these participant groups.

- ***Additional Safeguards for Vulnerable Subjects***: When some or all of the subjects are likely to be vulnerable to coercion and undue influence, such as children, pregnant women, human fetuses and neonates, cognitively impaired persons, prisoners, additional safeguards must be included in the research protocol to ensure protection of the rights and welfare of these participants.

- ***Informed Consent Requirements***: The IRB ensures that an effective and voluntary informed consent process will be implemented and that it is appropriately documented and conducted prior to any research related procedure. It also ensures that research projects that require the use any surveys, questionnaires, interview scripts, etc., may be waived from a signed informed consent form, has all the relevant information of an informed consent at the beginning of these documents.

- ***Privacy and Confidentiality:*** The IRB ensures that there appropriate measures put in place to provide confidentiality and security of research information collected and maintain anonymity of participants as applicable

- ***Data and Safety Monitoring***: The IRB ensures that adequate provisions for data monitoring will be instituted in order to ensure safety of human participants and provisions related to confidentiality of personal health information

- ***Payment to Research Participants***: The IRB ensures that no payment is implemented as part of coercion for participating in a research project.

1.3.2 IRB Decisions

For research projects reviewed by Expedited Review, the reviewer recommends the decision on the project to the IRB Chair and final decision is taken.

For research projects that require a full board review, a formal decision by the IRB requires an affirmative vote by a majority of the convened quorum as stated in the IRB Terms of Reference document.

Following a deliberation, the IRB Office will notify PIs in writing regarding one of the following decisions:

- ***Approval—*** If the IRB determines that all of the relevant regulatory requirements are satisfied and no additional changes required to the research project.
-
- ***Approval pending Modification***
    - The IRB may require that the investigator make modifications to the research protocol in order to meet relevant regulatory requirements.
    - The IRB delegate informs the PI in writing of the required modifications, comments, questions, or concerns about the research project and requests a reply and revised documents.
    - The PI's response, including revised documents, will be reviewed by the IRB Chair or a designated IRB member. **All revised documents must include tracked changes or highlighted changes when re-submitting to the IRB.**
    - The reviewer determines whether the modifications required by the IRB have been made and whether the modified documents meets the criteria for approval.
    - The research project may not proceed until the IRB approves the research.

- ***Deferral***
    - When the IRB needs additional information from the investigator in order to determine whether all of the relevant regulatory requirements are satisfied, the IRB will defer action until the information is provided and then review the response at a convened meeting.
    - When the IRB votes to defer action pending receipt of additional information, the PI is notified in writing and provided with a list of questions and concerns that need to be addressed as well as modifications required to the research proposal and or any study documents.
    - The PI is asked to submit a point-by-point response and revised documents to the IRB. **All revised documents must include tracked changes or highlighted changes when re-submitting to the IRB.**

- ***Not Approved***
    - If the IRB determines that the relevant regulatory requirements cannot be satisfied by making modifications to the protocol, the IRB may not approve the proposed research.
    - The PI is notified in writing of the basis for not approving the research project. The decision of the IRB cannot be overruled by any other institutional body. An investigator however, may appeal the decision of the IRB in writing directly to the IRB within 30 days of the review date.

PROCEDURE 1.4– CONFLICT OF INTEREST

The LAU IRB assesses the forms of conflict of interest that could affect the conduct of a research project while reviewing every research project. The PI should be aware and able to identify, manage and resolve potential conflict of interest that may affect the research conduct and review decision. This section guides individuals in identifying and disclosing potential conflict of interest and identifying ways to manage such conflict without compromising integrity.

1.4.1 Disclosure of Financial Conflict of Interest

Investigators are required to disclose financial interests, intellectual property, gifts, any activity that might seem to provide any form of conflict of interest, where such disclosure must be made at the time of submission to the IRB by the completing and signing the ***Investigator Financial Disclosure Form***.

Investigators must ensure that all those individuals who conduct research under their supervision must also adhere with this policy and disclose any conflict of interest with the outside organization by the completing and signing the ***Investigator Financial Disclosure Form***. The IRB ensures that any form of financial conflict of interest of the Researcher or Research staff, which could influence the conduct of research, is minimized or eliminated

All investigators conducting research under the auspices of LAU must ensure the following are disclosed:

- Personal financial interest
- Any activity that might seem to provide any form of conflict of interest
- Intellectual property
- Gifts

Investigators are to disclose the above of:

- The Investigator;
- The Investigator's family member;
- An Organization in which the investigator (or any Family member) has an ownership (even partial) in the organization or entity having the intellectual property of the funding agency

1.4.2 Disclosure of Non - Financial Conflict of Interest

The investigator must disclose non-financial or apparent conflict of interest in the following situations:

- Voting on a research project when the member of the IRB is the Principal Investigator, co-investigator or research coordinator on the study (also noted in the IRB Terms of Reference)

- Voting on a protocol when the member of the IRB has a spouse, child, family member or individual with whom the research project investigator or research coordinator has an apparent conflict of interest

- Voting on a protocol when the Principal Investigator is the IRB member's supervisor or advisor to the study

1.4.3 Financial Disclosure to research participants and the Research Community

1.4.3.1 Investigator must disclose to LAU and the IRB at the following times:

- Research funding submissions
- Research submissions to the IRB, through the Investigator Financial Disclosure Form
- Disclosure as mandated by LAU
- At any point when the investigator or research personnel establish a new outside relationship, or change an existing relations that might create a potential conflict of interest under this policy

1.4.3.2 Individual interests and activities, if applicable, might be also required to be disclosed

- Executive position
- In the informed consent document
- To the sponsor of the multi-center study
- To the research personnel working on the study with the investigator
- In publications or presentations

1.4.3.3 Investigator (s) or his/her spouse, child, family member or individual with whom the research project investigator (s) or research coordinator cannot have the following interest in an Organization and partake in a research project that is funded or supported by that organization such as:

- Equity interest;
- Is a member of the board
- To the IRB of other participating center

PROCEDURE 1.5– REGISTERING A CLINICAL TRIAL

The IRB provides guidance for investigators regarding registering clinical trials on Clinical Trials.gov. The purpose of Clinical Trials.gov is to disclose to the public key information about a clinical trial. It captures significant information about the research project before, during and study results after a study is completed. The U.S. Federal law and regulations as well as prominent journals such as International Committee of Medical Journal Editors (ICMJE) require that a PI register the IRB approved research project on any registry that is a primary register of the WHO International Clinical Trials Registry Platform (ICTRP) or in ClinicalTrials.gov, which is a data provider to the WHO ICTRP. Such registration of clinical trials in a public trials registry must be made at or before the time of first patient enrollment as a condition of consideration for publication

The IRB:

- Requires that the Sponsor registers any sponsored clinical trial
- Recommends that the PI registers any Investigator-Initiated interventional clinical trial on Clinical Trials.gov (as per applicable publication requirements) or WHO international at http://www.who.int/ictrp/network/primary/en/

For additional information, please visit the following link at http://icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html

IRB CHAPTER 2 - RESPONSIBILITIES OF THE INVESTIGATORS AND RESEARCH PERSONNEL

The purpose of this chapter is to describe the role and responsibilities of the investigator and study personnel during the conduct of a research project. It functions as a support for the investigators and study personnel to understand their responsibilities with respect to protecting human participants in research and ensuring the integrity of the data collected. Physicians, faculty, residents, students, personnel and staff at LAU and LAUMCRH can serve as Principal Investigators.

PROCEDURE 2.1 – ROLE AND RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR

2.1.1 Qualifications

The Principal Investigators (PI) must be qualified by education, training, and experience to assume the responsibility for proper study conduct; must meet all the qualifications and training requirements specified by the Institutional Review Board (IRB); and should provide evidence of such qualifications through up-to-date curriculum vitae and/or other relevant documentation requested by the IRB

2.1.2 General Responsibilities

The Principal Investigator has the following general responsibilities:

- **Supervising the Conduct of a Research Project**

  Investigators who conduct research **commit to personally conduct and supervise all study related procedures** (as applicable)**.** The PI may delegate study-related activities to members of the study team, but must adequately supervise study personnel to whom tasks are delegated. The PI should have a plan for supervision and oversight of the research. The degree of supervision depends on the capabilities of the study personnel conducting the research, the nature of the research, and the subject population.

  When supervising the conduct of research involving human subjects, the PI must ensure that study personnel:

  - Are qualified by training and experience to perform study-related tasks that have been delegated to them;
  - Have general understanding and familiarity of the research study and the protocol and are promptly informed of any changes to the protocol; and
  - Follow the IRB-approved research protocol, including the recruitment and consent procedures described in the research protocol.

- **Protecting the Rights, Safety, and Welfare of Research Subjects**

  Guided by the ethical principles of human participant's protection, the PI (and all study personnel under his/her supervision) are responsible:

  - For protecting the rights, safety and welfare of research subjects under their care during a clinical research project.
  - Should be available to study participants in order to answer questions or provide care during the conduct of the research.

- To ensure that all study staff adhere closely to the IRB approved research protocol, as failure to do so may expose participants to unreasonable risks.
- For not commencing a research without adequate resources to protect subjects participating in the research and should stop the research if the resources necessary to protect subjects become unavailable. These resources might include research personnel, space, equipment, time, and availability of medical or psychological care for any problems that arise during participation in the research.

- **Ensuring Adherence to Regulatory Requirements Related to the conduct of Research**

  The PI and all study personnel under his/her supervision are responsible for ensuring that all human-subjects research is conducted in accordance with the IRB approved research protocol, IRB requirements, and all applicable international, federal, local regulations, policies, and requirements.

2.1.3 Specific Responsibilities

The PI must ensure that:

- IRB approval is obtained prior to initiating a research project and a valid IRB approval is maintained for the duration of the research project. If IRB approval is expired, no research procedures should be conducted until the IRB re-approves the research or until special permission is obtained from the IRB to continue previously enrolled subjects because it is in their best interests to do so;
- The research is conducted in accordance with the IRB approved research protocol, including, when applicable, the approved recruitment and consent procedures;
- When informed consent is required, informed consent is obtained prior to the initiation of any study-related procedures;
- When written informed consent is required, informed consent is obtained and documented using the current IRB approved consent form;
- When investigational products are being investigated, they are used only in accordance with the IRB approved research protocol and in addition, they are managed and controlled as required by the local, federal and international policy
- Changes to the IRB approved research protocol and/or the research consent form are not initiated without prospective IRB approval unless necessary to eliminate apparent immediate hazards to the subject;
- Adverse events and unanticipated problems involving risks to subjects or others are reported promptly to the IRB as noted in the chapter related to reporting requirements
- When applicable, Data and Safety Monitoring Board/Data Monitoring Committee or other monitoring group reports are submitted promptly to the IRB for review
- Continuing review is conducted prior to expiration of IRB approval in accordance with IRB Policy; and that when the research has been completed or is being closed out prior to completion, a final continuing review report is submitted to the IRB;
- Comprehensive and accurate research records are retained as required by the IRB and, when applicable, by the sponsor or applicable regulatory agency; and
- Research records are made available to the IRB, the sponsor, and relevant regulatory agencies upon request for monitoring and oversight of the research.

PROCEDURE 2.2 – DELEGATION OF RESPONSIBILITIES

The PI may delegate certain study –related tasks and responsibilities to members of the study team, noting the following four major considerations.

- Appropriate Delegation of Study-related Tasks: The PI must delegate tasks to individuals based on their qualification by education, training, and experience to perform the delegated task.
- Adequate Training of Study Staff
- Adequate Supervision and Involvement in the Ongoing Conduct of the Study
- Complete oversight on the conduct of the research project

The PI must list all members of the study team on the IRB application. Furthermore, the PI can use the "Delegation of Responsibility Log" in Supporting Documents on the IRB website for detailed and documented delegation of responsibility.

IRB CHAPTER 3 - INFORMED CONSENT PROCESS AND ASSENT REQUIREMENTS

The purpose of this chapter is to describe the relevant considerations and requirements for informed consent related to research projects conducted within LAU / LAUMC-RH or by its faculty, students and staff. It includes the elements of an informed consent document, the informed consent process, documentation and records, requirements for special populations, exceptions to general requirements, and re-consenting research participants.

This chapter is adopted from the regulations pertaining to research involving human participants as referenced in the Reference Section of this document.

The **Informed Consent** policies and procedures apply to all investigators and study personnel involved in preparing and/or conducting an informed consent with a study participant including social/ behavioral research projects. Investigators must include relevant elements of the consent document in information sheets and introduction to surveys, questionnaires and interview scripts, as applicable.

PROCEDURE 3.1 – REQUIREMENTS FOR AN INFORMED CONSENT

The standard requirements for informed consent (or its waiver, alteration, or exception) applies to all IRB submissions regardless of the type of review – convened meeting, expedited or exempt.

3.1.1 The Informed Consent Document

The informed consent document is one aspect of the informed consent process; however, it is very important. The Informed consent document must:

- Be written in lay terminology and at a Grade 6-8 readability level. If you are using MS Word to develop the consent document, check the readability via Flesch-Kincaid Grade Level during spell check.
- Use element headings, sub-headings, or bolded first sentences to improve readability, logical, consistent formatting
- Be in a language that is understandable to the participant.
- Not contain any medical or scientific terminology. Please refer to the Glossary of Medical Lay Terminology for assistance in preparing the informed consent document
- Not contain any abbreviations and acronyms
- Be written in the second person: ie: You
- Be free of exculpatory language
- Use lay units of measure instead of metric units: (e.g., describe the amount of a blood draw in teaspoons rather than milliliters).
- Number each page of the document in the form of Page X of Y

Additionally the Informed Consent Document must include **signature and date lines** for:

- Participant
- Person conducting the Informed Consent Process (i.e. the investigator or study team member)
- Parent, guardian, or representative for studies involving children or individuals with impaired decision-making capacity

Note: In some cases, a witness signature line is required for example if a translator is used or if otherwise requested by the sponsor or IRB.

Please refer to the checklist in Section 3.1.2 as a guide while you are preparing your informed consent document. To assist the investigators in preparing the informed consent document, the IRB has generated an Informed Consent Template that addresses the elements (*Refer to Appendix Section*).

3.1.2 Elements of Informed Consent Document

Basic elements are required (45 CFR 46.116 and 21 CFR 50 Subpart B) for all informed Consent forms:

- A statement that the study involves research
- An explanation of the purposes of the research
- The expected duration of the participant's participation
- Study treatment if any and the probability for random assignment to each treatment as applicable
- A description of the procedures to be followed
- Identification of any procedures which are experimental
- A description of any reasonably foreseeable risks or discomforts to the participant
- A description of any benefits to the participant or to others which may reasonably be expected from the research. If none, state so
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the participant
- A statement describing the extent, if any, to which confidentiality of records identifying the participant will be maintained
- For research involving more than minimal risk, an explanation as to whether any compensation, and an explanation as to whether any medical treatments are available, if injury occurs and, if so, what they consist of, or where further information may be obtained
- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled, and the participant may discontinue participation at any time without penalty or loss of benefits, to which the participant is otherwise entitled
- An explanation of whom to contact for answers to pertinent questions about the research and research participants' rights, and whom to contact in the event of a research-related injury to the participant
    - ( ) Research Qs
    - ( ) Rights Qs
    - ( ) Injury Qs

Additional elements as appropriate

- A statement that the particular treatment or procedure may involve risks to the participant (or to the embryo or fetus, if the participant is or may become pregnant),
- Anticipated circumstances under which the participant's participation may be terminated by the investigator without regard to the participant's consent
- Any additional costs to the participant that may result from participation in the research
- The consequences of a participant's decision to withdraw from the research and procedures for orderly termination of participation by the participant
- A statement that significant new findings developed during the course of the research, which may relate to the participant's willingness to continue participation, will be provided to the participant
- The approximate number of participants involved in the study

3.1.3 Consent Document Templates and Glossary of Lay Terminology

The consent document must be written so that the intended population is likely to understand the important information and make an informed decision. The IRB website provides Consent Document templates,

which addresses the required elements and provides a Glossary of Lay terminology to assist investigators in preparing the informed consent documents and relevant information to participants. *(Refer to Supporting Documents)*

3.1.4 Informed Consent Process

Informed Consent is an ongoing process in which researchers provide information to potential participants regarding the details of a research project prior to their acceptance and continues throughout their involvement in the research project. **The PI and/or delegate must ensure that the IRB Approved stamped informed consent is used with participants when conducting an informed consent process or when circulating an informed consent document for review**

In order to obtain a valid informed consent, investigators, researchers and responsible study personnel must ensure that

- The participant is competent to begin the informed consent process,
- They have disclosed all relevant information about the research project to the participant,
- The potential participant understands the information and
- He/she is capable of making a decision voluntarily and free from coercion or undue influence.

If the potential participant in a research project is part of a vulnerable population (i.e. pregnant women, cognitively impaired individuals, illiterate, children, or prisoners) special protections are required.

The Principal investigator must consider the following when planning the informed consent process as follows:

- The information that is important to provide to potential research participants, both in writing and during discussions
- The individual(s) who will present the information; must be listed on the application submitted to the IRB
- The timing when this information will be provided to potential participants
- The methods for assessing participants' competency
- The individuals who will obtain the potential participants' signature or agreement

3.1.5 Documentation of Informed Consent

Documentation serves as proof that the informed consent process has taken place and also as a record that the participant has agreed to participate in the research. The PI must document Informed Consent by using an IRB-approved written consent document that is:

- Signed and dated by the subject or the subject's representative
- Signed and dated by the PI (or delegated study staff if approved by the IRB) who obtained the consent and
- Signed and dated by a witness, when applicable (required when a subject or subject's representative is illiterate or when the IRB authorizes the use of a short form written consent procedure for limited English/Arabic speaking individuals or use of a translator).

Signing the consent form is merely documentation that the full informed consent process has taken place and should not be considered the only necessary step in the process. The delegated study staff who obtained the consent must also document the obtaining of the consent in the study file as applicable. The signed original informed consent document must be filed in the study file with a copy of the signed document

given to the participant or participant's representative. In the event that the study is conducted at LAUMC-RH, a copy of the signed consent document must also be placed in the medical records.

3.1.6 Verbal Consent and Information Sheets

- Consent to participate may be obtained verbally when the IRB has approved a waiver of documentation of consent as stated in Section 3.3. Verbal consent requires that all of the information that is normally provided in written form is provided either orally or in writing and the participant agrees to enroll verbally or behaviorally. The only difference in verbal consent is that there is no "informed consent form" for signature. Verbal consent should be documented in either the written study record. Participants should be provided with an information sheet as described below except in cases where it is not possible, such as phone and email surveys, or if possession of the information sheet would increase the risk level for the participants. In the latter case, contact information for the investigator and IRB may be provided *(Refer to Supporting Documents).*

- When documentation of consent has been waived by the IRB as detailed in Section 3.3, investigators are still expected to provide consent information to participants in writing through an "information sheet." Information sheets provide the same information as would be required in an informed consent form with the exception of a location for the participant's signature. Information sheets are commonly used as the front page of anonymous surveys and questionnaires. Completion of the survey indicates the participant consent *(Refer to Supporting Documents).*

3.1.7 Special Considerations – Genetic Testing

If a specific research project includes genetic testing, the IRB requires that in addition to the elements of an informed consent stated above, the informed consent form for genetic studies should disclose but not limited to the following:

- What expected information will result from the research and that unexpected findings may result
- Whether extended family will be involved
- Risk specific to this type of testing, what are the implications and limitations
- What information will participants and their family members will receive
- If some information may be given to each participant and in which case
- Whether participants or their family members will be given the choice to receive or not to receive follow up study information, or information about themselves
- Whether there are any psychological risks, social risks
- Any possible clinical implications from the test results
- How data/samples will be handled and steps that will be taken to ensure participant confidentiality
- Steps if participant wishes to withdrawn from a genetic study at any point in time, including withdrawing his/her sample
- Whether or not personal identifiers will be maintained with the DNA specimen or not
- How samples are to be disposed
- Whether samples can be used for other studies
- Secondary use of samples - If participants have consented to storage of samples for future studies, where and how long their samples will be stored and whether they are stored anonymously and whether they have the option of being re-contacted to consider use of their sample in future studies

PROCEDURE 3.2 – CONSENT PROCESS FOR VULNERABLE AND SPECIAL POPULATION

3.2.1 General Requirements – Vulnerable and Special Population

Special considerations must be in place to protect the rights and welfare of potential participants likely to be vulnerable to coercion or undue influence. In certain projects, efforts should be made to recruit and include women and minorities in research projects, however the following safeguards must be employed.

The safeguards employed for vulnerable participants include, among many other strategies,

- Assessing the decision-making capacity of potential participants,
- Securing the involvement of a legally authorized representative,
- Requiring parental permission from a parent/ legally authorized representative and in some studies from both parent, in addition to the child's assent, and ensuring that incentives are not coercive.

3.2.2 Research involving Children

Children (in most jurisdictions those under 18 years of age) do not have the legal capacity to consent independently. However, children should be asked whether or not they wish to participate in the research, usually around the age of seven. The IRB requires additional protections on research involving children, including special consent and assent requirements, as described below (as detailed in 45 CFR 46, Subpart D).

Considerations for Assent by Children

- Research involving children usually requires the use of child assent and at least one parental/guardian consent. The IRB shall make the determination as to whether to require assent of older children before they are enrolled in a research study. Generally, children aged 7 and above may be asked to give their assent for participation
- In determining whether children are capable of assenting, the PI must take into account the ages, maturity, and psychological state of the children involved.
- In cases where the IRB requires assent from children, two documents need to be developed: one for obtaining the parent / representative's consent (Parental permission) and the other, which outlines the study in simplified language, for obtaining the child's assent. If a separate assent form is not prepared, the child should be asked to sign the parental consent form on a separate "assent" line.
- Parent/representative consent and child assent shall be documented by the use of a written consent/assent form approved by the IRB and signed and dated by the parent/child and the investigator obtained the consent/assent. A signed and dated copy shall be given to the person signing the form.

Waiver of Assent and/or Consent

Child assent may be waived by the IRB, upon the PI's request, for certain studies involving treatment for an illness or condition that is available only in the context of research study.

Parental consent may be waived by the IRB, upon the PI's request, for minimal risk research to be conducted in a classroom or if parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children). In this scenario, the IRB may devise an alternative mechanism to protect the child subjects.

3.2.3 Research involving participants with Impaired Decision Making Capacity

A person generally is legally competent to give informed consent to research when he/she understands the difference between treatment and research, understands the risks and benefits of a specific research protocol and appreciates the consequences of his/her participation in research. The following must be considered when planning to include participants with impaired decision making capacity:

- A qualified professional, who is not part of the research team, must first assess the individual's competency and determine in writing whether he/she is competent to give informed consent.
- A person with impaired decision-making capacity who cannot give informed consent may participate in research only after the investigator has obtained consent from a legally acceptable representative.
- The representative's consent shall be documented by the use of an IRB-approved consent form and signed and dated by both the representative and the investigator obtaining the consent. A signed copy shall be given to the person signing the form.

3.2.4 Research involving Illiterate Subjects

- A person who speaks and understands Arabic / English / French, but does not read and write, can be enrolled in a study by "making their mark" on the consent document.
- A person who can understand and comprehend spoken Arabic / English / French, but is physically unable to talk or write, can be entered into a study if they are competent and able to indicate approval or disapproval by other means.
- The consent form should document the method used for communication with the prospective subject and the specific means by which the prospective subject communicated agreement to participate in the study.
- If subject verbally agrees to participate in the study, if capable to do so, the subject signs or marks an X to signify consent and an impartial third party should witness the entire consent process and sign and date the consent document.

3.2.5 Research involving Pregnant Women

The IRB requires that additional protection provided to pregnant women involved in research (as detailed in 45 CFR 46, Subpart B). In particular, the following considerations for informed consent requirements must be satisfied:

Pregnant Women - The consent form clearly explains the reasonably foreseeable impact of the research on the fetus, and consent will be obtained from the appropriate individuals as follows:

- The pregnant woman or her legally authorized representative if: i) The research holds out the prospect of direct benefit to the pregnant woman, or, ii) The research holds out the prospect of a direct benefit both to the pregnant woman and the fetus; or iii) The research does not hold out the prospect of direct benefit for the woman or the fetus, but the risk to the fetus is not greater

than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.

- The pregnant woman and the father if i) The research holds out the prospect of a direct benefit solely to the fetus unless the father is unavailable, incompetent, or temporary incapacitated, or the pregnancy resulted from rape or incest. In cases where the father is not reasonably available, a statement to this effect must be signed by the mother.

- For minors who are pregnant, assent and permission are obtained in accordance with the provisions of research involving Children as noted above.

3.2.6 Research involving Employees and Students

Employees, students, and trainees at LAU and/or LAUMC-RH and other facilities under the jurisdiction of the IRB are considered vulnerable participants, in particular because of the risk of coercion and undue influence. The IRB has the same standards for approving research involving these groups as other vulnerable participants. Please refer to the LAU IRB Policy.

3.2.7 Research involving Prisoners

When dealing with prisoners, the PI must ensure the safety and confidentiality of the interview location. The PI must also secure a written informed consent from the prisoner; elements of informed consent as detailed at the beginning of this chapter and as detailed in 45 CFR 46, Subpart C

Informed Consent should explicitly state confidentiality of information and ways in which statements or data collected cannot not be used directly or indirectly as legal evidence against the research subject or anyone else. In case of minors, parents and/or legal guardians should provide written consent as well.

Furthermore, the PI must ensure appropriate approvals from the relevant government ministries and/or prisoners' facilities. In Lebanon, the Ministry of Interior and Municipalities (MOIM) remains in charge of prison management. The PI must, therefore provide the approval for MOIM's facilitation of interview's safety and location. Furthermore, the PI must provide approval from all relevant governmental ministries and centers / facilities where the study will be conducted.

PROCEDURE 3.3 – WAIVER OR ALTERATION OF INFORMED CONSENT REQUIREMENTS

3.3.1 Waiver or Alteration of Informed Consent Process

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 criteria under 45 CFR 46.116(c) or 46.116(d) are met. To approve such a request under 46.116(d), 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.

In some cases, research may involve some form of deception. In this case, the investigator may, with protocol-specific justification, request an alteration of the consent processes. The IRB may approve the research, including the request to alter the requirements of the informed consent if the investigator demonstrates that deception or incomplete disclosure is necessary to address concerns relating to participant protection, and in which case debriefing will occur after data collection

3.3.2 Waiver or Alteration of Informed Consent Documentation "waiver of signature"

The IRB may ***waive*** the requirement for documentation of Informed Consent with a signed written Informed Consent document for some or all Participants associated with a research project, when requested by the PI, and it finds one of the following (as detailed in section 45 CFR 46.117):

- The only record linking the subject and the research would be the consent document and the principal risk to participants would be the potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern whether such a link is made.

- 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.

Waiving the requirement for a written form **does not waive the requirement for informed consent**. Participants must be informed of the nature of the research, and their consent (or the consent of their representatives) must be obtained whenever appropriate. This is typically granted in circumstances in which participants are provided information about the study but a consent discussion does not occur such as online studies, surveys sent to participants via e-mail, and other types of research for which an informed consent process is not practical.

Although there is no direct interaction with participants, participants are given relevant information about the study and a chance to accept or decline participation via responding or not responding by completing the actual survey or questionnaire. Similar to an oral consent script, the email contact script, mailed contact letter or introduction on the survey or questionnaire itself should include information regarding the nature and duration of study procedures, risks and benefits, alternatives, cost to participants, voluntary participation and withdrawal without any loss of benefit and confidentiality of the data collected *(Refer to Supporting Documents - Sample Introductions to Surveys and Questionnaires).*

Even if a waiver of documentation is granted by the IRB, the investigator must provide the participant with all of the information described in section 3.1.2 required to constitute a complete and appropriate consent

It is important to note that for studies using investigational drugs, the FDA Regulations do not provide for a waiver or alternation of the informed consent process; the only exceptions to the informed consent requirements are for clearly defined circumstances of emergency use of a test article

PROCEDURE 3.4 – RE-CONSENTING RESEARCH PARTICIPANTS

It is the PI's responsibility to ensure research participants are provided in a timely manner with any new information about the research project. This includes any changes related to their participation, and any new findings that have developed during the course of the research project that may influence their willingness to continue participation or that might affect their long-term health after completion of study participation.

Any changes to the informed consent and research project must be submitted to the IRB for review and approval before implementation. The IRB will determine the process for disclosure of the significant new

information to the participants—based on the review of the new information, the new risks identified and the overall risks to the research study—and will then inform the PI of the process for disclosure following review of the new information presented.

The following list of significant new information or risks that require informing the participants and re-consenting during the course of the study includes but is not limited to:

- Increase in the frequency and/or severity of the procedures stated in the approved research project/informed consent
- New risks and adverse event reporting necessitating to revise the informed consent document
- New findings and information on the use of the investigational product, if applicable
- New alternatives to study participation
- Change in Principal Investigator
- The PI and/or other research team member(s) now have a financial interest in the study
- Change in Sponsor, if applicable
- Change in contact information

PROCEDURE 3.5 – ADDITIONAL GUIDELINES FOR ONLINE RESEARCH

The PI must takes special consideration for research to be conducted via the Internet including but not limited to use of emails, electronic boards, online survey and questionnaire soft wares, blogs, websites, etc). Furthermore, PI must use resources that reassures the participant their anonymity, when required, such online soft wares including but not limited to LAU BLUE, Survey Monkey, etc.

PI must ensure the following when planning to conduct research online:

- Presence of an Informed consent script
- Measures to confirm Anonymity
- Measures to reassure Confidentiality and Privacy

PROCEDURE 3.6 – OBSERVATION OF THE CONSENT PROCESS

As part of the IRB's role to protect the safety and well-being of research participants, the IRB, at its discretion, may require a staff member or an outside party to observe the consent process and determine:

- Whether the informed consent process has been appropriately completed and documented;
- Whether the participant has had sufficient time to consider study 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 conveyed in an understandable language.

Typically, the following kinds of selected protocols may be observed, at the discretion of the IRB:

- High risk studies
- Studies that involve particularly complicated procedures or interventions
- Studies involving special or potentially vulnerable populations (e.g., ICU patients, children, etc.)
- Studies involving study staff with minimal experience in administering consent to potential study participants, or
- Other situations when the IRB has concerns that consent process is/may not be proceeding well.

IRB CHAPTER 4 - GUIDELINES FOR CONDUCTING A RESEARCH PROJECT

The purpose of this chapter is to describe the general guidelines for the conduct of research throughout the life of the project. It highlights the processes required for efficient management and reporting of study procedures.

All investigators planning to conduct a research project must maintain adherence to the requirements set forth in this chapter. In addition, they are expected to employ measures to protect the rights and welfare of research participants

PROCEDURE 4.1 – RECRUITMENT PROCEDURES AND PARTICIPANTS' RIGHTS

As part of its oversight for the conduct of research, the IRB evaluates recruitment and participant selection to ensure that they are performed in a fair, equitable and ethical manner. Consideration for recruitment encompasses pre-screening, recruitment incentives, payments, methods of approach etc. Therefore, all recruitment strategies must ensure protection of potential participants' privacy, avoid any undue pressure and provide study related information accurately.

4.1.1 Pre-screening and Recruitment Considerations

The PI must consider the following elements while preparing the research protocol and when planning to identify research participants:

- ***Relevant Population*** —whether one can secure the appropriate sample population from the existing community
- ***Benefits*** —to the objective, the purpose of the study, the study team, and most importantly the potential participant(s)
- ***Barriers***—that may delay the process of subject recruitment
- ***Strategies*** - the selection of participant recruitment and retention strategies
- ***Sample size***—determining a statistically valid sample size
- ***Inclusion/exclusion criteria***
- ***Informational material***
- ***Recruitment Timelines***—whether over the course of the research project or over a certain period
- ***Timing of the consent process***, depending on the objectives of the research project

4.1.2 Recruitment Methods

The PI must consider the methods intended to be followed for approaching participants to take part in a specific research project and these methods must be detailed in the research proposal. When deciding on the methods to follow, PI's must do every effort to eliminate any form of coercion while approaching participants to take part in a specific research project. These can include:

- *Direct communication by a physician and/or investigator;*
- *Medical record or database search*
- *Recruitment letter*
- *Advertisement*
- *Referrals from other sources*
- *Other, should be detailed in the research proposal*

4.1.3 Advertisement Requirements

All advertisements must be consistent with the protocol and must be approved by the IRB before implementation. Investigators must submit recruitment materials, as they will be implemented, to the IRB for review along with the initial protocol submission, or as applicable.

The following is a reference guide for information to be included in an advertisement *(Please refer to appendices for sample advertisement)*

- The name and location of the institution and center/department conducting the research
- The name of the PI and departmental affiliation, if appropriate
- The word "research"
- The wording "you are invited" or "participants invited"
- Statement of the condition under study
- Brief and accurate description of the purpose of the research
- A factual description of the benefits to the subject from study participation
- A brief summary of the major eligibility criteria
- A brief list of the study procedures involved
- A statement of the approximate time commitment required, if appropriate
- A brief description of the payment offered without specifying monetary amount e.g. "study-related transportation costs will be reimbursed"
- Contact name for further information, with telephone number and email address

4.1.4 Special Considerations

Investigators must employ specific considerations when including students, faculty and staff in a potential research project. The investigator must be aware of the LAU IRB Policy highlighting the involvement of students, faculty and staff stating that *"**Faculty, staff and students can be included only in "no more than minimal risk studies", and their time should not be** invaded to the extent of creating conflicts with their scheduled work."*

PROCEDURE 4.2 – RISK AND BENEFIT ASSESSMENT

Investigators are required to assess the risk benefit ratio and ensure that they are developing measures in their research project to minimize those risks and maximize the benefits.

4.2.1 Identification of Risks

Investigators are responsible for identifying all possible types of risk. These risks could be physical, social, psychological and/or legal. All research involves to a certain degree some form of risk, however in some cases it might be very slight where as in others it might have a negative impact on the participant. The IRB will consider the extent to which the researcher has identified the potential risks and in what way the research has adapted measures to minimize those risks as much as possible without compromising or interfering with the validity of the research itself. Here is a list of some of the comment risks that night arise as a result of a specific research project:

- Inducement or coercion to participate
- Deception
- Disclosure of personal identifiable information
- Physical risk

4.2.2 Procedures to Reduce Risks

Investigators are responsible to detail in the research proposal information regarding methods to minimize risks such as:

- Ensure that the projected sample size is sufficient to yield the expected results
- Incorporate adequate safeguards into the research design such as a detailed safety and monitoring plan and a DSMB as applicable, procedures to maintain confidentiality of the data, trained research staff to assist participants and be able to answer to study related questions
- Provide a sufficient information in the research protocol regarding the experimental design and rational behind the proposed research along with supporting information and evidence

PROCEDURE 4.3 – HANDLING INVESTIGATIONAL PRODUCTS

All Investigational Products (IP) must be handled in compliance with the approved protocol and as highlighted in this document and related documents, and based on applicable local regulations including the Lebanese Ministry of Public Health (MOPH). IP may only be used in a research study as described in the IRB approved research protocol

4.3.1 General Considerations

- All IP must be handled as required by the investigational plan and as per the regulations set forth by the Lebanese MOPH
- Supplier of IP is responsible for any form of import/export of IP and must confirm with Good Manufacturing Practices
- Only the PI, identified on the IRB approved protocol, may execute a request in his/her name, for transfer of IP
- The protocol submission to the IRB must contain information how the IP is handled before, during and after a study
- The PI is responsible for ensuring that the IP is received, checked and accounted for, stored, administered and disposed in accordance with the applicable regulations, IRB approved protocol and institutional policy ***(please refer to the LAUMC-RH Policy for Managing Clinical Study Medication at LAUMCRH)***
- The IP must be used only in accordance with an IRB approved research protocol and after obtaining appropriate informed consent
- The IP may only be used by the participant under the PI's personal supervision or under the supervision of a physician as delegated by the PI

4.3.2 IP Handling requirements

The PI can delegate one or more of its duties for handling IP, however the PI is the ultimate person responsible for the overall management of the IP.

IP accountability is a regulatory requirement for all research activities that fall under this category. It involves documentation and compiling records of receipt, storage, dispensing, accountability, disposal/ return of IP. The PI or designee must follow the following guidelines when handling IP:

- Once the IP is received, the PI or designee must be notified in order to inspect and verify the content, confirm and sign off on the content and note any damage or discrepancy

- IP must be stored in a secure location and labeled as IP. Storage facility (namely the pharmacy) must be in compliance with all applicable facility, sponsor, local and international requirements for handling of IP
- The PI must comply with this document as well as pharmacy's internal policies and procedures for handling IP, as applicable
- Appropriate accountability and dispensing logs must be maintain at all times at the storage facility
- Ensure appropriate measures are in place for return or disposal of any unused or returned IP and maintain appropriate documentation of such

4.3.2 Randomization Code Handling requirements

The PI should follow these specific requirements for handling randomization codes:

- In the event the research study is blinded, the PI should follow the appropriate randomization procedures for dispensing IP and should ensure that the code is broken only in accordance with the research protocol. The PI should maintain the randomization codes in a safe location or should be aware of un-blinding procedures in any event necessitating code breaking
- The PI should notify the IRB promptly in the event of un-blinding and breaking the randomization code.

PROCEDURE 4.4 – DATA HANDLING AND DATA AND SAFETY MONITORING

This section describes the scope of handling data, data and safety monitoring in the conduct of a research project. It highlights the requirements for establishing a Data and Safety Monitoring Plan (DSMP) as part of a research project as well as the role of the Data and Safety Monitoring Board (DSMB).

4.4.1 Privacy and Confidentiality of Research Records

The PI is required to maintain confidentiality of personal and identifiable information about research participants and is requested to provide information to the IRB regarding their proposed measures to safeguard the data collected for the life cycle of the project – that is from data collection, to data use, analysis, dissemination, retention and disposal.

The PI must ensure several measures to maintain confidentiality of the data collected and must provide detailed explanations for any limitations:

- Use of code numbers to identify results obtained from participants
- Ensure that participants' name does not and will not appear on any data collection tool
- Keep all source data in a locked cabinet
- Identify, and note on the IRB submission, all personnel who will have access to the data or other identifying information
- Specify in the protocol how records and documents will be handled during the course of the study and once the research project is completed
- Specific permission and coding for participants being audio-taped, video-taped or photographed for the purpose of a research project

In the event the PI will be collecting data anonymously, this means the PI cannot link individual responses with the participants' identity. This applies to data collected via surveys and questionnaires that fall under exempt category B.

4.4.2 Data and Safety Monitoring Plan

A Data and Safety Monitoring Plan (DSMP) is a guiding system and a quality assurance plan for a research project. It prospectively identifies activities to protect the safety of participants and the validity of the data to be collected.

A DSMP must be included in all interventional research projects and are unique to each research project. The type of DSMP and the frequency of monitoring activities should include but not limited to the following considerations:

- Nature, size and complexity of the research project
- Type of study procedures
- Expected risks of the study
- The type of participant population

A Data and Safety Monitoring Plan (DSMP) can include the following components – *you can also refer to the appendix for a table to assist you in developing a DSMP as part of your research proposal*

- Safety monitoring – this is important in order to minimize potential risk to the participant and should include parameters for safety observation, frequency of safety monitoring, appropriate measures for reporting adverse events, stopping rules for terminating participant's involvement in the research project
- Data monitoring – this is conducted to ensure adherence to the IRB approved research protocol as well as the validity of the data collected. This should include informed consent documentation, participant eligibility confirmation and data accuracy verification
- Product accountability – if the study involves the use of an IP, a plan is crucial to account for managing of IP including receipt, dispensing, disposal/return as well as the overall inventory accounting for the IP
- Privacy and confidentiality – the plan should highlight on how data will be protected, who will have access to the study files and what steps will be taken to prevent unauthorized access. Furthermore, in the event biological samples are taken, how to handle confidentiality and privacy.

The National Institute of Health (NIH) requires that a Data and Safety Monitoring Plan include the following essential elements when applying for NIH fund for medicinal research:

- Monitoring the progress of trial and the safety of participants
- Description of the mechanism for reporting adverse events to the IRB, FDA and NIH (that is, to the NLM program official responsible for the grant)
- Plans for assuring data accuracy and protocol compliance.

https://www.nlm.nih.gov/ep/dsm.html

4.4.3 Data and Safety Monitoring Board

All clinical studies require safety monitoring throughout the duration of the research, but not all studies require monitoring by a Data and Safety Monitoring Board (DSMB). DSMBs may be critical for studies intended to save lives, prevent serious disease progression, or reduce the risk of a major adverse health outcome. DSMBs are particularly important in studies where interim data analysis is required to ensure the safety of research participants *(as noted by NIH Data and Safety Monitoring Policy / WHO - Requirement – refer to reference section).*

If there is no DSMB set up, the IRB may request the formation of a DSMB, on a case by case basis, as follows:

- Typically before a study begins
- Based on the complexity of a specific research project
- Depending on the level of risk to the participants

Please contact the IRB for further details

PROCEDURE 4.5 – RECORD KEEPING AND RECORD RETENTION

Record keeping and retention of complete, accurate, and retrievable research data is essential for verifying the quality of study data, demonstrating investigator compliance with Good Clinical Practice (GCP) guidelines and applicable regulatory requirements while ensuring the integrity of study data.

4.5.1 Study Document Management

Investigators are advised to understand and adhere to the following study document management requirements:

- The PI should ensure the accuracy, completeness, legibility, of all research-related information in order to be able to reconstruct the research and sequence of events, at a future date.

- Any change or correction should be made by crossing a straight line through and should be dated, initialed, and explained (if necessary) and should not obscure the original entry; this applies to both written and electronic changes or corrections.

- All study-related documents must be available for audit/inspection by the IRB and other relevant regulatory authorities, as required.

4.5.2 Essential Documents

Essential documents are generated throughout the various stages of a study and must be maintained by study personnel. In general, investigators should establish **two categories of essential documents for each study**, as follows:

- Regulatory Documents include, not limited to the following:

    - The IRB-approved Protocol (all versions)
    - All IRB Study-related Correspondence and Documentation
    - All Study Site Personnel-related Documentation
    - All Study-related Logs
    - Laboratory Documents
    - Data Collection Documentation
    - All Study-related Agreements and Contracts
    - Monitoring Documentation and Monitoring Log, as applicable
    - Other Study Site and Study Team-related Documentation
    - Clinical Study Report or Statistical Analysis (at study completion)

- Study file for each participant

    - Case Report Forms (CRFs) and supporting data including, for example, signed and dated consent forms and medical records (progress notes of the physician, the individual's chart(s) and accompanying notes).
    - Documentation that informed consent was obtained prior to the individual's participation in the study.
    - Original signed copies of informed consent forms

The Essential Documents Summary Table (according to ICH-GCP Section 8) for clinical studies—included in the Appendix—provides a complete list of essential documents and includes a description of the purpose and/or requirement of each document and who is responsible for retaining each document.

4.5.3 Record Retention

The following must be taken into consideration upon closing a research project

- Research records must be retained for at least **3 years** from the time the study has been completed (or longer depending on regulatory/sponsor/funding agency requirements, type of research, and archival/historical value). In many instances, most investigators retain research data and records for a longer period than the minimum requirement.
- In addition to this requirement, researchers should be aware of, and adopt, the relevant practices/codes within their research discipline that establish norms or best-practice for the retention of research data and records. For example, research records from clinical trials must be retained for a minimum of fifteen years from the date of termination of the study and preferably for the lifetime of the product.
- PI is responsible to document the location of study files after a study has been completed/closed
- Confidential research data and records must be destroyed in the most effective way possible in order to ensure complete destruction of the information. For example, paper format should be shredded, electronic data/records should be destroyed by reformatting or rewriting, data and records on audio-visual tapes can be subject to a 'magnetic field bulk eraser' to remove the recording.

IRB CHAPTER 5 - REPORTING REQUIREMENTS

The purpose of this chapter is to highlight what constitute an adverse event (AE) and unanticipated problem (UAP) involving risks to participants. It also states the requirements regarding appropriate timelines for the principal investigators (PI) to report AEs and UAPs to the Institutional Review Board (IRB).

This chapter defines requirements adopted from the OHRP website for managing adverse events.

All investigators conducting research that has been approved by the LAU IRB is subject to the requirements set forth in this policy and procedure.

PROCEDURE 5.1 – REPORTING OF ADVERSE EVENTS AND UNANTICIPATED PROBLEMS

5.1.1 General Considerations

Adverse events (AEs) can encompass both physical and psychological harm and can occur most commonly in the context of biomedical research, although on occasion, they can occur in the context of social and behavioral research. AEs may be the result of:

- The interventions and interactions used in the research;
- The collection of identifiable private information in the research
- An underlying disease, disorder, or condition of the subject; and/or
- Other circumstances unrelated to either the research or any underlying disease, disorder, or condition of the subject

5.1.2 Assessing Unanticipated problems

Unanticipated problem (UAP) is not clearly defined under the regulations for Good Clinical Practice (GCP), however the Office of Human Research Protection (OHRP) considers UAP to include any incident, experience of outcome that meets **all** of the following criteria:

- Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
- Related or possibly related to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggest that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

OHRP notes that an incident, experience, or outcome that meets the three above criteria generally will warrant consideration of substantive changes in the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of subjects or others. Examples of corrective actions or substantive changes that might need to be considered in response to an unanticipated problem include:

- Changes to the research protocol initiated by the investigator after obtaining IRB approval to eliminate apparent immediate hazards to subjects;
- Modification of inclusion or exclusion criteria to mitigate the newly identified risks;

- Implementation of additional procedures for monitoring subjects;
- Suspension of enrollment of new subjects;
- Suspension of research procedures in currently enrolled subjects;
- Modification of informed consent documents to include a description of newly recognized risks; and
- Provision of additional information about newly recognized risks to previously enrolled subjects.

Furthermore, there are other types of incidents, experiences, and outcomes that occur during the conduct of a research project that represent unanticipated problems but are not considered adverse events. For example, some unanticipated problems involve social or economic harm instead of the physical or psychological harm associated with adverse events. In other cases, unanticipated problems place subjects or others at increased *risk* of harm, but no harm occurs.

5.1.3 Assessing Adverse Events as Unanticipated Problems

The Principal Investigator must assess the Adverse Event based on the following criteria:

- Whether the **AE is unexpected** – not foreseeable risk associated with the procedure involved in the research that are described in the IRB approved documents or the unexpected progression of the underlying disease, disorder or condition of the participant
- Whether the **AE is related or possibly related to participation in the research**

The first step in assessing whether an adverse event meets the third criterion for an unanticipated problem is to determine whether the adverse event is *serious*.

In this guidance document, as per OHRP and GCP, defines **Serious Adverse Event (SAE)** for interventional research projects as any adverse event that:

1. Results in death;
2. Is life-threatening (places the subject at immediate risk of death from the event as it occurred);
3. Results in inpatient hospitalization or prolongation of existing hospitalization;
4. Results in a persistent or significant disability/incapacity;
5. Results in a congenital anomaly/birth defect; or
6. Based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).

5.1.4 Requirements for documenting Adverse Events

All adverse events must be captured and documented, it is recommended to be documented on a tracking sheet per participant, for each participant who signs an informed consent. *If the research project is a sponsored study, the PI can use the sponsor's form*.

For all **reportable adverse events**, the *Adverse Event and UAP Reporting Form* must be used *(see section 5.1.5 for Reporting Requirements of Internal adverse events and UAP)*. It is recommended to track all AEs reported to the IRB. The IRB may impose additional reporting requirements when it reviews the plan for data and safety monitoring described in the research protocol, on a case-by-case basis.

5.1.5 Requirements for Reporting Internal Serious Adverse Events and Unanticipated Problems

The PI is required to document and report the following adverse events to the IRB within 10 calendar days by completing the *Adverse Event and UAP Reporting Form.* The following diagram from the OHRP website can guide the investigators to assess which adverse events should be reported.

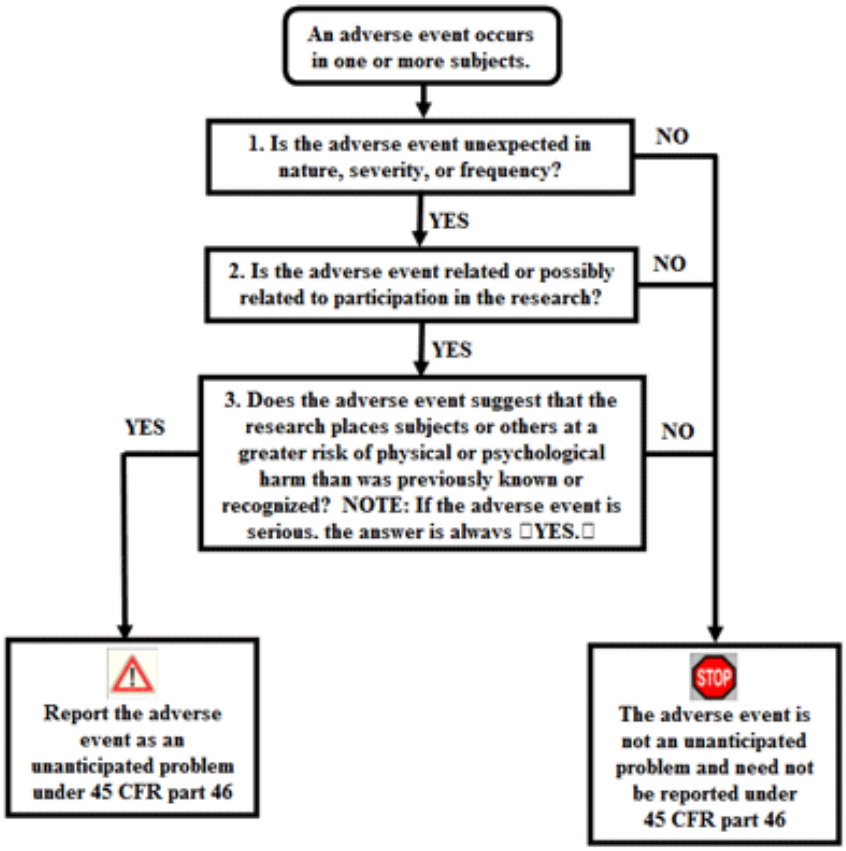

Diagram from the OHRP website

5.1.6 Requirements for Reporting External Serious Adverse Events and Unanticipated Problems (Sponsored Studies)

For research projects that are sponsored, the PI typically becomes aware of an external adverse event upon notification and receipt of a report from the sponsor, coordinating center or other monitoring group, such as a Data and Safety Monitoring Board (DSMB)/Data Monitoring Committee (DMC), or collaborating investigator at another site. These are typically referred to as **IND/IDE Safety Reports** such as CIOMS (WHO) or Medwatch Reports (FDA).

By regulation, sponsors are required to notify all participating investigators and relevant local, federal, and international regulatory agencies (such as FDA , for example) **of any adverse event that is serious, related (or possibly related) and unexpected**.

The LAU requirement for reporting External Serious Adverse Events and Unanticipated Problems is as follows:

- All investigators **must** review the sponsor's safety report and report **all external adverse event reports (blinded and un-blinded)** to the IRB in a consolidated report **twice a year**

- Other external AE reports do not need to be reported to the IRB. The PI must review, initial, date and file these reports with the research regulatory documents. These reports must be made available to the IRB upon request.

PROCEDURE 5.2 – RESEARCH PROJECT DEVIATIONS

This section describes research project deviations and highlights the

- Requirements for requesting research project exceptions from the IRB
- Reporting research project violations to the IRB

5.2.1 Request for Exceptions

The PI must submit a request to the IRB for protocol exceptions, for review and approval. This request must be submitted before initiating the deviation, except when necessary to eliminate apparent immediate hazard / risk to the participant.

5.2.2 Reporting Research Project Violations

The initiation of a protocol deviation prior to IRB submission, review and approval is considered a protocol violation. The qualification of a protocol violation as "major" or "minor" depends heavily on the specific facts of the deviation. The examples of major and minor protocol violations listed below are not all-inclusive. Any of these examples of minor protocol violations could qualify as major if, under the specific circumstances, the violation may impact subject safety, affect the integrity of study data, and/or affect subjects' willingness to participate in the study.

REFERENCES

- OHRP – Code of Federal Regulations, 45 CFR 46
- FDA – Code of Federal Regulations, 21 CFR 50
- ICH Good Clinical Practice – E6
- Office of Human Research Protection website
- US Office of Human Research Protection – Unanticipated Problems involving risks and Adverse Event Guidance
- National Institute of Health
- Operational Guidelines for the Establishment and Functioning of Data and Safety Monitoring Boards (World Health Organization)
- Definitions – Glossary Clinical Trials Terminology

SUPPORTING DOCUMENTS

- LAU Constitution and Bylaws - Faculty Bylaws, *Article X Institutional Review Board*
- LAU Policy for Institutional Review Board
- LAU Code of Ethical and Legal Conduct in Research
- LAUMC-RH Human Research Protection Policies
- IRB Types of Review (Full, Expedited Categories and Exempt Categories)
- Applications and Supporting Documents on the LAU IRB website
- IRB Processes
    - IRB PRO 1. Research Project Submission
    - IRB PRO 2. Classroom Project Submission