INVESTIGATOR'S MANUAL

INSTITUTIONAL REVIEW BOARD

POLICIES AND PROCEDURES

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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 to participate in research given by an individual not competent to give legally valid informed consent.

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 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, determine its scientific and ethical validity and ensure the safety of subjects.

Disability is 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 is 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 document. The PI can submit a request for exempt status, confirmation of which must be granted by the IRB Chairman or designee.

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

Illiterate Subjects are individuals that have 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 primary site, under LAU IRB jurisdiction

Investigational Products are products 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 – are also known as MedWatch Form 3500A under FDA or CIOMS (WHO). These written reports are used by the sponsor to notify the FDA and all participating investigators of any serious and unexpected adverse event that is associated with the research, or of any finding from tests in laboratory animals that suggests a significant risk for human subjects including reports of mutagenicity, teratogenicity, or carcinogenicity.

IRB – Institutional Review Board is an independent body constituted of medical, scientific, and non-scientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a research study by, among other things, reviewing, approving, and providing continuing review of trial protocols and amendments, and of the methods and materials to be used in obtaining and documenting informed consent of the trial subjects.

Major Protocol Violations are violations that may impact subject safety, affect the integrity of study data and/or affect subject's participation in the study.

Minimal Risk is when the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

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

Minor Protocol Violation is 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: the person responsible for the overall conduct of a research project at a site.

Protocol Amendment is a written description of a modification to or formal clarification of a research project.

Protocol Exceptions are 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 Deviations are any alteration/modification to the IRB approved protocol. The protocol includes all research related documents, such as consent form and advertisement.

Protocol Violation is any protocol deviation that is not previously approved by the IRB before implementation.

Randomization is the process of assigning trial participants to treatment or control groups using elements of chance to determine assignments in order to reduce bias (International Council for Harmonization -ICH).

Randomization Code is the code used during randomization which documents the assigned arm or group.

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

Reimbursement: is a 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 and the funding source must be included in the study budget.

Related/ Unrelated Adverse Events *Refer to section 5.1.3.*

Remuneration is payment for participation in research.

Research personnel is anyone assigned by the Principal Investigator to one or more research-related tasks

Risk is the probability of harm or injury (physical, psychological, social or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant.

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

Source Documents are 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 Populations consist of individuals who are relatively (or absolutely) incapable of protecting their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests.Examples are members of a group with a hierarchical structure, patients with incurable diseases or in nursing homes, children and minority groups, refugees, and individuals incapable of giving consent.

PURPOSE AND SCOPE

This document defines the policies and procedures for the oversight of research involving human participants at the Lebanese American University (LAU) and the LAU Medical Center - Rizk Hospital (LAUMC-RH). This document details the required policies and procedures for the conduct of research.

APPLICABILITY

The Investigator's Manual - 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/biospecimens or personal health information. All individuals involved in research must be knowledgeable about the bylaws, policies and the requirements detailed in this document.

In this document, "Research" is defined as a systematic investigation designed to produce or contribute to generalizable knowledge and "Human Participant" is defined as a living individual about whom information is obtained or with whom there is an interaction.

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, as defined above, conducted at LAU and/or the LAU Medical Center - Rizk Hospital (LAUMC-RH) or by LAU Faculty/Staff and students at outside premises must be submitted to the LAU Institutional Review Board (IRB) Office for review and approval **prior** to data collection or study initiation.

The IRB determines if a certain activity is research involving human participants, as defined above, and whether such research is considered exempt under applicable regulations, as defined in this document. In addition, the IRB specifies that such activities are not considered research such as quality improvement, program evaluation, surveillance activities, and others.

Furthermore, this document should be read in conjunction with the LAUMC-RH Policies and Procedures for research to be conducted at the hospital.

PURPOSE AND OBJECTIVES

The purpose and objectives of this document are 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 LAU and/or LAUMC-RH faculty, staff and/or students at outside premises.

Consistent with its purpose, the objective of this document is to assist the university in developing its policies, procedures and research oversight based on the ethical principles and regulatory requirements highlighted below, 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
ii) Foster 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 (IRB)

The IRB is 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 responsible for the Investigator's Manual - Policies and Procedures manual.

The primary administrative responsibility for the day-to-day operation of the oversight of research involving human participants lies with the IRB Office.

For any comments or concerns regarding the role of the LAU IRB, its policies and procedures, please contact the Dean of Graduate Studies and Research.

COMPLIANCE WITH THE ETHICAL REQUIREMENTS FOR RESEARCH

The LAU IRB office is responsible for communicating to the LAU and LAU Medical Center – Rizk Hospital leadership and community, through the Dean for Graduate Studies and Research, and ensures that the LAU community abides by the following:

- Commitment to protect human participants / subjects participating in research
- Compliance with LAU Faculty Bylaws and Institutional Review Board Policy
- 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

In the event of Non-Compliance with the IRB requirements, the Principal Investigator should meet with the IRB Administrators in order to resolve such conditions. IRB Approval cannot be granted until non-compliant issues have been resolved.

The LAU IRB Office will notify the Dean of the Graduate Studies and Research in the event of any unresolved serious and continuing non-compliance with institutional, local and applicable international regulations and requirements.

EDUCATION AND AWARENESS

The LAU IRB office mandates that all those involved in a research project be listed on the LAU IRB application and complete the training mandated by the LAU IRB office on the Protection of Human Participants in Research, under CITI training at https://gsr.lau.edu.lb/irb/education-training.php

The LAU 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 through, but not limited to, the following:

- New faculty meetings and orientations
- Individual School orientations
- Hospital grand rounds
- Medical Student Educational program
- Include in the LAU curriculum lectures for master students and senior students
- Quality Improvement - as requested by the IRB

ASSESSING QUALITY, EFFICACY AND EFFECTIVENESS OF THE HRPP

The LAU IRB Office conducts audits, surveys and post- approval 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 applies 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 and procedures are governed by ethical principles described in the following guiding principles and regulatory documents. The LAU IRB follows the regulatory requirements set forth under the U.S Office of Human Research Protection of the Common Rule (45 CFR 46) for research submission and oversight, and the Lebanese Ministry of Public Health (IRB Minister Decision No.141 Date 27/1/2016) for its jurisdiction.

- **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—including informed consent, properly formulated scientific experimentation and beneficence towards participants—were further elaborated 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 the 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 or 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 by judging 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

- U.S. Department of Health and Human Services – Office of Human Research Protection

The Office of Human Research Protection has developed and published a variety of policy and regulatory guidance material to assist the research community in conducting ethical research that is compliant with and follow the DHHS regulations.

- Office of Human Subject Protection website
- Human Subject Protection – 45CFR46
- International Requirements for Human Subject Protection

- Food and Drug Administration

The Food and Drug Administration has developed and published a set of policy and regulatory documents for those that fall under its jurisdiction and must follow the FDA regulations:

- Food and Drug Administration
- 21CFR 50 (Human Subjects)
- 21CFR 56 (IRB)
- 21 CFR 312 (IND)
- 21CFR 812 (IDE)
- Information Sheet Guidance for IRBs, Clinical Investigators and Sponsors
- A Guide to Informed Consent – Information Sheet

- ICH Good Clinical Practice – Efficacy Guidelines (E6)

The first version of the International Council for Harmonization (ICH) Section E6 Good Clinical Practice (GCP) Guideline was finalized in 1996, describing the responsibilities and expectations of all participants in the conduct of clinical trials, including investigators, monitors, sponsors and IRBs. GCP

covers aspects of monitoring, reporting and archiving of clinical trials and incorporating addenda on the Essential Documents and on the Investigator's Brochure.

This harmonized guideline has been amended in 2016 with an integrated Addendum to encourage implementation of improved and more efficient approaches to clinical trial design, conduct, oversight, recording and reporting while continuing to ensure human subject protection and reliability of trial results. Standards regarding electronic records and essential documents intended to increase clinical trial quality and efficiency have also been updated.

- World Health Organization

Standards and operational guidance for ethics review of health-related research with human participants (Document)

- Lebanese Ministry of Public Health

The Lebanese Ministry of Public Health issued a law that requires institutions that conduct research to have an Institutional Review Board responsible for the oversight of research and should follow the requirements set forth under the Ministry Decision No.141 Date 27/1/2016

Ministry of Public Health (Clinical Trials and IRB Authorization)

- National Council for Scientific Research (CNRS)

Charter of Ethics of Scientific Research in Lebanon: Charter that defines the basic ethical and scientific principles for responsible conduct of research (click here to check the Charter)

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 but are 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. **Submission to the IRB and IRB approval 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 Application and related documents (refer to section 1.1.2). This is a mandatory cover form for all research conducted by LAU Faculty / Staff. Principal investigators must also ensure securing the necessary signatures on the form – For faculty, the Chair and the Dean of the School must sign on the form, whereas for Staff, the immediate Supervisor must sign in place of the Dean Signature section.

This form is not required for student projects. For student submission, the advisor must sign on the relevant LAU IRB application noted in section 1.1.2

1.1.2 Preparing and Submitting the Initial IRB Application and supporting documents

Investigators/ Researchers 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 LAU IRB shall not, at any time, provide a retroactive approval for a research already started or completed, with the exception of review of retrospective studies.

Investigators / Researchers can refer to the checklists on the LAU IRB website for guidance:

- IRB Submission Checklist for Faculty and Staff
- IRB Submission Checklist for Students

For Student Research Projects, please refer to Guidance for Student Research Projects and Classroom Projects section 1.1.3

For case reports, please refer to section 1.1.6

Investigators / Researchers shall submit the following documents when requesting approval from the LAU IRB:

- Relevant LAU IRB application, **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*

- **If the proposed research project is to be conducted at LAU Medical Center – Rizk Hospital**, the PI must complete **LAUMC-RH Research Signature Page** and secure the relevant signatures to submit along with relevant IRB application

- **If the proposed research project is to be conducted at the Simulation Center,** the PI must complete **Simulation Center Signature Page** and secure the relevant signatures and submit along with the relevant IRB application

- **If the proposed research project is to be conducted at any site or center outside LAU and /or its affiliates,** the PI must secure the relevant and applicable approvals and submit along with the relevant IRB application. If study is to be conducted outside Lebanon, PI must check with national and local authorities and secure institutions' ethical boards approval where available

- Below is a list of relevant documents **to be submitted along with the relevant IRB application**
    - 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, for sponsored or funded studies
    - 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

- **The investigator must submit all documents electronically, scanned signature pages and all other documents as word documents.** Each application has a list of documents at the beginning of the application to identify what documents must be submitted

Any non-LAU researcher or student seeking to conduct research at LAU or LAU Medical Center – Rizk Hospital or involving faculty, staff or students, must have an LAU Faculty to serve as SPONSOR of the research project.

1.1.3 Guidance for Student Research Projects and Classroom Projects (Information to Students and Faculty)

LAU students conducting research project at the Lebanese American University (LAU) or LAU Medical Center–Rizk Hospital (LAUMC–RH) must receive the necessary approval from the Institutional Review Board (IRB) at LAU as detailed below.

LAU students, conducting their research outside LAU or LAUMC–RH, must receive approval from the IRB at LAU as well as approval from the relevant committee responsible for approval of research involving human subjects where the study will be conducted.

Students are subject to the same requirements and policies set forth for the conduct of research as stated in this document.

There are 2 categories under which student projects fall:

- Category 1- Student Research Project

Student research activities include, but are not limited to, projects that result in undergraduate honors theses, masters theses, or doctoral dissertations.

In this category, student researchers have the same submission requirements as any investigator. They may submit as Principal Investigator (PI) with a faculty advisor as co-investigator, which may be appropriate for new projects where the student has a leading role.

Student researcher, co-investigators (if a group) and faculty advisor / classroom instructors are required to have current research ethics training certification.

- Category 2 – Classroom project

The IRB recognizes that graduate and undergraduate research methodology courses are designed to teach students research skills through a combination of readings, lectures and research activities or projects. The expectation of such research projects is for the student to apply what is being taught (i.e. use skills outside of the classroom) rather than to substantially contribute to existing research literature in a field. Accordingly, the IRB has developed special guidelines for such class projects.

The Class Project Research IRB Application form must be completed and signed by the course instructor and submitted to the LAU IRB Office at least one (1) week before the research is to begin. No student research project involving human subjects may begin until the instructor has submitted the application and it has been approved by the IRB.

An instructor who wishes to make use of this abbreviated review procedure must:

- Diligently review each student's proposal to determine its acceptability
- Submit a complete Classroom Project Application along with all applicable informed consent form and data collection tool for limited review
- Ensure necessary ethical training in respecting the privacy of individuals and the confidentiality of the data. Such training must be listed in the course syllabus and submitted to the IRB
- Ensure that instructor and all teaching assistants have completed the online required online training for the protection of human participants in research and have submitted their completion certificate to the IRB

Instructors are encouraged to contact the LAU IRB for guidance about ways to handle topics such as privacy, confidentiality, informed consent, and professional ethics when class projects are part of the course syllabus. These issues may still remain even when IRB approval is not required, in which case instructors, advisors and their department play an even greater role in providing the appropriate guidance and oversight.

Note: Students planning to use a class-based project as part of an undergraduate senior/honor's thesis, master's thesis, doctoral dissertation, independent study project, or for submitting it for off campus publication or presentation must follow the IRB review procedures before commencing the project (see Student Research Category 1 above)

1.1.4 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 and an explanation on when each must be used:

- **Continuing Review Application** – *for all research projects that have been approved under Full or Expedited review and require **renewal to continue** after the expiry date noted in the LAU IRB 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 during the LAU IRB Approval time period, 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.*

1.1.5 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 as critical points assessed by the IRB– ***See Supporting documents - Research Protocol Template, for easy reference:***

- Study rationale and objectives (including background information)
- Targeted participant population and justification
- Sample size justification
- Eligibility criteria (study population / inclusion and exclusion criteria)
- Methods of recruitment and approaching participants
- Informed consent procedure and process
- 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
- Steps taken to protect participants and measures to ensure confidentiality
- Adverse event management and reporting, as applicable
- Types of statistical and clinical analyses that will be performed to evaluate the significance of the results

1.1.6 Guidance for Case Report Forms

Institutional policies and regulations require IRB approval for all research involving human participants. Case report forms are a unique form of research where the research presents a case about one or a few participants. If the case report can somehow lead to identifying the participant, then appropriate IRB approval and participant consent is required. If the case report does not identify the participant and is a case report of 1-2 participants, then IRB is not required. If the journal requires a letter from the IRB to

confirm that above applies, please contact the IRB and provide all relevant information. Otherwise, IRB submission should be required.

1.1.7 Acknowledgement receipt – Office of the IRB

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

1.1.8 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 contact the GSR office / IRB Office for further details.

PROCEDURE 1.2 – TYPES OF REVIEW

Each submission undergoes either full or expedited review as summarized in the following table and detailed below *(Please refer to Appendix 1. IRB Types of Review)*:

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 as determined by the IRB. Please refer to Appendix 1. IRB Types of Review for details on what studies are considered exempt or fall under expedited review.

- **Initial Protocol Application**

  The PI must submit **all documents by email** including the applicable *Initial Protocol Application* and all required documents, as outlined in the form at least one month prior to the upcoming meeting scheduled (please refer to the meeting schedule on the IRB website). 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.

An amendment to an approved research protocol includes but is not limited to the following:

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

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 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 **all documents by email including** 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 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 **all documents by email including** 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 and designee for confirmation of the exempt status with limited review, 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, or to end research where the risk/benefit ratio or adverse events turns out to be too high, as determined by the PI/sponsor **or** the IRB. Once terminated, all study activities must cease.

PROCEDURE 1.3 – IRB DELIBERATIONS AND DECISION

1.3.1 IRB Review

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, where 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 they have attempted 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 if any, 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, refugees or 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 of any surveys, questionnaires, interview scripts, etc., where signed informed consent may be waived to have all the relevant information of an informed consent at the beginning of these documents.

- ***Privacy and Confidentiality:*** The IRB ensures that appropriate measures are in place to provide confidentiality and security of research information collected, and to 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, however reasonable financial compensation to cover cost of involvement should be acceptable. This is reviewed by the IRB on a case by case basis

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 are 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 meet the criteria for approval.
    - The research project may not proceed until the IRB approves the research.

- *Provisional Approval*

    - The IRB might provide provisional approval to a research protocol in the event an approval is required for funding purposes or to secure clearance from the participating site where the research will occur.

- Once pending documents are provided to the IRB's satisfaction, an official final approval will follow the provisional approval, along with the stamped approved documents.

➢ ***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. However, the investigator may appeal the decision of the IRB in writing directly to the IRB within 30 days of the review date, as noted in Section 1.3.3.

PROCEDURE 1.4– CONFLICT OF INTEREST

The LAU IRB assesses the forms of conflict of interest (COI) that could affect the conduct of a research project while reviewing every research project. COI is defined as 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.

The PI should be aware and able to identify, manage and resolve potential conflicts of interest that may affect 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 and any activity that might seem to constitute 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 individuals who conduct research under their supervision must also adhere with this policy and disclose any conflict of interest with the outside organization by completing and signing the ***Investigator Financial Disclosure Form***. The IRB in coordination with the PI 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 from the funding agency or sponsor

These disclosures pertain to the investigator, the investigator's family member, or 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 Principal Investigator, co-investigator, research coordinator or any research personnel on the study are a member on the IRB

- Voting on a protocol when the investigator, a spouse, child, family member or individual with whom the research project investigator or research coordinator is a member of the IRB and therefore 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 relation 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 disclose in the informed consent document, to the sponsor of the multi-center study, to the research personnel working on the study with the investigator, and in publications or presentations

PROCEDURE 1.5– RESEARCH AT LAU MEDICAL CENTER –RIZK HOSPITAL

The LAU IRB is responsible for the review and oversight of research involving human participants within its affiliated medical centers. The LAU Medical Center – Rizk Hospital has delegated to the LAU IRB and the Assistant Dean of Research at the School of Medicine the governance of human research protection and the oversight of research within the hospital. The governance and oversight as well as the policies developed within the hospital are in line with the new accreditation requirements for hospitals under the Lebanese Ministry of Public Health.

Please refer to the Human Research Protection Policies and Protocol instructions at LAU Medical Center – Rizk Hospital for the conduct of research within the hospital. These documents are available on hospital *laserfiche*.

PROCEDURE 1.6– REGISTERING A CLINICAL TRIAL

The IRB provides guidance for investigators regarding registering with clinical trial platforms. The Lebanese Ministry of Public Health launched the Lebanese Clinical Trial Registry (LCTR) in July 2019. This platform is now an official registry platform recognized as a primary registry under the World Health Organization (and is equivalent to Clinical Trials.gov).

Researchers planning to conduct their own research projects, or Lead PIs on investigator-initiated clinical trials to be conducted within Lebanon, can now register their study under the LCTR platform instead of clinicaltrials.gov. Registering with LCTR is an easy, fast and free of charge alternative to clinicaltrials.gov which might no longer allow registration of projects from Lebanon.

The purpose of LCTR, Clinical Trials.gov or other registering platforms is to disclose to the public key information about a clinical trial. Registration 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 bodies such as the 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.

Important note:

- Please note that some funding agencies might still request that you register under clinicaltrials.gov, please keep that in mind when planning your research project as you might have to register under 2 platforms.
- If you are taking part in a multi-center sponsored study, the sponsor is required to register the study under LCTR and add all participating centers.

The IRB requires that the Sponsor to register any sponsored clinical trial for collaborative studies and the PI to register any Investigator-initiated interventional clinical trial on the LCTR and if required on the Clinical Trials.gov (as per applicable publication requirements).

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

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:

- **Overall responsibilities**

  Investigators and researchers designing their own projects should ensure that their research will most likely develop or contribute to generalizable knowledge. Whereas, investigators that don't design the research project must ensure that the research design is sound and meet the study's objectives

- **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) is responsible for:

  - Protecting the rights, safety and welfare of research subjects under their care during a clinical research project.
  - Being available to study participants in order to answer questions or provide care during the conduct of the research.
  - Ensuring that all study staff adhere closely to the IRB-approved research protocol, as failure to do so may expose participants to unreasonable risks.
  - Refraining from starting research without adequate resources to protect subjects participating in the research and, stopping the research if the resources necessary to protect subjects become unavailable, including 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:

- LAU 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 maintain 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 local, federal and international policies
- 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 Section 5.1 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 LAU 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 introductions 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, one has the option to check readability level during spell check.
- Use element headings, sub-headings, or bolded first sentences to improve readability, and rely on logical, consistent formatting
- Be in a language that is understandable to the participant.
- Not contain any unnecessary 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 the following:

- 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
- A brief explanation of the 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 no benefits are expected, this should be clearly stated.
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the participant
- A statement describing the extent, 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 or 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, and 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
    - Questions related to the Research
    - Questions related to the participant's Rights
    - Questions in case of Injury

Additional elements as appropriate might include:

- 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 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.
- Informed consent is provided in a language understandable to the participant. Furthermore, the participant shall be able to provide oral/written consent as approved by the IRB. In the event that the participant is not capable of providing consent, the participant shall have a legally authorized representative to consent on their behalf.

If the potential participant in a research project is part of a vulnerable population (i.e. pregnant women, cognitively impaired individuals, illiterate, children, prisoners or refugees) 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 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. *(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 – Psychological support and counseling statements

Optional statements to be included in the informed consent form in the event of psychological distress:

We recommend that if you are worried about your health, including your mental health, you should seek advice from the student health/counselling services at your university or call on the hotline 1564 to seek help from the mental health department at the Ministry of Public Health.

We recommend that if you feel any kind of distress, you should seek advice from a health/counselling service or contact the researcher.

We recommend that if you feel any kind of distress while completing the questionnaire, you should seek advice from a health/counselling service or contact the researcher.

3.1.8 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 the following:

- What expected information will result from the research and if unexpected findings may result

- Whether extended family will be involved
- Risk specific to this type of testing, 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 or social risks
- Any possible clinical implications from the test results
- How data/samples will be handled and which steps will be taken to ensure participant confidentiality
- Steps if participant wishes to be withdrawn from a genetic study at any point in time, including withdrawing his/her sample(s)
- Whether or not personal identifiers will be maintained with the DNA specimen or not
- How samples will be disposed if applicable
- 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

Sample of informed consent section for genetic studies:

Please check the appropriate box for blood or tissue sample:

Permitting coded use of biological materials for the proposed study only, with no further contact permitted to ask for permission to do further studies,

Permitting coded use of biological materials for the proposed study only, with further contact permitted to ask for permission to do further studies,

Permitting coded use of biological materials for the proposed study only and anonymized use for any kind of future study.

PROCEDURE 3.2 – CONSENT PROCESS FOR VULNERABLE AND SPECIAL POPULATIONS

3.2.1 General Requirements – Vulnerable and Special Populations

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, inclusion of women and minorities in research projects is desirable, however the following safeguards must be employed.

The safeguards employed for vulnerable participants must 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 parents, in addition to the child's assent, and ensuring that incentives are not coercive.

3.2.2 Research involving Children

Children (in most jurisdictions persons 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 starting at 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 to 11 may be asked to give their oral assent for participation, whereas children aged 12-17 me be asked to give written consent
- 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. In certain cases, both parents must give consent, as deemed appropriate by the IRB. 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. For involving students as research participants, please refer to Section 4.2 of this document.

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 assurance that 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 MOIM's approval for facilitation of interview. 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 determine that:

- 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 are necessary. In these cases, 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 alteration 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 – DEBRIEFING PROCESS GUIDANCE

In certain research projects and primarily in Social and Behavioral Research (SBER), a researcher might find that the use of deception or incomplete disclosure of certain aspects of a research project in an informed consent is a necessary tool for their study to take place. For that matter, a short paragraph should be prepared as a debriefing after data has been collected where deception was approved as part of the research project. This information must be shared with the participants after data collection. The participant has the right to withdraw the collected data. All debriefing information must be also reviewed and approved by the IRB

PROCEDURE 3.5 – 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/or 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 3.6 – ADDITIONAL GUIDELINES FOR ONLINE RESEARCH

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

PI must ensure the following when planning to conduct research online and when uploading their survey/questionnaire:

- Presence of an Informed consent script at the beginning of the survey or questionnaire
- Measures to confirm Anonymity
- Measures to reassure Confidentiality and Privacy

When the study will be sent via an electronic platform such as LAU BLUE, Survey Monkey or other electronic platform, the PI should make sure to either upload the IRB APPROVED STAMPED introductory consent, or add the following statement at the end of the consent section. The statement to be added: "This study has been reviewed and approved by the LAU IRB" where the PI will be required to add the LAU IRB approval reference tracking number. This number can be found on the LAU IRB approval letter.

PROCEDURE 3.7 – 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,
- That the information presented to the participant reflects the content of the consent form and is conveyed in an understandable language.

Typically, the following kinds of studies may be selected for observation, 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 the consenting process may not be proceeding well.

IRB CHAPTER 4 - GUIDELINES FOR DEVELOPING AND CONDUCTING A RESEARCH PROJECT

The purpose of this chapter is to describe the general guidelines for the development and conduct of research throughout the duration 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.

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, and others. 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 the relevant population is adequately chosen
- ***Benefits*** —to scientific knowledge, 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 treating physician and/or investigator;*
- *Medical record or database search*
- *Recruitment letter*
- *Advertisement*
- *Referrals from other sources*
- *Others, 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 potential 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",
- If monetary reward is included, it should not be emphasized or the amount bolded or enlarged.
- 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 the understanding that their time should not be invaded to the extent of creating conflicts with their scheduled work."*

4.1.5 Participants' Rights

Participants shall

- Have the right to know that their privacy and welfare will be protected to the best reasonable manner.

- Have sufficient time to decide whether or not to take part in a research study, and to make that decision without any pressure from the people who are conducting the research.

- Have the right to refuse to take part in the study at all, or to stop participating at any time after they have signed consent and/or begin the study. If they decide to stop participating in the study, they have a right to continued, necessary medical treatment.

- Be told what the study is trying to find out, what will happen to them, what they will be asked to do if they are in the study and if it is a clinical trial, what drug/device will be used in the study.

- Be told about the reasonably foreseeable risks of being in the study.

- Be told about the possible benefits of being in the study.

- Be told whether there are any costs associated with being in the study and whether they will be compensated for participating in the study.

- Be told who will have access to information collected about them, and how their confidentiality will be protected.

- Be told whom to contact with questions about the research, about research-related injury, and about their rights as a research participants.

- If the study involves treatment or therapy:
  - Shall be told about the other non-research treatment choices they have
  - Shall be told where treatment is available should they have a research-related injury, and who will pay for research-related injury treatment.

- Receive a copy of the consent form that they will sign or copy of the information sheet.

- Be able to ask any questions they may have.

PROCEDURE 4.2 – STUDENTS AS RESEARCH SUBJECTS: HOW TO AVOID UNDUE INFLUENCE AND COERCION

This section highlights the key elements a researcher should carefully review when considering approaching students as research participants in order to minimize the possibility of coercion and undue influences.

Although students often provide a ready source of potential research participants to faculty and staff, they are not always an appropriate or representative study sample as compared to other subject groups. Attention should be given as to whether they are being solicited because they are a convenient and accessible sample, rather than as a representative sample for the research inquiry. Furthermore, this is to ensure that students are not unduly influenced to participate due to concerns about grades, favoritism or any other factor of such relationship.

This document is in line with the LAU IRB Policy and provides guidelines to assist investigators who engage in research projects in which students will be asked to take part in a research study.

The following considerations must be followed and incorporated into the research protocol (mainly under study design, recruitment and consent section) and in the relevant submission documents to the LAU IRB.

a. Clear explanation or justification should be provided to the LAU IRB as to why students are the most appropriate participants for the study
b. The research must present no more than minimal risk to the participants.
c. The research represents a potential educational opportunity for participants.
d. The recruitment/consent language contains clear statements to address and minimize coercion and undue influence.
e. The recruitment and/or consent process will be conducted by someone who does NOT have a status relationship with the potential subjects. Therefore, the involvement of a neutral third party may be an effective way to address any perceived coercion or undue influence. The involvement of a third party may only be tasked with collecting and temporarily holding documents and does not need to be added to the study team.

f. If the research is conducted within the classroom setting, the instructor is blinded to the identity of participants - at least until grades are posted.
g. No extra grades or course rewards should be offered to the students who choose be involved in the research.
h. Participants may also be recruited through the posting of LAU IRB approved flyers/ads, or through LAU IRB approved communications sent out to a large group (such as mass mailings like emails or letters).
i. The consent process should be conducted by a coInvestigator who is not involved in grading of course activities as well.

If you have questions on how to minimize the potential for coercion or undue influence in your research and who may be an investigator, please contact the LAU IRB Office for guidance.

PROCEDURE 4.3 – 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.

4.3.1 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 whereas in others it might have a clear 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 common risks that might arise as a result of a specific research project:

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

4.3.2 Procedures to Reduce Risks

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

- Ensuring that the projected sample size is sufficient to yield the expected results
- Incorporating adequate safeguards into the research design such as a detailed safety and monitoring plan and a Data Safety Monitoring Board (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 rationale behind the proposed research along with supporting information and evidence

4.3.3 IRB's assessment of Risk and measure for AE management

The IRB will assess the type of risk and what measures have been considered by the PI to manage any form of Adverse Event (AE) resulting from participating in the research study. For biomedical research

and clinical trials, the IRB will communicate with the PI the need for insurance coverage to cover for any related AE that might occur to the participants as part of their involvement in the study.

PROCEDURE 4.4 – HANDLING INVESTIGATIONAL PRODUCTS

All Investigational Products (IPs) 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

4.4.1 General Considerations

- All IPs must be handled as required by the investigational plan and as per the regulations set forth by the Lebanese MOPH
- Supplier of IPs is responsible for any form of import/export of IPs and must conform to Good Manufacturing Practices
- Only the PI, identified on the IRB approved protocol, may execute a request in his/her name, for transfer of IPs
- The protocol submission to the IRB must contain information how the IPs are 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-Rizk Hospital Policy for Managing Clinical Study Medication)***
- The IPs must be used only in accordance with an IRB approved research protocol and after obtaining appropriate informed consent
- The IPs 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 or following appropriate training as deemed fit by the IRB and the investigator.

4.4.2 IP Handling requirements

The PI can delegate one or more of its duties for handling IPs, however the PI is the ultimate person responsible for the overall management of the IPs ***(please refer to the LAUMC-Rizk Hospital Policy for Managing Clinical Study Medication)***

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 IPs. The PI or delegate must follow the following guidelines when handling IPs:

- Once the IP is received, the PI or delegate 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 maintained at all times at the storage facility
- Appropriate measures must be in place for return or disposal of any unused or returned IP and documentation of such

4.4.2 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 IPs 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 4.5 – DATA HANDLING AND DATA AND SAFETY MONITORING

This section describes the scope of data handling 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).

4.5.1 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 participants' name does 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
- Secure 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.

4.5.2 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 is unique to each research project. The type of DSMP and the frequency of monitoring activities should include the following considerations:

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

A Data and Safety Monitoring Plan (DSMP) can also include the following components – *you can 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 IPs including receipt, dispensing, disposal/return as well as the overall inventory accounting for the IP
- Privacy and confidentiality – the plan should highlight 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, measures to maintain confidentiality and privacy must be described.

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

4.5.3 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 4.6 – COLLECTION OF HUMAN BIOLOGICAL SPECIMENS

In the event investigator wants to collect human biological specimens for research, IRB review is required and may begin when the following are met:

- Systematic investigation designed to contribute to generalizable knowledge
- Study involving the collection of information about a living individual through interaction or intervention, with the individual or access to the participant's private information, medical records, etc.

Examples of biospecimen research requiring IRB review that fall under one of the following review criteria: exempt, expedited, or full board review

- *Prospective collection of biospecimens for a specific research study*
- *Prospective collection and storage of biospecimens for future research use*
- *Secondary use of identifiable biospecimens. Example includes obtaining blood/tissue samples along with identifiers from a biobank or repository*
- *Secondary use of coded biospecimens when the investigator collected the specimens him/herself for another research project*
- *Secondary use of coded biospecimens when the investigator has access to the code that would allow linkage of the specimens to identifiable information*
- *Secondary use of de-identified or coded biological specimens in a project that will generate or collect data that will or may be submitted to the FDA*

PROCEDURE 4.7 – IDENTIFIABLE INFORMATION AND DE-IDENTIFIED DATA

The IRB ensures that appropriate measures are in place to ensure confidentiality and confirm anonymity when dealing with de-identified data. The following data sets can be added to the data being collected as de-identified such as year of birth or age, gender and sample collection or visit date, however the list of identifiers noted below should not be collected unless IRB approval has been secured and appropriate consent has been granted from the participant. In this case data is not considered de-identified.

1. Names (Full or last name and initial)
2. Geographic identifiers: Address (street, city, village, postal code, etc. – initial 3 digits if geographic unit contains less than 20,000 people, or any other geographical codes)
3. Dates (except for years), including date of birth, admission dates, etc.
4. Telephone numbers
5. Fax numbers
6. Email addresses
7. Governmental identification numbers such as social security number, passport number, etc.
8. Medical record numbers
9. Health insurance numbers
10. Account numbers
11. Certificate or license numbers
12. Vehicle Identifiers, license plate and Serial numbers

13. Device Identifiers and Serial Numbers
14. Web Uniform Resource Locators (URLs)
15. Internet Protocol (IP) address numbers
16. Biometric Identifiers (e.g. finger, retinal and voice prints)
17. Full face photographic images and any comparable images
18. Any other unique identifying number, characteristic, or code except the unique code assigned by the investigator to code the data

PROCEDURE 4.8 – 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.

4.8.1 Study Document Management

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

- The PI should ensure the accuracy, completeness and legibility of all research-related information to allow reconstruction of the sequence of events at a future date.

- Any change or correction should be made by crossing a straight line through, 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.

4.8.2 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 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.

4.8.3 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. It is advisable that the researcher maintains all study records for auditing purposes.
- 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 documents should be shredded, electronic data/records should be destroyed by reformatting or rewriting, data and records on audio-visual tapes can be subjected 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 are 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
- Suggestions 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 any of 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 participants 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. This is particular for Biomedical research and Clinical Trials:

- 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

It is recommended that all adverse events must be captured and documented on a tracking sheet per study, 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 that are serious or unanticipated, as detailed above**, 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 and report them 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 / Site specific Serious Adverse Events and Unanticipated (unexpected) Problems

The PI is required to document and report any unanticipated (unexpected) AE and ANY Serious Adverse Events (SAE) to the IRB immediately and promptly followed by a follow up notification with additional information no later than 24 hours after occurrence/realization by email, 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. The PI is required to send follow up information as new information becomes available. The LAU IRB shall notify hospital Risk Management office of such an AE within 24 hours of the IRB being aware of such an event.

Please refer to the hospital specific procedures for managing adverse events

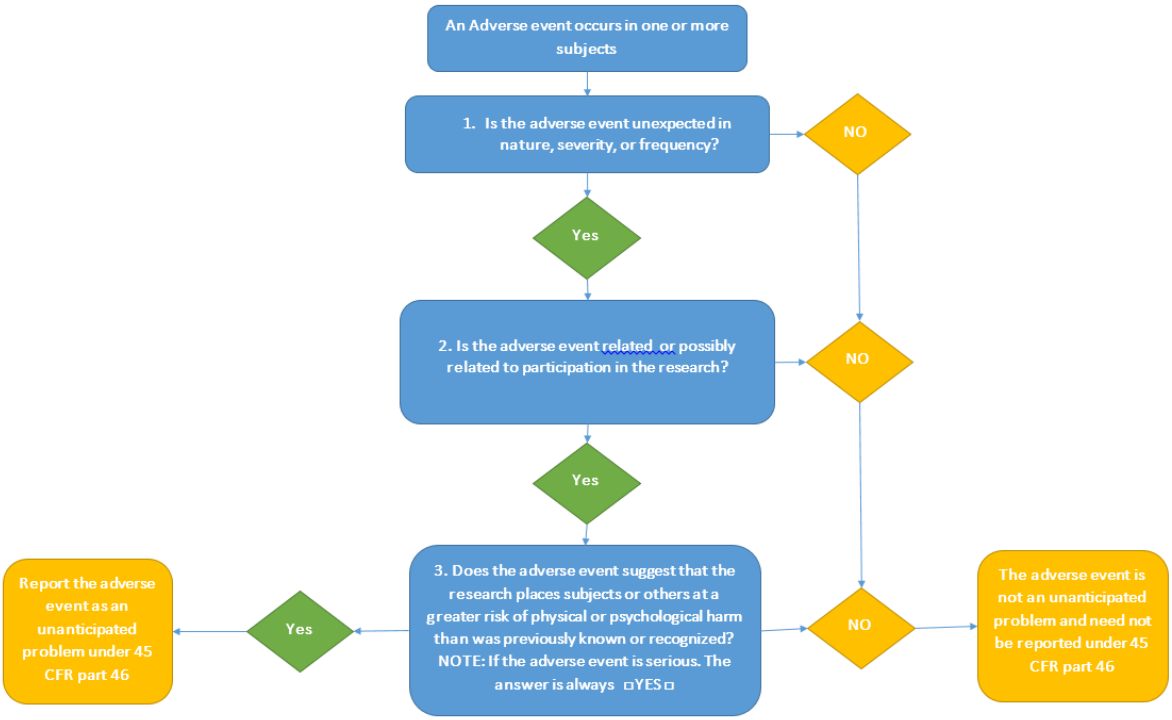

Diagram from the OHRP website

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 following sponsor's safety report: **all external serious adverse event reports (blinded and un-blinded), related (or possibly related) and unexpected referred to as Suspected Unexpected Serious Adverse Reaction (SUSAR) and report** 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.

5.1.7 Requirements for Reporting urgent safety measures or study termination

The PI/sponsor should promptly notify the IRB of any findings that could adversely affect the safety of the participants, impact the conduct of the study/trial or alter the IRB's approval /favorable opinion to continue the trial (as per ICH GCP)

PROCEDURE 5.2 – RESEARCH PROJECT EXCEPTIONS, DEVIATIONS AND VIOLATIONS

Protocol exception, deviation and violation occur when there is a change between the already approved LAU IRB research protocol and the actual performance of the research project. Regulations require that the IRB reviews any changes in the research activity before implementation, except when necessary to eliminate any harm to the participants.

This section describes research project exceptions, deviations and violations and highlights the

- Requirements for requesting research project exceptions or deviations for an already approved research protocol from the IRB
- Process for 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 and deviations, 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. Any 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. The PI must report to the LAU IRB promptly upon being aware of the violation and within no more than 5 calendar days, if the violation is affecting participant safety, otherwise all other violations should be reported within 20 calendar days.

A protocol violation may arise to the level of non-compliance. This occurs when there is a deliberate or inadvertent violation or failure to comply with the regulations for the conduct of research as detailed in this document. Reporting non-compliance to the LAU IRB must be done within 5 calendar days from being aware of the incident.

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
- LAUMC-RH Human Research Protection Policies (on hospital lazerfiche folder)
- Applications and Supporting Documents on the LAU IRB website

APPENDICES

- Appendix 1. IRB Types of Review (Full, Expedited Categories and Exempt Categories)

Appendix 1 - IRB Types of Review

Exempt, Expedited, Full IRB Review

The IRB follows three distinct review types while reviewing research involving human subjects. These types are based on the regulations governing research and relate to the degree of risk to research subjects. For Full and Expedited review, please use the Initial Protocol Application and for Exempt review, please use the Protocol Exempt Application.

Exempt Review

Some human subject research might fall under an Exempt review process. In order to assess if your research project fits one of the exemption criteria, please see list below or 45CFR 46 101 (b) at http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html. The IRB office will make the final determination if your research project falls under an Exempt Review.

Research may be exempt from review when the only involvement of human subjects in the research falls into one of the following categories:

- Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
- Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior unless: (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation. (However, when a study involves children being interviewed, questioned or surveyed, that study must be reviewed by the IRB and may not be exempt. Similarly, studies involving children and observation of public behavior in which the Principal Investigator (or other investigator) participates in the activities being observed must be reviewed by the IRB)
- Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures (e.g. anonymous questionnaire), interview procedures, or observation of public behavior that is not otherwise exempt if: (i) the human subjects are elected or

appointed public officials or candidates for public office; or (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

- Research, involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
- Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.
- Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the federal health authority or food inspection agency

Expedited Review

Some human subject research might fall under an Expedited Review process. The categories for Expedited review process are noted below and can be found at http://www.hhs.gov/ohrp/policy/expedited98.html

Applicability

- Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.
- The categories in this list apply regardless of the age of subjects, except as noted.

- The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects= financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
- The expedited review procedure may not be used for classified research involving human subjects.
- Investigators are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review—expedited or convened—utilized by the IRB.

Research Categories

- Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
    - Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
    - Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
- Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
    - from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
    - from other adults and children2, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.
- Prospective collection of biological specimens for research purposes by noninvasive means. Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions

(including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

- Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

  Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject=s privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.
- Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)
- Collection of data from voice, video, digital, or image recordings made for research purposes.
- Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

- Continuing review of research previously approved by the convened IRB as follows:
    - where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
    - where no subjects have been enrolled and no additional risks have been identified; or
    - where the remaining research activities are limited to data analysis.
- Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

In addition, expedited review is appropriate for minor changes in protocols and consent forms proposed for previously approved research during the period (one year or less) for which approval is authorized. Changes affecting risk, benefit, discomfort, or subject protections are not "minor" changes. Minor modifications include, for example, administrative changes to the protocol, changes to add follow-up calls when gathering initial data by telephone, or certain changes in the scheduling of medications.

Full IRB Review

Human subject research that does not fit any of the Expedited or Exempt review categories will require a Full IRB review at a convened meeting. The IRB meets once a month or as requested by the IRB chairman. Research applications are placed on the agenda and will be discussed at the next scheduled meeting. The IRB chairman might cancel a full IRB meeting if

- There are insufficient number of applications to be discussed,
- Inability to secure a quorum,
- University holiday; or
- Other reasons that may arise that makes a meeting unnecessary or inappropriate

The IRB uses a primary reviewer system for full IRB review. Application materials are sent to the IRB members scheduled to attend a meeting at least one week in advance of the meeting. Two members are selected by the chair, one as the primary reviewer and the other as a secondary reviewer for a research project.

The primary reviewer leads the discussion of each project at the full IRB convened meeting. The secondary reviewer adds any other relevant comments or clarifications. The members determine whether the project meets the criteria for approval or whether revisions to the study design are required. The Informed Consent Document is reviewed for accuracy, clarity, and inclusion of required and optional elements of consent. During the meeting, voting is by show of hands. By a majority of those present at the meeting, each project is either: (1) approved as submitted; (2) approved pending receipt of required minor revisions to study procedures, Informed Consent Document(s), or other written materials; (3) tabled pending review at a subsequent full board meeting after receipt of significant additional information or revisions, or (4) disapproved.

Written minutes of each full IRB meeting include: (1) attendance, (2) the number of votes to approve, table, disapprove, or abstain (without individual identification), (3) the basis for requiring changes in or disapproving the research, (4) the length of time until the next review, and (5) a summary of the discussion of controverted issues and their resolution.